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The role of water-soluble contrast in the management of adhesive small bowel obstruction

Saleh M Abbas

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Abstract

Adhesions are the most common cause of small bowel obstruction (SBO) in western countries. Ninety-three per cent of adhesions are caused by a previous abdominal operation. They are particularly common after colorectal resection and ileal-anal pouch reconstruction.

In recent years water soluble media have been demonstrated to help in the diagnosis of bowel obstruction and also in predicting the likely success of non-operative resolution. Some authors have also suggested a therapeutic value for water-soluble contrast.

This aim of this thesis is to investigate the role of water-soluble contrast media in the management of adhesive SBO.

An attempt to quantify the burden of adhesive SBO in New Zealand was made by retrospectively reviewing the experience at a major teaching hospital. This was followed by a systematic review and meta-analysis of the published literature. A randomised controlled trial to evaluate the therapeutic role of water-soluble contrast (Gastrografin) in adhesive SBO was then conducted. This was followed by assessment of the impact of routine use of Gastrografin on the management of adhesive SBO.

The retrospective review showed that the New Zealand experience is similar to that overseas. The systematic review showed that Oral administration of Gastrografin was safe and when followed by abdominal X-ray helps to triage patients to surgical and no-operative management. It also suggested a therapeutic role in this setting.

The randomised controlled trial confirmed that Gastrografin has therapeutic value in adhesive SBO. The final study showed that the routine administration of Gastrografin did not shorten hospital stay probably related to significant breaches of protocol.

In conclusion, SBO is a common problem. Gastrografin has an important triage role and hastens resolution of SBO. If Gastrografin is to make an overall difference to SBO management in a hospital then breaches in protocol need to be addressed.

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Chapter 1

Small bowel obstruction

Extent of the problem

Any patient who undergoes abdominal surgery, that involves opening of the peritoneal cavity, will have an increased lifetime risk for formation of adhesions which may cause bowel obstruction at any point in time. Adhesions are the most common cause of small bowel obstruction (SBO) in western countries, these are the cause of 70% of admissions with small bowel obstruction, and the rest are due to hernias and, tumours of the small bowel, lymphoma, and secondary malignancies(1-3). It is thought that 93% of adhesions are caused by previous surgery, 7% are thought to be congenital and 2% are inflammatory.(4)

Weibel et al. studied 752 autopsies and they found that 67% of those who had abdominal surgery developed intra-abdominal adhesions compared with 28% of those who did not have previous abdominal surgery (2). In another prospective study Menzies et al(4) analysed 210 patients undergoing elective laparotomy; they found in patients who had previously had one or more abdominal operations that 93% had intra-abdominal adhesions that were considered as a direct result of their previous surgery. This compares with 10.4% incidence of adhesions in patients who had first-time laparotomy(4). Elsewhere it has been reported that almost 95% of patients who have abdominal surgery will have a certain, albeit variable, degree of intra-abdominal adhesions (5).The true proportion of patients who develop adhesions after abdominal surgery may never be accurately known as shown by this selected references from the literature. Furthermore the numbers of these

patients that progress to small bowel obstruction over the years will never be possible to assess accurately(5-7).

The cost

Small bowel obstruction is a common surgical problem; Ellis et al. reported a 24 years' experience with adhesive small bowel obstruction at Westminster. They reported that intestinal obstruction accounted for 0.9% of all admissions, 3.3% of major laparotomies and 28.8% of cases of small bowel obstructions (8). A well-known study (SCAR) is a large scale epidemiological study performed with the Scottish Medical Record Linkage Database. The SCAR study prospectively followed a cohort of 52,192 patients undergoing a laparotomy in Scotland in 1986. It reported a 1 in 3 risk of re-admission with a possible adhesion-related problem 10 years after laparotomy; and a 5% rate of adhesion-related admission(9). In North America, there are 300,000 hospital admissions annually for small bowel obstruction that requires adhesiolysis, accounting for nearly 850 000 days of inpatient care(10)(11,12)

Predisposing risk factors

It has been suggested that some procedures have a higher risk of postoperative adhesive obstruction, In general, procedures in the lower abdomen and the pelvis and operations resulting in damage to a large peritoneal surface area tend to have a higher risk for developing adhesions. Another factor is pelvic surgery (13-17), and colonic resections that remove large parts of the colon leaving most of the area below the transverse mesocolon exposed (4, 15-25). The likelihood of bowel obstruction occurring following elective upper abdominal surgery is thought to be a lot less than that involving surgery below the transverse mesocolon (20).

In a recent review of 446,331 patients from the literature It was found that patients who had undergone ileal pouch-anal anastomosis were associated with the highest incidence of small bowel obstruction (19.3%) followed by open colectomy (9.5-14.3%) (15-17, 25-30). Gynecological procedures were associated with an overall incidence of 11.1% (0.1% after cesarean section to 23.9% in open adnexal surgery) (10, 16, 24-31), while elective colonic resections resulted in a 3.6% incidence of small bowel obstruction(31-33) .

The incidence of small bowel obstruction is generally greater in open surgery than laparoscopic surgery except in appendectomy. The incidence was 7.1% in open cholecystectomies compared with 0.2% in laparoscopic cholecystectomy; 15.6% in open total abdominal hysterectomies vs. 1% in laparoscopic hysterectomy. There was no difference in SBO following laparoscopic or open appendectomies (1.4% vs. 1.3%) (32-34). After colectomy approximately 58% of those who developed small bowel obstruction were readmitted in the first year and 22% of these patients required surgery (32). Other identified surgical risk factors for developing adhesions include foreign bodies, glove powder, mesh, suture materials, postoperative leak, and spilled gallstones (14, 35).

Although advantages such as quicker postoperative recovery and decreased hospital stay have been attributed to laparoscopic surgery(36) , it has not consistently shown a difference in the incidence of SBO within the 1st year of surgery compared with open colorectal surgery(36, 37) .

Economic impact

The consequences of adhesion formation include a significant economic burden, and the treatment of adhesive small bowel obstruction consumes a significant

amount of health resources (5, 38-41). As the cost of health care continues to escalate with increasing numbers of aging patients requiring surgery, it is likely that the cost of caring for patients with adhesive small bowel obstruction will increase (38, 40-42) . In the United States the estimated financial impact for patient treatment related to adhesion-related disorders was US\$1.3 billion for the year 1994 (10).

In a selected cohort of patients with proven intra-abdominal adhesions from Sweden, the economic impact was higher than reported previously; the annual cost of adhesion-related problems was estimated as 39.9-59.5 million euros, and the cost of inpatient care was almost equal to that for gastric cancer, these results are comparable to what is reported in from the United States and the United Kingdom(43-45).

Recurrence

Menzies et al. followed patients for a long period and reported that following laparotomy and division of adhesions for small bowel obstruction about 32% will have a recurrence of small bowel obstruction (4). Recurrence of adhesive small bowel obstruction is a particularly challenging problem. Adhesions seem to affect relatively young patients with a high risk for lifetime risk for recurrence. It is thought that the risk of adhesions is less with age. There is a possible role for a decrease in gastrointestinal motility with aging in postoperative adhesion formation, which may be responsible for higher risk in young patients(46-48) . The interval between laparotomy and admission for small bowel obstruction is variable with a median of 5.5 years (11 days-34.7 years)(39) .

The annual incidence of small bowel obstruction following laparotomy is around 1%; and 20% of those who develop small bowel obstruction will develop this more than 10 years after the index operation(4, 8, 39). Menzies et al found that 39% of those who developed small bowel obstruction did so within the first year after surgery and 20% within one month (4).

Approximately 30% of patients admitted with small bowel obstruction will require surgical intervention (49). The rest usually settle with non-operative management, but there remains a significant recurrence rate. The five year recurrence rate varies between 10-29% of those managed with surgical intervention and 17-53% of those managed non-operatively (50, 51). These rates are variable and seem to depend on definitions of small bowel obstruction and completeness of follow up. In many studies there is incomplete follow up, missing data, inappropriate analyses, selection bias and most studies are retrospective. Variation in the reported rates may also be explained by variation of inclusion criteria such as inclusion of patients with recurrent abdominal malignancy, a history of abdominal radiation and inclusion of causes of small bowel obstruction other than adhesions(49, 50) . The number of previous admissions may greatly influence the risk of readmission for adhesive SBO also.

Recurrence of small bowel obstruction is reportedly higher in patients with multiple admissions and those with shorter intervals between attacks of bowel obstruction (51). It is thought that patients who require surgery for adhesive small bowel obstruction constitute a specific risk group for recurrence of obstruction and these patients may be particular candidates for the preventive use of anti-adhesion agents, particularly when other risk factors of recurrences are present, such as age

between 16 and 40, complications after the index operation and matted adhesions.(4, 51-54).

The time interval to obstruction tend to vary according to type of the index operation, its longer after open appendectomy than after colorectal and pelvic surgery(1, 55, 56) . Colorectal surgery and vertical incisions tend to predispose to multiple matted adhesions rather than an adhesive band (49, 57) and this is associated with higher recurrence rate. Patients with an adhesive band had a 25 % readmission rate, compared with a 49% rate for patients with matted adhesions (6). The number of previous operations does not appear to affect the risk for recurrence of obstruction(49, 57) .

Surgery for small bowel obstruction is associated with significant mortality, which depends on age of the cohort and associated comorbidities(58) . Margenthaler et al. reported a 30 day mortality rate of 7.3% in a veteran's institution. Elsewhere, the 30 day mortality has been reported to be less than 3%. However, some of these series reported in-hospital mortality while others reported 30 day mortality (50, 52, 53, 55, 58, 59). Historically the mortality used to be much higher. Improvements in surgical and postoperative care have helped to reduce mortality from 50% to less than 3%(50).

It has been reported that age over 75 years old and ASA \geq III, medical complications and strangulated small bowel, that required resection, are associated with a higher risk of mortality (54, 58, 59). A comparison was performed of 30-day morbidity and mortality between patients undergoing adhesiolysis versus those undergoing small bowel resection with anastomosis. Stepwise logistic regression analysis was used to construct models predicting 30-

day morbidity (defined as one or more complications) and 30-day mortality. Sixty-eight preoperative clinical parameters were examined. The overall 30-day mortality rate following surgery for SBO was 7.3% for adhesiolysis and 9.7% for small bowel resection, although, as noted above other series have reported rates less than 3%(3, 49, 50, 55, 60, 61).

Morbidity associated with small bowel obstruction is significant and increases with associated comorbidities. The reported complication rate varies from 18%–30% following division of adhesions and 22%–40% following small bowel resection (50, 52-54, 60-63). Common encountered complications after division of adhesions and small bowel resection are pneumonia, prolonged ileus, respiratory failure, wound infection, urinary tract infection, systemic sepsis, and wound dehiscence(4, 52, 55, 60-65). The rates of morbidity and mortality seem to increase exponentially with age.

Patients above the age of 60 have predicted morbidity rates of 40% to 56% and the predicted mortality rate is 6% to 24% (62). Among the factors that increase morbidity and mortality are respiratory disease, renal impairment, ASA class \geq III, intraoperative contamination and raised white cell count(57, 62). In elective surgery the presence of adhesions during surgical exploration makes surgery difficult and increases the risk of complications. They also make common laparoscopic surgery such as elective cholecystectomy difficult or impossible.

They are associated with prolonged operating time, more blood loss and other complications. The risk of inadvertent enterotomy increases and leads to an increasing rate of septic complications, intensive care admission and adverse outcome(15, 17).

In summary small bowel obstruction is a common surgical presentation, usually caused by adhesions related to previous abdominal surgery. It constitutes a significant burden on the healthcare system with extensive use of hospital resources. Adhesions are two types, either a band which has a low risk for recurrence or matted, which tends to have multiple recurrences. Other factors associated with high risk of recurrence include recurrent attacks of small bowel obstruction, young age and complications after abdominal operations.

Loss of small bowel

An initial trial of non-operative management in the form of no oral intake, nasogastric suction, pain control and intravenous fluid and electrolyte resuscitation is the standard practice for most adults with an acute admission for small bowel obstruction. Early operative intervention is mandated for patients who present with signs and symptoms of strangulation. This approach results in successful resolution of 40-70% of cases. However, the safety and efficacy of non-operative management remains largely unproven in the paediatric and adolescent populations (2-20). In this age group operative treatment is undertaken in about 80% of patients and 16% will require small bowel resection (49, 54, 66, 67). The rational is to avoid any bowel resection caused by ischemia. Delayed diagnosis is a recognised cause for more loss of bowel length (68, 69).

Small bowel obstruction in the early postoperative period

Although it comprises only 3% of the admissions of small bowel obstruction, readmission for small bowel obstruction in the early postoperative period (the first six weeks after laparotomy) is a difficult clinical problem that is associated with significant morbidity. The diagnosis is difficult due to postoperative pain, ileus and ongoing use of narcotic analgesics (18, 20, 70-73). The most frequent index

operation is surgery for adhesive small bowel obstruction (43%) with a median interval of 24 days (8-50 days)(63). Colorectal operations are another high risk group for this type of small bowel obstruction (18-20, 70). Adhesions are the most common cause for this type of small bowel obstruction, which constitutes 80% of the cases (63, 72). 23% - 62% of these patients require surgical intervention and most of these are due to matted adhesions rather than a single band (49, 63, 73, 74). The five years recurrence rate after surgical treatment is 57% to 63% after non-operative treatment(63).

Pathophysiology of adhesions

Formation of adhesions after abdominal surgery breaching the peritoneum may be both beneficial and harmful(15, 42, 75). The extent of adhesions varies from one patient to another and this mostly depends on the type of the operation and whether the patient develops postoperative complications(33). Adhesions may localize or isolate an infectious process or contain minor leakage from an anastomotic line, thus preventing the spread of the infection. On the other hand, they may contribute to the common clinical problem of intestinal obstruction. As discussed above small bowel obstruction may occur from several days to up to 40 years after the initial laparotomy(5, 76).

The process of adhesion formation is complex and involves different cell types, cytokines, coagulation factors and proteases, all acting together to effect a healing process (77, 78). This process involves complex interactions between inflammation, tissue repair, angiogenesis and remodelling (14). Activation of the coagulation cascade results in conversion of fibrinogen to fibrin which is deposited on raw surfaces. This is followed by activation of fibrinolysis. This process allows for proliferation of mesothelial cells and prevents adhesion of adjacent

structures(14, 15). If fibrinolysis does not occur in the first few days fibrin will persist and forms a base for infiltration of collagen producing fibroblasts (15, 42, 79).

There are two types of fibrinolytic system activators: tissue plasminogen activator and urokinase like plasminogen activator. Plasmin is a protease capable of degrading various molecules including fibrin (77, 80, 81). Normally fibrinolytic capacity exceeds coagulation, but this changes after surgery (81-83). Up regulation of adhesions of molecules such as intracellular adhesion molecule (ICAM-1) and vascular cell adhesion molecule (VCAM-1) and up regulation of transforming growth factor beta and interleukin-1 are thought to contribute to adhesion formation probably by reducing fibrinolytic activity (80, 84-89). Substance P seems to play a significant coordinator role in this process (7, 90, 91).

Prevention

It is almost certain that any abdominal operation will be followed by formation of adhesions. There is no effective treatment the prevent recurrence of adhesions. Laparoscopic surgery has been suggested to reduce adhesions (92, 93).

Preventive techniques and special barriers has been considered in high-risk patients with variable results(33). Reduced levels of plasminogen activator in the peritoneum after surgery are thought to be a causative factor and some experimental studies have suggested the benefit of using plasminogen activator to reduce adhesions (75, 78, 85, 94-96). Seprafilm membrane has been tested clinically and it appears to be effective in reducing the severity of postoperative adhesions after major abdominal surgery. However it does not reduce the incidence of adhesions. Some authors recommend using Seprafilm when second-

look intervention is planned. Long-term studies are needed to assess the cost-effectiveness and value of Seprafilm in preventing bowel obstruction (97). Hyaluronic acid-carboxycellulose membrane can reduce the incidence of adhesions(76). Other materials that have been tried, with variable, success are steroids, non-steroidal anti-inflammatory drugs, Dextran 70 adenosine, dextran, hydropolymeric coating and heparin (7, 93, 98-102).

Pathophysiology of small bowel obstruction

There are two types of obstruction; simple presenting with obstipation, abdominal distension (however abdominal distension may be absent in very proximal obstruction), colicky abdominal pain, nausea and vomiting, and strangulated obstruction, which presents with constant abdominal pain, tachycardia, fever, peritoneal irritation, and may be associated with leucocytosis, hyperamylasemia, and metabolic acidosis(1, 103-106). These are pathophysiologic responses to ischemic necrosis of the wall of the small bowel. The process of ischemia results from venous occlusion that results in increasing tissue oedema and increasing pressure on the arterioles and capillaries that eventually results in complete cessation of the microcirculation with tissue hypoxia and necrosis. In addition the venous occlusion leads to high pressure in small venules that eventually rupture and this result in intramural and intraluminal haemorrhage.

In closed-loop or strangulated intestinal obstruction, a loop of bowel is occluded at two different points along its course. The obstruction is the result of a simple constrictive band or internal hernia that compresses the intestinal lumen and also constricts the related small-bowel mesentery in the same process. A variable length of the small bowel is involved in this process. Because of the localized obstruction of the bowel at two different points the isolated bowel loop becomes

increasingly distended and the intervening mesentery becomes constricted with its narrow pedicle. This anatomic configuration may also result from twisting of an isolated loop that is fixed at two points along its long axis, producing a small-bowel volvulus. The volvulus tends to result in high grade or complete obstruction, but once developed, it further aggravates the obstructing mechanical process. Progressive ischemia will result that will progress to necrosis of the wall and perforation if no surgical treatment is undertaken. Strangulation occurs in about 10% of the cases of bowel obstruction and results in a mortality of 10-37%; however all available data are prior to 1990 (19, 104, 107-113).

A definite pathological distinction should always be made between non ischemic closed-loop obstruction and strangulation. These are related phenomena but separate pathologic entities. Strangulation almost always develops because of a closed loop obstruction; however, a closed loop particularly if operated on early may not be associated with strangulation (107, 114-117).

More commonly small bowel obstruction is less severe and is described as a subacute presentation. The bowel proximal to the transition point becomes dilated due to increased secretion and accumulation of swallowed air. The physiologic response, in addition to increased secretions and delayed absorption, is increased frequency and intensity of peristalsis proximal and distal to the obstruction which results in abdominal pain and, early in the course, frequent small and loose bowel motions(102, 118, 119). The increased intraluminal pressure results in distension and this contributes to increased hydrostatic pressure in the capillaries and subsequent oedema, which can significantly contribute to increased fluid and electrolytes in the interstitial space. There is also increased bacterial proliferation

in the proximal lumen which is mainly caused by E. Coli. Bacterial translocation will subsequently occur to the regional lymph nodes due to microvascular and permeability changes(102, 118, 119) .

Presentation

Patients with small bowel obstruction usually present with abdominal pain. Typically there is a past history of abdominal surgery which could be anywhere from few weeks to few decades previously (39). The pain is typically colicky and episodic and centred around the central part of the abdomen. Vomiting of green coloured fluid is a common symptom usually preceded by a severe cramps and sometimes nausea. Vomiting is the main symptom in proximal obstruction. Later the vomit may become brown and feculent. Intestinal peristalsis may cause audible bowel sounds usually described by patients as rumbling sounds. Typically patients have loss of appetite and they feel thirsty. Constipation and obstipation is found in most patients. Abdominal distension becomes evident after several hours from the onset of pain; distension may not be evident in proximal obstruction. Constant pain is a warning sign that the patient may have a closed loop obstruction or ischemic injury of the affected small bowel(9). Perea et al. prospectively studied 100 patients with adhesive SBO and found that the presenting symptoms were vomiting (77%), abdominal pain (68%), and absence of passage of flatus and/or faeces (52%), and constant pain (12%). Abdominal distension was the most frequent clinical sign, with a prevalence of 56%. The same author reported abdominal pain (92%), vomiting (82%), abdominal tenderness (64%), and distension (59%) as the most frequent symptoms and signs(12).

On clinical examination the patient is usually in distress with pain, there is a certain degree of dehydration and tachycardia. Important signs are central abdominal distension. Visible peristalsis may be seen in slim patients and some may have visible incisional hernia at the scar of previous surgery. Palpation usually shows a soft abdomen and tenderness is a warning sign of small bowel strangulation. On auscultation there are prominent small bowel sounds and sometimes peristaltic rushes; the rectum is usually empty on digital rectal examination, but this sign is not consistent(9).

Diagnosis

Small bowel obstruction is usually suspected on the basis of history and clinical examination. A prospective study of over 1300 patients with acute abdominal pain was undertaken in Finland and found that the presence of previous surgery (relative risk (12.1) and the type of pain (colicky versus constant, RR risk 2.4) were the most accurate predictive symptoms in the diagnosis of acute small bowel obstruction. The most accurate clinical signs were abdominal distension (RR 13.1) and hyper active bowel sounds (RR 9). Clinical diagnosis of small bowel obstruction in that study had sensitivity of 75% and specificity of 99%(120).

Abdominal X rays often secure the diagnosis with visibly dilated small bowel loops and multiple air fluid levels. Occasionally these sighs are subtle and the confirmation requires administration of water soluble contrast followed by abdominal X rays or CT scan. There are no reliable laboratory investigations to confirm or rule out strangulated small bowel obstruction. However there is sometimes raised white cells count.

There are three important decisions to be made early in the management of a patient with small bowel obstruction. The first is to establish that the patient does have small bowel obstruction. The second is to rule out strangulation of small bowel. The third is to discriminate between partial and complete small bowel obstruction in the setting of adhesions caused by previous surgery. Patients who are suspected to have strangulated small bowel on clinical grounds with symptoms and signs such as uncontrolled or continuous pain, a tender abdomen, and a raised white cell count or fever are managed surgically after initial resuscitation and correction of the fluid and electrolyte disturbances.

Generally those who do not require surgery immediately on admission are given a trial of non-operative management for 2-3 days (121). A variety of clinical indicators have been used to assess patients' progress and the need for surgery based on passage of bowel motions and flatus, output of the nasogastric tube, extent of the pain and abdominal distension(121). However these clinical variables are notoriously inconsistent (67).

Radiology

Plain abdominal films are commonly used to secure the diagnosis. Abdominal radiographs are usually reliable in the detection of acute small bowel obstruction with recent reports of sensitivity and specificity for both of 83%(110), although earlier studies reported sensitivity and accuracy of only 50-60%(107, 110). Classical findings on X-Ray include dilated centrally located small bowel loops, multiple air fluid levels and absence of gas in the colon. Normal abdominal X rays, however, do not rule out small bowel obstruction.

Both erect and supine abdominal films are usually obtained when small bowel obstruction is suspected. Usually an erect or lateral decubitus film is taken to see air fluid levels(122, 123).This has also been challenged by the argument that an erect film may add no additional information to the supine film(124). The lack of erect or lateral decubitus abdominal X ray does not seem to influence the detection or exclusion of small bowel obstruction(110, 125). Lappas et al. found that the two most specific radiographic signs of small bowel obstruction were air-fluid levels of different heights or an air-fluid level width of 2.5 cm or more. Lappas et al. also found that when both of these signs were present, the obstruction is likely to be high grade and complete(125). Overall, plain films are diagnostic in 50-60% of the cases, equivocal in 20-30%, and non-specific in 10-20% (126-128).

Some authors have attempted to define the use of abdominal films in differentiating simple from complete and strangulated intestinal obstruction by relying on signs such as the coffee bean sign, the distended air-filled closed loop, the pseudotumor sign produced by the overly distended fluid-filled closed loop, and a nodular luminal contour of the affected bowel. These signs are seldom seen and are difficult to interpret (129, 130). In most cases, findings on scout abdominal films cannot differentiate between simple small bowel obstruction and complete or strangulated small bowel obstruction (117, 131-134).

To address the inadequacy of plain abdominal X rays in the diagnosis and management of small bowel obstruction a number of approaches have been studied. Nelson et al., in 1965, found barium to be a safe method for diagnosing small bowel obstruction, provided there was no clinical evidence of bowel strangulation or perforation (77). Small bowel-follow through and enteroclysis

using diluted barium are considered as a reliable methods of evaluating small-bowel disease and can be obtained relatively quickly (128). It has an accuracy of 85% in the diagnosis of small-bowel obstruction (128). The disadvantages are that enteroclysis is an invasive procedure, is difficult to perform in frail and ill patients, and is not safe in patients with complete obstructions or in those with suspected strangulation or closed-loop obstruction(135, 136). Dixon et al. performed a retrospective 10 year review of their experience with then use of small bowel contrast in 1465 patients and reported a sensitivity of 93.1% and a specificity of 96.9% (29) for the diagnosis of complete small bowel obstruction(137).

Oral water soluble contrast small bowel studies have been introduced more recently for the diagnosis of small bowel obstruction, and have been proved to be safe (138-140), although complications related to the use of water soluble contrast such as pneumonia, renal failure and anaphylaxis have been reported (141, 142,143). Water soluble contrast is a hypertonic solution. It promotes small bowel peristalsis by smooth muscle stretch perhaps due to increased intraluminal pressure. It has been advocated as an examination that should be used in all patients unless they clearly need surgery or are clinically resolving(9, 128). This approach may help to achieve an accurate diagnosis, and CT scanning therefore could be reserved for complex cases, particularly where the small bowel obstruction may not be caused by adhesions (9).

Small bowel contrast studies have also been reported to be useful to discriminate between partial and complete small bowel obstruction. The patient is given 100 ml of oral water soluble contrast (which can also be given via the nasogastric tube) and a single abdominal X ray is taken 4-24 hours after administration(138, 144-

151). The evidence suggests that, if the oral contrast reaches the colon within 4–24 hours after administration, complete obstruction is unlikely and non-operative management is likely to be successful (145-151).

Chung et al. correlated radiological findings with clinical outcome and reported high accuracy of prediction of resolution of small bowel obstruction after oral water soluble contrast and abdominal X ray after 4 hours(152). Another prospective study, that enrolled 112 patients, reported similar results with 40ml of oral contrast and an abdominal film after 24 hours. The procedure predicted resolution or need for surgery with a sensitivity of 98% and a specificity of 100% (153). In these studies the patient outcome (need for laparotomy or resolution on non-operative management) was regarded as the standard against which the accuracy of water soluble contrast as a diagnostic tool was evaluated (145-151).

CT scan has also been compared with plain abdominal X-rays, by Maglinte et al., who reported superior specificity with CT (79% versus 57%) but similar rates of sensitivity and accuracy(154). A CT scan has the advantage of detecting other pathological process such as malignant causes for obstruction and this may be the only advantage(116, 155-159). It has been suggested that CT scanning is highly specific in the diagnosis of strangulation in adhesive small bowel obstruction showing signs of ischemia such as reduced mural enhancement, presence of peritoneal fluid and mesenteric congestion. However, these signs are not very sensitive(156). The CT criteria commonly used to differentiate non complicated simple SBO from complicated or strangulated obstruction (bowel wall necrosis) such as bowel wall thickening are associated with difficulties related to the precision of this measurement (160-162). A 3mm threshold has been suggested

by some authors,(156, 160, 162) whereas a 2 mm threshold was used by Frager et al. as suggestive of ischaemia (163). Other signs are delayed wall enhancement of the involved loop compared with the homogeneous enhancement of adjacent normal bowel(163), pneumoperitoneum or bowel wall pneumatosis(116, 164, 165), bowel wall thinning (characterized by a wall thickness less than 1mm), congestion of small mesenteric veins characterized by enlargement of small serpentine blood vessels in the mesentery(160, 162, 164), peritoneal fluid of variable amount(160-163, 166) and the beak sign characterized by beaking of the bowel loop at the site of obstruction(167).

More recently multi-detector CT scanning has been increasingly incorporated in management algorithm of small bowel obstruction (164, 168-174). The diagnosis of bowel obstruction on CT scan and the differentiation from an adynamic ileus are based on the detection of a definite point of transition, with dilated fluid and/or air-filled loops of small bowel proximal to the site of obstruction and collapsed loops of small bowel and colon distal to the obstruction (167). The reported sensitivity and specificity of CT for bowel obstruction is 90-96% and 96% respectively, with accuracy of 95%(175, 176).

Balthazar suggested that the presence on CT of one sign such as radial distribution with stretched mesenteric vessels converging, toward twisted, U-shaped or C-shaped dilated bowel loop, two adjacent collapsed, round, oval, or triangular loops, beak sign whirl sign diagnose closed loop obstruction with 79% sensitivity(167, 177). It was also suggested that the presence of one of strangulation signs such as, circumferential thickening, increased attenuation,

target or halo sign, pneumatisosis, haziness of mesenteric vessels, obliteration of mesenteric vessels is diagnostic of strangulation with sensitivity of 62%(167) .

Jones et al. performed a retrospective review of CT findings in 96 patients with adhesive small bowel obstruction and tried to devise a score to predict the need for surgery using signs such as dilated small bowel loops, a clear transition point, and free peritoneal fluid. The resulting score was less sensitive than X ray with oral contrast with a sensitivity of 65-77%(178). Also in that study the operative rates were relatively higher than those reported elsewhere at 55%.

Recently a predictive model was developed to predict the need for surgery depending on four signs, which were a history of obstipation and features on CT of intra-peritoneal free fluid, mesenteric oedema, and lack of the small-bowel faeces sign (179). When three of those features were present (mesenteric oedema, lack of small bowel faeces sign and obstipation) the model predicted with high sensitivity the need for surgical exploration(180). The sensitivity and specificity to predict the need for exploration when all 3 features were present concurrently were 37% and 94%, respectively. The positive and negative predictive values were 86% and 59%, respectively, with an accuracy of 65%. The corresponding figures for strangulation were 46% and 82%, respectively, whereas the positive and negative predictive values were 29% and 91%, respectively, with an accuracy of 77%(179-181).

The risk of strangulation in adhesive band obstruction is as high as 38% (163). Closed-loop obstruction is also considered as an emergent indication for surgery even when there is no evident ischemia at diagnosis because it tends to twist the mesentery (whirl sign on CT scan) and is prone to lead quickly and unpredictably

to strangulation(167, 177). On the basis of the clinical significance of band adhesions with different risks of closed-loop obstruction and strangulation, which are most often caused by adhesive bands, Delabrousse et al. (182) investigated the role of CT scan to differentiate between bands and matted adhesions on 67 patients. CT findings were compared between the two types of adhesions with regard to simple obstruction patterns (single abrupt transition zone which indicates dilated proximal bowel loops and collapsed distal bowel loops, a beak sign and a "fat notch" sign (182, 183), which correspond to the extrinsic compression of the bowel at the transition point by an extramural band) that are associated with band adhesions (167, 177). In this study the mentioned signs correlated highly with band adhesions. The results of this study however, were not correlated to the clinical outcome of that cohort of patients, in terms of resolution of the obstruction or the need for surgery. Although closed loop obstruction is only seen in 28% of patients with band adhesions it was found to be the most specific sign for adhesive band obstruction (182). In this study it was also found that in patients with matted adhesions, the transition zone is more likely to be in the pelvis rather than the abdomen and also they are more likely to have a small bowel feces sign. CT signs of a single adhesive band were clearly associated with strangulation on surgical exploration with 41% cases of bowel ischemia and 26% of patients with bowel necrosis. These findings are useful as indicators for emergency surgical exploration, but are less useful in the management of less urgent cases.

Ultrasound (uss) has been investigated in small bowel obstruction and described as more accurate than plain abdominal radiography (184, 185) in the diagnosis of the level of obstruction. It has also been claimed to be able to identify strangulation(186). Progressive interval increase of bowel wall thickness on uss at

admission and 24 hours later was used as an indicator for need of surgery with sensitivity of 92% and a specificity of 100 % (187) but these results have not been able to be reproduced. There is no clear evidence that uss can discriminate between partial and complete small bowel obstruction and in the absence of randomised trials it is not clear whether ultrasound is of any added value(185, 187-189).

Magnetic resonance imaging has also been proposed as a tool for the diagnosis of small bowel obstruction as an accurate and sensitive imaging modality(190, 191). Using the HASTE sequence, it has not been able to differentiate between partial and complete obstruction. Also MRI is not readily accessible, it is more expensive and currently does not add further details to those obtained by other imaging modalities. The role of MRI remains limited to those patients in whom CT scan is contraindicated such as patients with renal impairment and allergy to iodinated contrast media.

Treatment

The traditional treatment of small-bowel obstruction was originally based on the principle that, “the sun should never rise and set on a complete small bowel obstruction”(103, 192) . The usual criterion for operative intervention in small bowel obstruction was the presence of a complete obstruction, defined as a lack of gas in the distal small bowel or colon on a plain abdominal radiograph(193). However, over the years there has been much progress in the experience of non-operative management. Currently the focus of initial management is on non-operative treatment in the form of nasogastric tube decompression of the gut, fluid and electrolyte resuscitation so long there are no signs of small bowel strangulation(179, 180, 194, 195,196).

Most patients with adhesive small bowel obstruction will settle down with non-operative treatment(130, 197-199). In addition to patients with strangulation, patients who had surgery within the six weeks before admission for small bowel obstruction, patients with proven carcinomatosis, patients with irreducible hernia are generally not treated conservatively (200). Mortality rates for SBO have decreased from 50% to less than 3% over the past 100 years (50). This dramatic improvement is attributed mainly to advances in non-operative management. The downfall of non-operative treatment is the possibility of strangulated small bowel being missed with a consequent increased need for bowel resection, prolongation of hospital stay and risk of complications (179, 180). Of those managed non-operatively 17% will ultimately require operative intervention for small bowel obstruction over an average follow-up duration of 4.4 years (50).

Some authors recommend a limited observation period of only 24–72 hours, whilst others recommend an upper limit of five days (111, 201). Age has significant impact on the outcome and thus patients above the age of 75 should be treated aggressively and promptly to reduce the rate of complications(202). In patients with frequent recurrence and multiple previous laparotomies, prolonged conservative treatment including parenteral nutrition may be adopted to avoid a complex and morbid procedure (203). Thus a usual pathway is to pursue a conservative management of small bowel obstruction in absence of clinical and CT signs of strangulation. Such patients are considered to have non strangulated obstruction and can be managed safely with intravenous fluids and electrolytes, nasogastric tube decompression (either with long or usual length). These patients are potential candidates for water soluble contrast medium with both diagnostic

and therapeutic purposes. The appearance of water-soluble contrast in the colon on X-ray 6- 24 hours from administration predicts resolution.

The contrast may be administered either orally or via NGT (50-150 ml) either at admission or after an initial attempt of conservative treatment of 48 hours. The time length of non-operative treatment is not standardised; in absence of signs of strangulation or peritonitis, non-operative management can be tried up to 72 hours; on day 3 if the nasogastric aspirate exceeds 500ml with no signs of resolution operation is recommended unless there are significant operative risks(203-205). Oral contrast does not seem to affect recurrence rates or recurrences needing surgery when compared to traditional conservative treatment.

Recently, models have been devised to predict resolution or otherwise for those who undergo nonoperative management (121, 180, 206, 207). These models have a sensitivity of 72% and specificity of 96% and they include signs detected on CT scanning in addition to clinical and laboratory parameters such as white cells count and C reactive protein (206, 208).

In 1933, Wangensteen and Paine reported an operative technique of advancing a long tube through the jejunum down to the point of obstruction. This relieved obstruction in 80% of patients without any further treatment(209). This technique was later accomplished through a non-operative technique, utilizing a tube that was passed through the nose. The major disadvantage of this technique was the delay in passage of the tube from the stomach into the duodenum. This problem was overcome by using upper gastrointestinal endoscopy to advance the tubes into the small bowel and eliminate the delay in small bowel decompression. Recently the reported success rate was 90% following a trial of long tube

decompression for 48 to 72 hours in selected patients(210). This approach may be still useful in some patients who are deemed to be high risk for surgical intervention when they fail to respond to non-operative management (209, 211, 212). Long tube decompression, although it was safe, did not show any advantage over nasogastric tube decompression in a randomised trial(213) .

There remains a particular subgroup of patients who are defined to have high grade obstruction, this group forms about 10% of all cases of small bowel obstruction(214), in this group almost half of the patients will settle down on non-operative management, but there is significant recurrence of 24% vs 9% in those presented I the same manner and managed with laparotomy (214).

Laparoscopy was introduced in the 1990s in the form of laparoscopic or laparoscopic assisted adhesiolysis. It has been shown to be safe and feasible in a selected group of patients with potential diagnostic and therapeutic value (215-218). The clinical outcome has been compared with open adhesiolysis in two retrospective studies. One study reported that patients managed with open surgery had a significant higher morbidity (40.4 vs 16-19%) and longer postoperative hospital stay (18.1 vs 11.3 days) when compared with laparoscopy. Conversely, the surgical operating time was longer in patients treated laparoscopically (103 vs 84 min) (106). The second was a case control clinical trial and included 62 patients. Laparoscopy and laparoscopy-assisted adhesiolysis was performed on 31 patients and showed a significant lower morbidity (16 vs 45%), shorter postoperative hospital stay (5 vs 9 days), and earlier first bowel movement (3 vs 6 days). There was no difference in the surgical operating time between the laparoscopic and open approaches (78 vs 70 min) (215)

This topic has been the subject of a recent systematic review; the authors concluded that in the absence of randomised controlled trials the values of laparoscopic surgery and its potential benefit are yet to be determined (219.220) . Factors such as laparoscopic training and availability of resources may also affect the laparoscopic approach(190). Thus open surgery remains as the preferred method for surgical treatment of strangulating obstruction as well as after failed conservative management. In selected patients, a laparoscopic approach can be attempted using an open access technique. Access in the left upper quadrant should be safe. Laparoscopic adhesiolysis should be attempted preferably in case of first episode of obstruction especially if single band is anticipated. A low threshold for open conversion should be maintained (76).

The fact that water contrast media have high osmolarity and act as osmotic laxatives, by absorbing water from the bowel wall, has led to investigation of its potential therapeutic value. Few randomised controlled studies have reported the therapeutic benefits of administration of water-soluble contrast to patients who do not require immediate surgery with faster resolution and a shorter hospital stay(136, 144, 150-153, 221, 222). Administration of water-soluble contrast did not seem to reduce the need for surgical intervention. However, these studies were not blinded because the investigators had access to x-rays of patients after administration of Gastrografin (water soluble contrast) (136, 149, 150, 221).

Nelson et al. and Harris et al. in the 1960s suggested that iodinated radiopaque media in the small bowel may cause loss of fluid from the interstitial space of the small bowel into the bowel lumen, precipitating hypovolaemia and dehydration, which may be significant in the elderly with cardiovascular disease and in patients

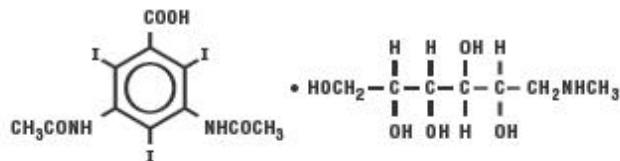
with severe dehydration. Nevertheless there are no such complications reported from their clinical use. This also may indicate that these contrast media may work as osmotic laxatives (223, 224).

Another adjunct that has been studied is oral magnesium oxide. *L. acidophilus* and simethicone may hasten the resolution of conservatively treated partial adhesive small bowel obstruction, reduce the need for surgery and shorten the hospital stay (225, 226).

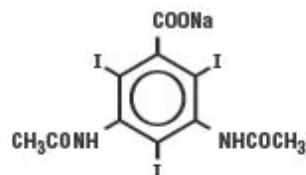
Water soluble contrast media: Chemical characteristics

The most commonly used water-soluble contrast is Gastrograffin® (BayerAG, Berlin, Germany). Gastrograffin has been used primarily for detection of anastomotic leaks from oesophageal and bowel anastomoses. Its advantage over the traditional use of barium is that it is safe and does not lead to a fibrotic inflammatory reaction when it leaks outside the gut lumen.

Gastrograffin contains sodium amidotrizoate 100 mg/mL and meglumine amidotrizoate 660 mg/mL (www.Bayer.com.au). It also contains disodium edetate, saccharin sodium, polysorbate 80, anise oil and purified water. The relatively high atomic weight of Iodine contributes sufficient radiodensity for radiographic contrast with surrounding tissues. Diatrizoate meglumine is designated chemically as 1-deoxy-1- (methylamino)-D-glucitol 3,5-diacetamido-2, 4,6-triiodo-benzoate (salt); diatrizoate sodium is monosodium 3, 5-diacetamido-2, 4,6-triiodobenzoate (see Figure 1).

Figure 1. Chemical composition of Gastrografin

diatrizoate meglumine
 $\text{C}_{11}\text{H}_9\text{I}_3\text{N}_2\text{O}_4 \cdot \text{C}_7\text{H}_{17}\text{NO}_5$
MW 809.13
Organically Bound Iodine: 47.1%
CAS-131-49-7



diatrizoate sodium
 $\text{C}_{11}\text{H}_8\text{I}_3\text{N}_2\text{NaO}_4$
MW 635.90
Organically Bound Iodine: 59.9%
CAS-737-31-5

Following oral administration, only about 3% of the amidotrizoic acid is absorbed from the stomach and intestines. This portion, and any further contrast medium that might have reached the abdominal cavity or surrounding tissue through perforations of the gastrointestinal tract, are eliminated mainly via the kidneys. The osmolarity of Gastrografin is 1900 mOsm/L, which is approximately six times that of extracellular fluid (i.e., the interstitial space). It promotes shifting of fluid into the bowel lumen, which increases the pressure gradient across an obstructive site. The bowel content is diluted, and in the presence of the wetting agent, passage of bowel contents through a narrow intestinal lumen is enhanced. It is also thought to reduce oedema of the bowel wall and enhance bowel motility (141, 150, 224, 227).

Study Design

The aim of this thesis is to evaluate the available evidence, investigate the therapeutic role of a water-soluble contrast agent in patients with adhesive SBO,

and assess its clinical benefit in routine application. It begins with a retrospective review of the management of SBO at Middlemore Hospital from 1999–2007, and highlights the significance of the problem in clinical practice, including admissions, recurrence, mortality, and operative rates.

Then a systematic review and meta-analysis of studies in the literature that investigated the diagnostic and or the therapeutic role of water soluble contrast media in the management of adhesive small bowel obstruction was conducted.

Then a randomized controlled trial was conducted to assess the therapeutic role of water soluble contrast media in small bowel obstruction. The primary outcomes of the trial were hospital stay, rate of resolution, need for surgical intervention and time from admission to first bowel movement of flatus or motion.

Finally the clinical impact of routine use of water soluble media both as diagnostic and therapeutic agent in adhesive small bowel obstruction was assessed. The end points were hospital stay, rates of resolution and need for surgical intervention.

Chapter 2

A retrospective review of small bowel obstruction at Middlemore Hospital

Introduction

As discussed in chapter 1, the most common cause of SBO (70% of cases) in Western countries is postoperative adhesions.(3). Previous studies have demonstrated peritoneal adhesions in about 70%–90% of patients who have had previous abdominal surgery that required opening of the peritoneal cavity(2, 4). Studies of the natural history of adhesive SBO have shown that about 80% of cases resolve with conservative treatment in the form of nasogastric suction, intravenous hydration, and electrolyte management (49, 52). Accurate early recognition of intestinal strangulation in patients with SBO is important to decide whether emergency surgery is needed or to allow safe non-operative management of carefully selected patients.

Although a large proportion of patients are successfully managed with non-operative measures early recognition of strangulated intestinal obstruction requiring emergency laparotomy is vital to save patients' lives because delay in treatment results in increased mortality (50,179,180). Bowel strangulation is an independent risk factor for complications and mortality, and the mortality rates for patients with strangulated obstruction are up to 10 times higher than those for patients with simple SBO(105, 228). The risk of recurrence remains high, and the literature reports a wide ranging rate of overall recurrence (8.7%–53%) from three years onwards(229). This study was undertaken to evaluate the experience at

Middlemore Hospital and compare these results with those reported in the literature.

Patients and methods

Patients admitted to Middlemore Hospital with a diagnosis of SBO between July 1999 and April 2007 were retrospectively reviewed. Patients' clinical notes and radiology reports were reviewed to verify the clinical diagnosis of small bowel obstruction. Data gathered included gender, age, whether the index operation was for malignancy or not, type of index operation, recurrence of SBO, need for laparotomy or resolution, complications, mortality, number of recurrences, hospital stay, admission to intensive care unit, and type of adhesions found at the time of surgery; also the type of surgical procedure required, whether adhesiolysis or small bowel resection with anastomosis. Patients who were admitted with SBO but without previous abdominal surgery were excluded. Patients who had obstruction as a result of recurrence of malignant disease or as a result of groin or abdominal wall hernia were also excluded.

The rates of resolution on operative treatment versus nonoperative treatment were compared. The relationship between the risk of recurrence and type of adhesions, primary operation, spontaneous resolution or need for surgery, gender and age of the patient, complication at index operation (such as leak, bleeding or intra-abdominal collection), or whether the index operation was for sepsis as a result of perforated viscus was then investigated. All analyses were performed using the Chi-squared test and SPSS® version 13 for Windows (SPSS Inc, Chicago, IL). A p value of <0.05 was accepted as statistically significant.

Results

Nine hundred and ninety-four admissions of 648 patients with adhesive SBO during the study period were identified. The median age was 64 years and 362 patients (56%) were women. There were 322 episodes of recurrence among 176 patients. Sixty-nine patients (10%) required laparotomy; of those 14 required small bowel resection and anastomosis and 55 required only division of adhesions . The rate of recurrence in this series was 27% and the laparotomy rate was 10%.

The most common types of operations associated with SBO were colorectal and pelvic procedures. In this cohort 62% of these patients had the index operation for pelvic organs particularly rectal resection and resection of gynaecologic malignancies.

The non-operative treatment group group had a significantly lower frequency of comorbidities compared with those who needed laparotomy and adhesiolysis with or without small bowel resection small bowel resection group, including history of abdominal surgery for cancer (4% versus 9%). The operative group had higher frequency of chronic obstructive airway disease (3%) compared with the non-operative group (1%). There were no significant differences between the 2 groups with respect to other comorbidities Table 1.

Table 1. Comparison between patients who required adhesiolysis plus/ minus bowel resection and those require small bowel adhesiolysis with or without resection with respect to comorbidities and type of previous surgery.

Comorbidity	Adhesiolysis (%)	Small bowel resection (%)	P
Previous surgery for pelvic organs and rectal cancer	2	9	0.001
Cardiovascular disease	3	4	0.4
Chronic renal failure	1	1	0.9
Chronic obstructive airway disease	21	39	0.03
Cerebrovascular and neurologic disease	3	4	0.3
Previous chemotherapy or radiotherapy	2	2	0.4

The median SBO recurrence rate was one (range 0–13). Of the 176 patients who developed recurrence, 28 required a laparotomy on readmission (15%). There were 50 deaths (7%) in this series (all deaths were caused by complications related to small bowel obstruction), with a complication rate of 12%. The median hospital stay was three (range 1–49) days. The median hospital stay for those who required surgery was 6.5 days, and for those who resolved without surgery three days. None of the factors analysed influenced the recurrence of SBO (Table 2). Sixty-nine patients (12%) required laparotomy.

Table 2. Factors analysed for recurrence (These factors are based on known risk for recurrence from literature review)

Factor	Recurrence	No recurrence	p value
Age (years)			
<50	54	121	
>50	123	194	0.126
Complicated index operation			
Yes	29	70	0.467
No	139	410	
Index operation for cancer			
Yes	75	160	0.396
No	124	289	

Table 3. Factors that may influence resolution on first attack

Factor	Laparotomy	Resolution	p value
White blood cell count			
>10	33	236	0.319
<10	36	343	
Index operation for cancer			
Yes	34	200	0.02
No	35	379	
Complications following index operation			
Yes	17	94	0.02
No	52	487	

Patients who had their index operation for cancer and those with index surgery complicated by sepsis, bleeding and anastomotic leak were more likely to need laparotomy on the first admission (Table 3).

Logistic regression analysis was performed on factors thought to have influence of the rate of 30 days mortality rates. The results are shown in table 4.

Table 4. Logistic regressions analysis for 30 days mortality

Variable	Parameter	P	Odds Ratio
ASA 4	0.78	0.02	4.45
History of cancer	0.82	0.004	2.3
Anaemia	0.73	0.002	2.02
Renal failure	0.75	0.001	2.17
COPD	0.9	0.001	2.8
Age 50-59	0.2	0.5	1.2
Age 60-69	0.6	0.1	1.8
Age over 80	1.3	0.02	3.7

Discussion

This study has shown that a considerable number of acute surgical admissions are related to SBO caused by adhesions. There were 994 admissions in the specified time period. In most cases, the predisposing cause was previous surgery, which was most commonly colorectal or pelvic surgery. Mortality is still high at 7% in this series and the morbidity was 12%. These figures are comparable to what is reported in the literature.

The recurrence rate for SBO in this study was 27%, which is comparable with other reports. The rate of laparotomy was relatively low at 10%. None of the clinical variables measured was associated with recurrence of bowel obstruction, although the patient was more likely to respond and resolve without surgery if the index surgery was for benign disease.

In this study the resolution rate with nonoperative treatment was 90%. Many studies have investigated the influence of the original abdominal operation on the course of the adhesive SBO, the response to conservative treatment, the need for surgical intervention, and rates and risks of recurrence (197, 230, 231). These studies have concluded that adhesive SBO following a previous small bowel resection is more likely to be complete and require operative intervention than adhesive SBO following other types of surgical intervention, such as appendectomy, colorectal resection, gastric resection, and gynaecologic and pelvic surgery(197, 230, 231). Such differences were not seen in this study.

The interval between a patient's most recent laparotomy and initial admission for adhesions is quite variable. In a series of over 2000 patients followed for more than 10 years after abdominal surgery, Ellis et al. noted that 1% of patients developed SBO secondary to adhesions within one year of the first operation. However, 20% of patients who ever developed SBO had the diagnosis more than 10 years after the index abdominal surgery(230). Due to the nature of our moving population and lack of readily available data, we were unable to calculate this interval for all patients in this study

The literature indicates that approximately 70% of patients with SBO resolve with conservative treatment.(52, 72, 232). The management of patients with acute SBO varies and depends on individual presentation; patients suspected to have small bowel strangulation with evidence of peritonism usually require an emergency laparotomy. For those who have no evidence of small bowel strangulation, management is usually in the form of nasogastric suction, intravenous hydration, management of pain, and electrolyte balance, but there are no uniform strategies

regarding timing of surgery(52, 64, 130, 229). A large proportion of this group of patients is successfully managed with non-operative measures.

A major clinical problem with SBO is its propensity for frequent recurrence, given that adhesive obstruction commonly follows previous abdominal surgery(103, 233, 234). This retrospective study has failed to support previous studies identifying predictive factors for recurrence of adhesive SBO. A low rate of laparotomy was seen in this study population, with a significantly greater need for laparotomy when the index operation was for cancer. However, there were no factors (72, 232) that predicted the possibility of recurrence in a reliable manner.

Chapter 3

Systematic review and meta-analysis of oral water-soluble contrast for management of adhesive SBO

Introduction

As discussed in chapter 1 and chapter 2 adhesive SBO is a major cause of hospital admission in New Zealand and elsewhere, imposing a considerable burden on hospital resources(49, 72, 232). It may follow any abdominal operation but is most common after appendectomy and colorectal surgery.(52) Although obstruction in most patients resolves with conservative treatment (235), identifying those who require surgery is difficult. The conventional approach is to offer conservative treatment for 48 hours, because most cases that are likely to resolve do so within this time frame(52).

Several studies have evaluated the role of water-soluble contrast agents in predicting the need for surgical treatment in adhesive SBO.(108, 236, 237). The aim of these studies was to determine whether water-soluble contrast agents can differentiate complete from partial SBO, and whether partial obstruction resolves without surgery. Gastrografin is the most commonly used water-soluble contrast agent. It comprises a mixture of sodium diatrizoate and meglumine diatrizoate, with an osmolarity of 1900 mOsm/L. Gastrografin activates movement of water into the small bowel lumen, and also decreases oedema of the small bowel wall and enhances smooth muscle contractility(55, 142, 153, 238).

Passage of Gastrografin into the large bowel may allow the judicious selection of appropriate patients for nonoperative management. Some authors have reported

that conservative treatment is indicated if contrast can be detected in the right colon 4–6 hours after ingestion(152, 239).

Other studies have attempted to assess whether the administration of Gastrografin® has a therapeutic role and can relieve adhesive SBO without surgery, but the results are conflicting (60, 141, 221). This systematic review and meta-analysis examines the role of Gastrografin in the diagnosis and treatment of adhesive SBO.

Methods

Search strategy

Relevant primary studies were identified from the Cochrane Central Register of Controlled Trials (Central), Cochrane Library 2006 (Issue 1), Medline (from 1966 to April 2006), Embase (from 1980 to April 2006) and the Cochrane Colorectal Cancer Group Specialised Register (October 2005). The following search terms were used to search Central, the Specialised Register and Medline; the latter combined with the Cochrane Collaboration highly sensitive search strategy for identifying randomised controlled trials and controlled clinical trials. Search terms were: (1) intestinal obstruction(2) water-soluble contrast,(3) 1 and 2,(4) intestinal or bowel (as key word) (5) obstruction or adhesions.mp, (6) 4 and 5,(7) contrast media or Gastrografin or water soluble.mp,(8) 6 and 7, and (9) 3 or 8. To identify primary studies from Embase, the search was limited using the terms above to randomised and clinical controlled trials by using: "randomisation" all subheadings, "controlled study" all subheadings, and "clinical trial" all subheadings. Reference lists of included studies were scrutinized and relevant conference proceedings were searched. There were no language restrictions.

Selection of studies

All prospective clinical trials that included patients with probable adhesive SBO who received oral water-soluble contrast media were identified. Patients who had undergone abdominal surgery more than six weeks before admission and who were admitted to hospital with abdominal pain, vomiting and abdominal distension with dilated small bowel loops and air fluid levels on abdominal radiography, without signs of large bowel obstruction, were considered to have adhesive SBO.

Two types of intervention were assessed, i.e., administration of water-soluble contrast in patients with a diagnosis of adhesive SBO followed by interval abdominal radiography to identify contrast in the colon, and administration of contrast to patients with adhesive SBO to assess its ability to resolve without surgery.

Review methods

Two reviewers (S Abbas and I Bissett) independently assessed each study identified by the search and selected those that met the inclusion criteria. Disagreement was resolved by consensus. The two reviewers assessed the quality of the methodology used in each clinical trial. The method of randomisation where appropriate, nature of interventions, co-interventions and follow-up were critically appraised. Each non-randomised trial was scored as being of good, fair, or poor quality. The quality of the randomised controlled trials was assessed using a scale devised by Jadad et al. (240) ranging from 0 to 5.

Data collection and analysis

Data were gathered and checked by the reviewers. The results of each trial were summarised on an intention-to-treat basis in 2×2 tables for each outcome.

Duplicate publications were identified, and data were included only once.

Statistical analysis

Sensitivities, specificities, and positive and negative likelihood ratios were calculated for evaluation of the diagnostic value of the contrast. The results were pooled, and a summary receiver-operator characteristic curve was constructed using the formula described by Moses et al(241). The optimal timing of interval radiology was critically appraised. The clinical homogeneity (external validity) of the studies was evaluated.

Where appropriate, studies that examined contrast as a therapy were stratified for meta-analysis of the primary outcome, which was resolution of obstruction or need for surgery. Hospital stay was considered as a secondary outcome measure and was analysed as a continuous variable. Other outcome data collected were time from admission to resolution of adhesive SBO, time from admission to surgical intervention (analysed as continuous data), mortality, small bowel strangulation, bowel resection, septic complications, shock and extra-abdominal complications (all analysed as dichotomous data). The control and intervention groups were compared with respect to these variables.

The statistical heterogeneity of the results of the meta-analysis was assessed by graphical presentations of the confidence intervals (CI) on Forest plots and by performing a Chi-squared test for heterogeneity, in which $p < 0.100$ was regarded

as significant heterogeneity (Rev Man®, The Nordic Cochrane Centre, Rigshospitalet).

Sensitivity analysis was performed by including and excluding poor quality studies, those of doubtful eligibility, and studies that appeared to be outliers. Both fixed-effects and random-effects models were used to assess the robustness of the data, and disparities between the results were described. Data from randomised controlled trials were entered into Metaview in RevMan 4.2, and dichotomous variables were compared using the Mantel-Haenszel test. The results were presented as an odds ratio or risk difference. For continuous variables, the weighted mean difference was calculated from mean (\pm standard deviation) values.

Results

Characteristics of selected studies

Of 14 studies identified, three were subsequently excluded, one because patients were randomised to surgery or contrast, (141) one that was a duplicate study,(238) and one that was a retrospective review(239). Another study (152) included some patients who did not have previous abdominal surgery. A study by Biondo et al. was analysed in both the diagnostic and the therapeutic arms of the review, so there were six studies in each arm (222). Exclusion criteria were similar for all the studies, and included patients who had had surgery within the six weeks before the episode of SBO, those with signs of strangulation or peritonitis, carcinomatosis or irreducible hernia, as well as patients who showed signs of resolution of obstruction at the time of admission. One study that analysed the therapeutic role of Gastrografin excluded patients with no gas in the large bowel (complete obstruction).(221)

Studies that used water-soluble contrast to differentiate between partial and complete SBO, and hence to predict the probability of resolution, administered Gastrografin 50–100ml. Abdominal radiography was performed at four hours by Chung et al, Brochwickz-Lewinski et al, and Joyce et al. (138, 146, 152), at eight hours by Chen et al. (238), and at 24 hours by Onoue et al. and Biondo et al. (144, 222). The obstruction was considered partial if contrast was seen in the colon and complete if contrast did not reach the colon. The relationship between resolution of obstruction/need for surgery and radiological findings was investigated.

Studies that examined the therapeutic role of Gastrografin randomised patients to Gastrografin 100mL or placebo orally or via a nasogastric tube, which was then clamped for 60 minutes. Patients were otherwise treated similarly.(149, 151, 222, 242)

Quality of included studies

Six studies that examined the diagnostic role of Gastrografin were included, all of which were prospective in nature.(141, 144, 146, 152, 153, 222) The methodological quality was considered good, but the timing of abdominal radiography varied between four and 24 hours (see above). There was no "gold standard" against which to evaluate the diagnostic role of water-soluble contrast in SBO, but the eventual outcome for individual patients and the need for surgical intervention or resolution was regarded as the standard against which the accuracy of the diagnosis was evaluated.

The five studies that addressed the therapeutic role of Gastrografin were described as prospective randomised trials.(69, 150, 151, 222, 242) Each of these

scored 2 on the Jadad scale(240). None was described as blinded and their overall quality was only fair, given that randomisation methods and allocation concealment were not described. Dropouts and withdrawals were described in all studies and analysis was on an intention-to-treat basis. The decision to operate was made on clinical grounds, i.e., failure of resolution of obstruction or the onset of signs of strangulation. Although this was independent of the initial radiology, further radiography was performed to assess on going obstruction. The radiography results may have influenced the decision to operate in the study by Biondo et al, because patients who needed surgery in the Gastrografin group underwent surgery significantly earlier(222). Time allowed for non-operative resolution varied from 48 hours(151) to five days(221).

Results of studies examining the diagnostic role of Gastrografin

The sensitivity, specificity, positive likelihood ratios, and negative likelihood ratios were calculated for each study (Table 1). The presence of contrast in the colon indicated that the obstruction would resolve without surgical intervention with a sensitivity of 90%–100%, a specificity of 67%–100%, a positive likelihood ratio of 2.44–62.83, and a negative likelihood of 0.014–0.104. The pooled sensitivity and specificity was 97% and 96%, respectively, with positive and negative likelihood ratios of 25.098 and 0.036, respectively (Table 3).The timing of abdominal radiography differed between the studies, in the range of 4–24 hours after administration of contrast. The positive and negative likelihood ratios in studies with a delay of 4–8 hours were similar to those that had a delay of 24 hours. However, there was only one false-negative result among the 141 patients who had a 24-hour delay compared with 12 of 312 patients who had a delay of eight hours or less ($p=0.06$); there was no increase in the rate of complications in the

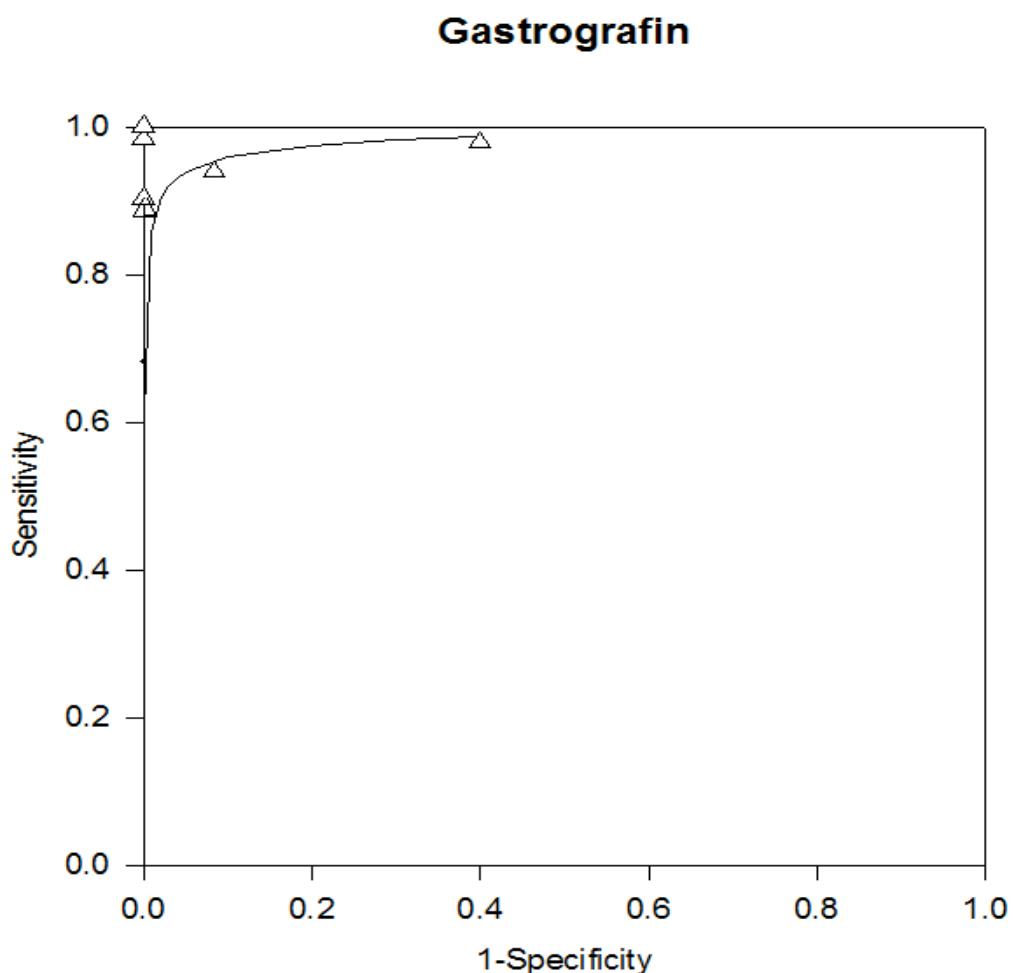
group that waited for 24 hours. A summary receiver-operator characteristic curve was constructed from the pooled data, using both non-weighted and weighted analyses. The area under the curve was 0.98 (see Figure 2 for weighted analysis).

Table 5. Prediction of resolution after administration of Gastrografin

Study	Total	TP	FP	FN	TN	Sens	Spec	LR+	LR-
Chung12	45	31	1	2	11	93	91	11.273	0.066
Chen15	116	74	0	8	34	90	100	NA	0.097
Brochwicz-Lewinski18	24	16	0	0	8	100	100	NA	NA
Joyce19	127	112	0	2	13	98	100	NA	0.017
Onoue20	97	90	2	1	4	99	67	2.44	0.036
Biondo21	44	39	0	0	5	100	100	NA	NA
Pooled	453	362	3	13	75	97	96	25.098	0.036

Abbreviations: TP, true positive; FP, false positive; FN, false negative; TN, true negative; Sens, sensitivity; Spec, specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NA, not applicable

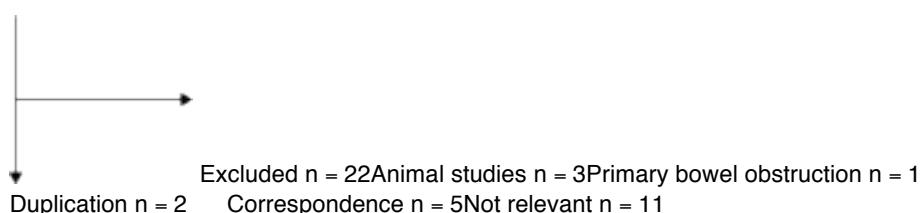
Figure 2. Receiver-operator characteristic curve for the diagnostic role of Gastrografin



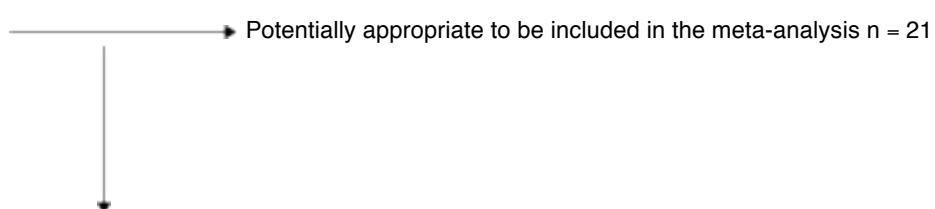
Therapeutic role of Gastrografin

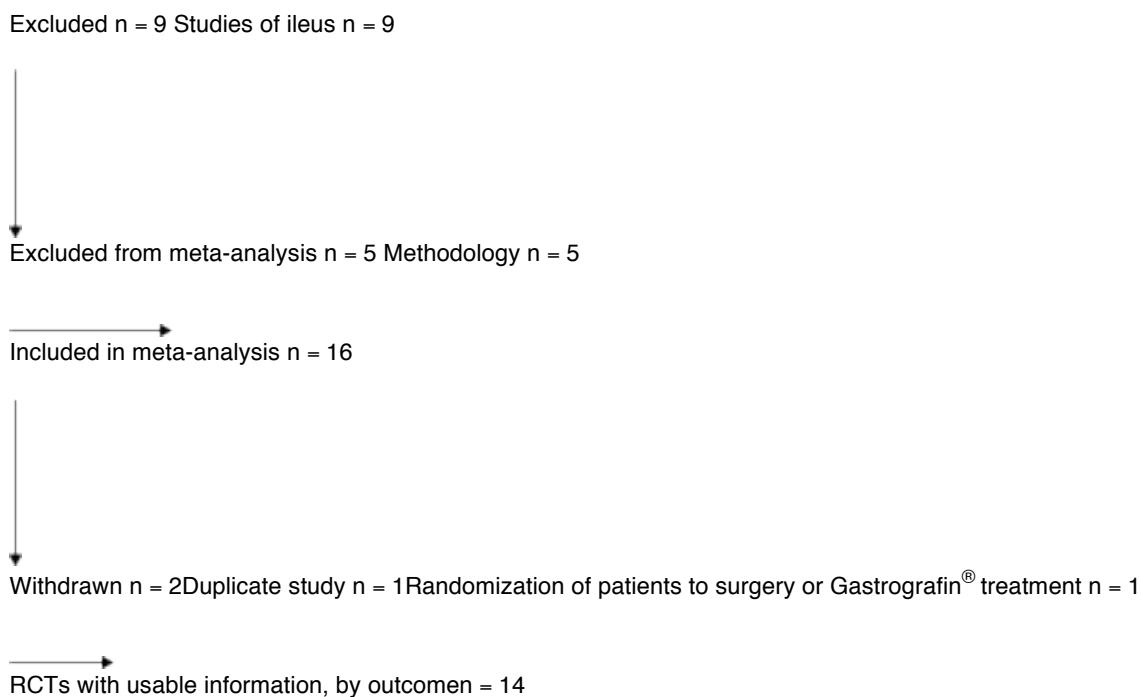
Flow chart of the search results and exclusion and inclusion

Potentially relevant RCTs identified and screened for retrieval = 52



Retrieved for more detailed evaluationn = 30





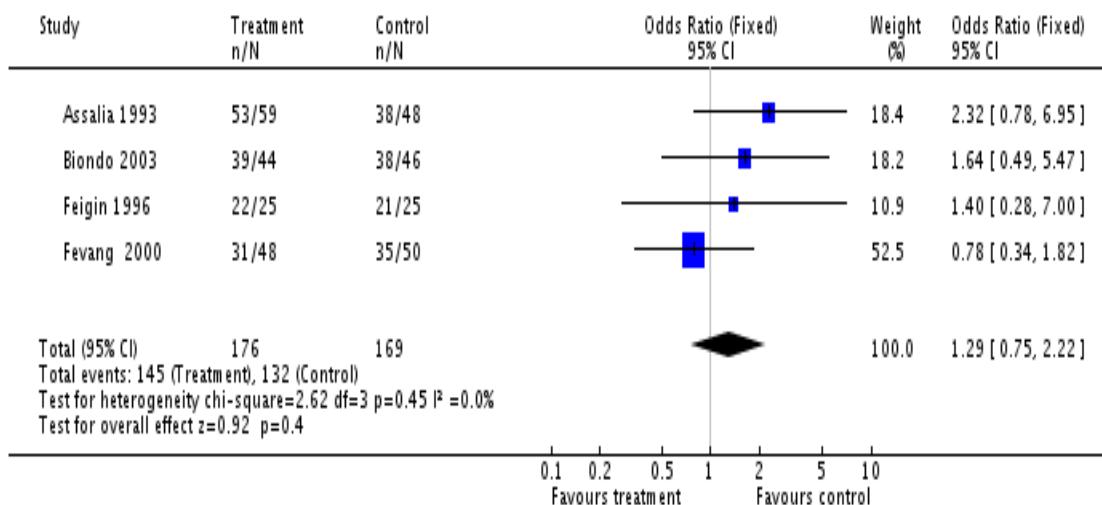
Resolution of obstruction or surgery

Resolution or operative treatment

All four studies in the therapeutic arm addressed this question. The Mantel-Haenszel test showed that there was no significant difference between Gastrografin and placebo with regard to resolution of SBO without surgery (Figure 3). The odds ratio was 1.29 (95% CI 0.75 to 2.22, $p=0.36$), and there was no heterogeneity between the included studies ($p=0.45$, comparison 01 01).

Figure 3. Comparison of numbers of patients who required surgery in both groups

Review: Oral water soluble contrast for the management of adhesive small bowel obstruction
 Comparison: 01 Resolution or Laparotomy
 Outcome: 01 Comparison of numbers of patients who had resolution of bowel obstruction without operation in both groups



Hospital stay

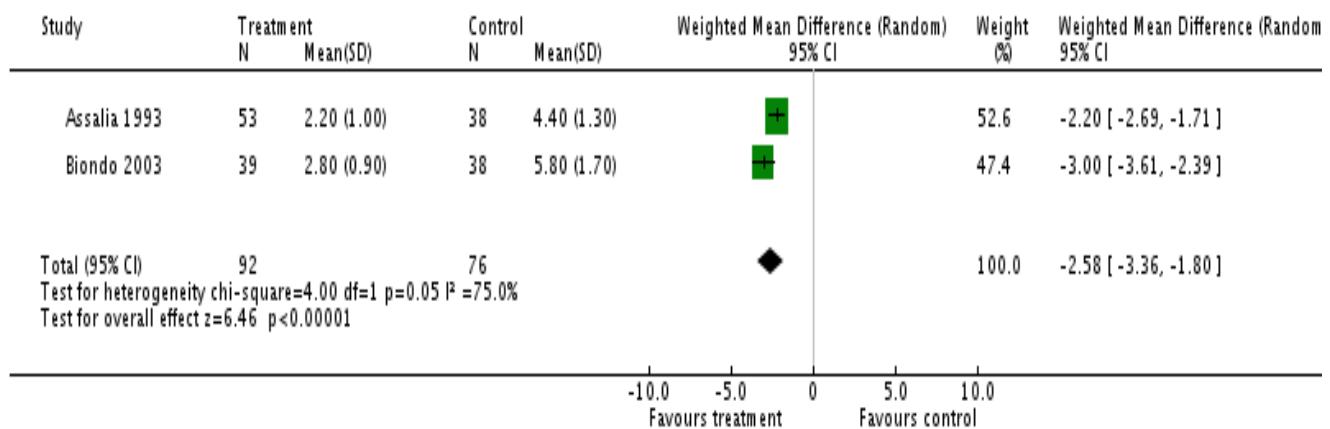
Two studies (151, 222) reported the mean (\pm standard deviation) length of hospital stay for patients who did not require surgery. These studies were used for meta-analysis, using the weighted mean difference and fixed-effect model (Figure 4). Patients who had Gastrograffin had a shorter duration of hospital stay, with a weighted mean difference of -2.58 (95% CI, 1.8–3.4, $p<0.0001$). Two studies(221, 242)^{150,151} were excluded from the meta-analysis because they contained inadequate data for inclusion. These individual studies did not show any statistically significant difference in length of hospital stay.

Figure 4. Length of hospital stay (in days) in both treatment and control group for non-operated patients

Review: Oral water soluble contrast for the management of adhesive small bowel obstruction

Comparison: 02 Hospital stay in days

Outcome: 01 Length of hospital stay (in days) in both treatment and control group for non-operated patients

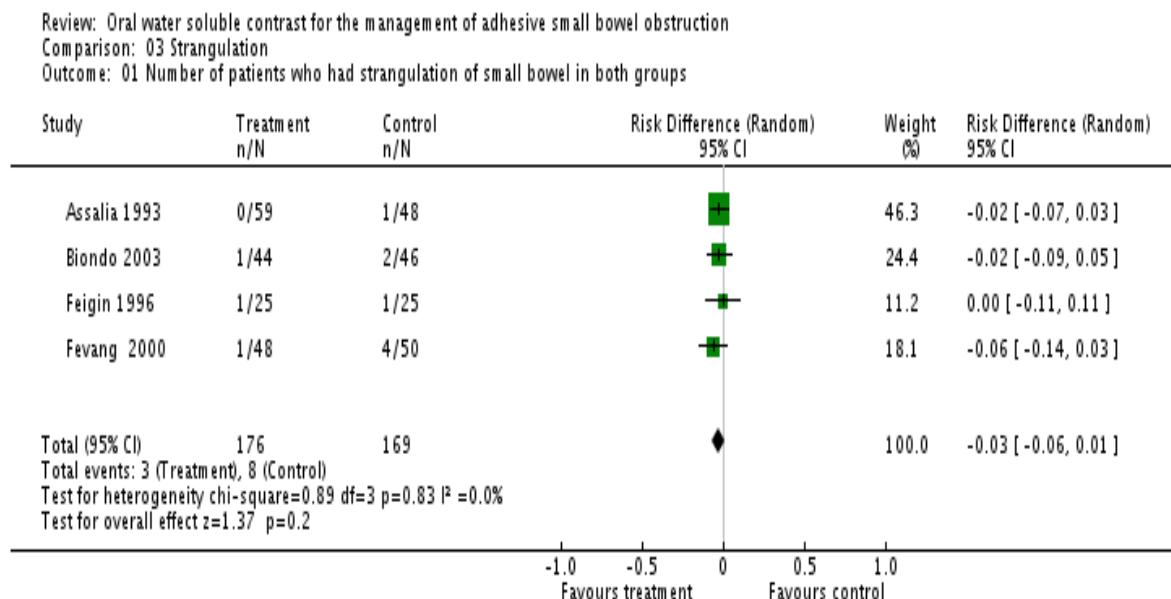


Time from admission to resolution of obstruction

Two studies (151, 222)^{33,152} reported time between admission and resolution, which was defined as the time of first bowel motion after admission. There was significant heterogeneity between the two studies ($p < 0.0001$). Studies differed with respect to reporting on patients with gas in the colon, which was the reason for exclusion of one study by Assalia et al.(151) This made a meta-analysis inappropriate for this variable.

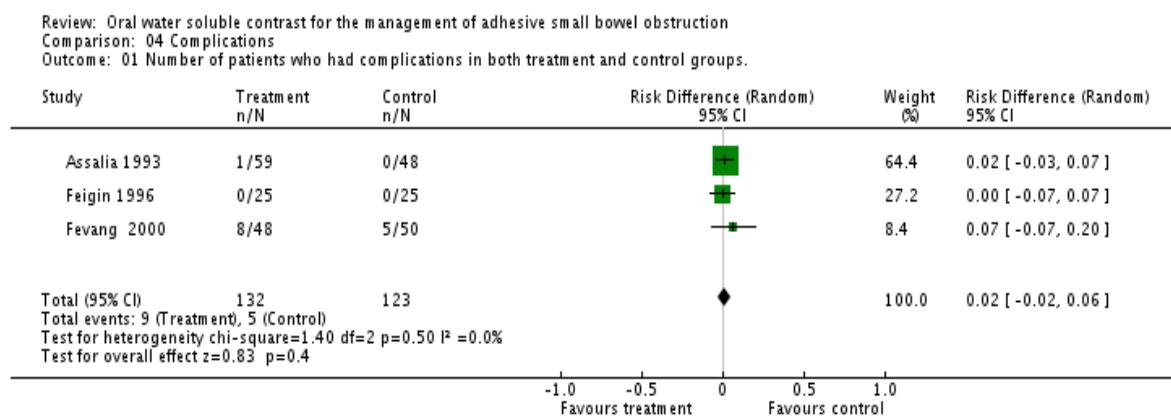
Small bowel strangulation and resection

Three studies (149, 151, 221) reported the number of patients who had small bowel strangulation (Figure 5). No difference was found between the Gastrografin and control groups (risk difference 0.03 [95% CI, 0.01–0.08], $p=0.17$).

Figure 5. Number of patients who had strangulation of small bowel in both groups

Overall complication rates

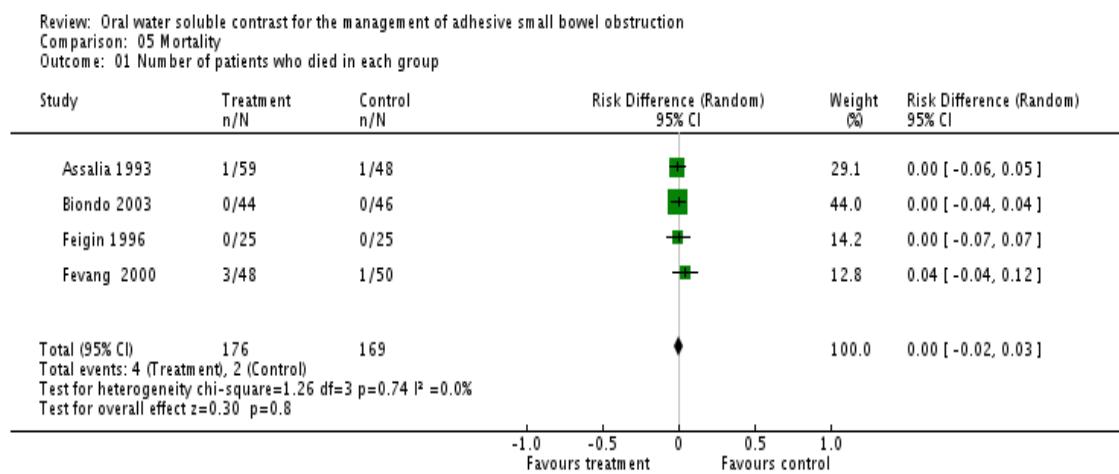
All studies reported overall complication rates. There was no difference between the two groups for complication rates, with 10 of 151 patients in the Gastrograffin group having a complication compared with eight of 139 in the control group (Figure 6) Meta-analysis using the Mantel-Haenszel test with both fixed effect and random effect models showed a risk difference of 0.02 (95% CI, 0.02–0.06, $p=0.41$).

Figure 6. Number of patients in the treatment and control groups who had complications

Mortality

All studies reported mortality rates (Figure 7) There was no difference in mortality rates between the Gastrografin and control groups, although the studies were not adequately powered to detect a difference (risk difference 0.00 [95%CI, 0.02–0.03], $p=0.76$).

Figure 7. Number of patients who died in each group



Time from admission to surgery

Although four studies (150, 221, 222, 242) reported the time between admission and surgery for those who required surgery, there were insufficient data to include this variable.

Discussion

This review provides compelling evidence for the value of Gastrografin as a means of identifying patients with adhesive SBO who require surgery. The area under the receiver-operator characteristic curve of the combined diagnostic studies, and the pooled sensitivity, specificity, and positive and negative likelihood ratio values indicate that it is a very accurate predictor of the likelihood of nonoperative resolution of SBO.

Patients with SBO, but no indication for immediate surgery, are suitable for evaluation with 100mL of water-soluble contrast given via a nasogastric tube or orally, and abdominal radiography 4–24 hours later. The presence of contrast in the colon at that time is indicative of partial SBO, which will probably settle with conservative treatment. On the other hand, if contrast does not reach the colon, the bowel obstruction is considered to be complete and is unlikely to resolve without surgical intervention. The results of a randomised trial of surgery versus Gastrografin in patients whose symptoms failed to resolve after 48 hours of conservative treatment support this approach.(141)

The results of this meta-analysis indicate that Gastrografin does not reduce the need for surgical intervention, however. Four studies were included in a meta-analysis of hospital stay after administration of contrast. This showed that the hospital stay was shorter in the Gastrografin group. The analysis of hospital stay included only patients who did not require surgery, so it appears that administration of the contrast agent was responsible for the reduction in hospital stay in this group rather than factors related to surgery or postoperative stay. However, this review was unable to assess whether Gastrografin actually hastens resolution of SBO because the studies were not strictly comparable in this regard. Only one study described the method of randomisation and provided adequate blinding with respect to the treatment given. In the other five studies, the decision of the clinician might have been influenced by the presence or absence of contrast on radiographs.

There are potential pitfalls in the use of water-soluble contrast in this setting. The administration of full-strength Gastrografin may lead to difficulty in interpreting the

results of subsequent computed tomography because its high density may cause radiological artefacts. Severe pneumonia from aspiration of Gastrografin is a recognised complication, and it would be unwise to administer this agent to patients who do not have an empty stomach or who continue to vomit. Routine gastric drainage by nasogastric tube prior to administration should prevent this(181, 187). Rarely, intravasation of contrast might occur if the nasogastric tube is not properly placed, which may lead to renal failure or anaphylaxis(181). This can be avoided by ensuring that the nasogastric tube is in the stomach before administration of contrast.

The optimal timing of radiography after administration of contrast is not clear, but there appears to be little advantage in terms of specificity and sensitivity in waiting longer than 4–6 hours. However, a potential advantage of waiting for 24 hours is that the obstruction may resolve in some patients and a radiograph will no longer be needed.

Based on the findings of this review, the management of patients with adhesive SBO can be simplified according to whether water-soluble contrast agent appears in the colon, with the potential for a reduced hospital stay. Gastrografin was safe, and did not increase the rate of overall morbidity or mortality or the incidence of small bowel strangulation.

These studies, however, do not answer the question as to whether or not Gastrografin has a specific therapeutic effect over and above its role in triaging patients to an operative or non-operative case.

Chapter 4

Randomised controlled trial of the therapeutic effect of Gastrografin in adhesive SBO

Introduction

While Gastrografin is beneficial in the early triage of patients into those who will settle quickly without surgery and those who will not, it is also possible that Gastrografin has a specific therapeutic effect. Water-soluble hyperosmotic solutions draw fluid into the lumen of the bowel and increase intestinal motility. The osmolarity of Gastrografin is 1900 mOsm/L, which is approximately six times that of extracellular fluid. It promotes shifting of fluid into the bowel lumen. The bowel content is diluted, and in the presence of the wetting agent, passage of bowel contents through a narrow intestinal lumen is enhanced. It is also thought to reduce oedema of the bowel wall and enhance bowel motility(139, 243).

The hypothesis that Gastrografin acts therapeutically in SBO has so far not been confirmed because previous studies have not specifically addressed this issue. And have confounded results by use of x ray when attempts to answer these questions. Biondo et al. studied the diagnostic role of Gastrografin in SBO and that showed shorter hospital stay in patients who had the Gastrografin, which raised the possibility of therapeutic effect, however, the result are likely to be related to early operation for patients with complete obstruction (222). More recently the use of water soluble contrast was found to hasten resolution of the obstruction by shortening the time interval between admission and the first bowel movement(147). This study aimed to address definitively the issue of whether or not Gastrografin has a therapeutic role in the treatment of SBO. It was aimed at

patients admitted to the hospital with subacute small bowel obstruction who did not require an immediate laparotomy.

Methods

The Auckland Regional Ethics Committee and the Counties Manukau and Auckland District Health Boards approved the study. Patients with clinical and radiological evidence of adhesive SBO suitable for initial conservative management were randomised to receive Gastrografin or placebo via a nasogastric tube as soon as practical after diagnosis, resuscitation, and emptying of the stomach. The admitting surgical registrar randomised patients to receive either Gastrografin or placebo.

The pharmacy supplied Gastrografin or placebo in identical 100 ml bottles that were given certain numbers and placed all the bottles (placebo and Gastrografin) mixed in a locker in the emergency department. The admitting surgical registrar randomly selected a bottle, and a nurse, who was not subsequently involved in the patient's care, administered the bottle's contents via the nasogastric tube. The bottle number was recorded on an information sheet. The nasogastric tube was then clamped for one hour. The patient was subsequently treated as per the admitting surgeon's preference. Usually this was by nasogastric tube drainage and intravenous fluids.

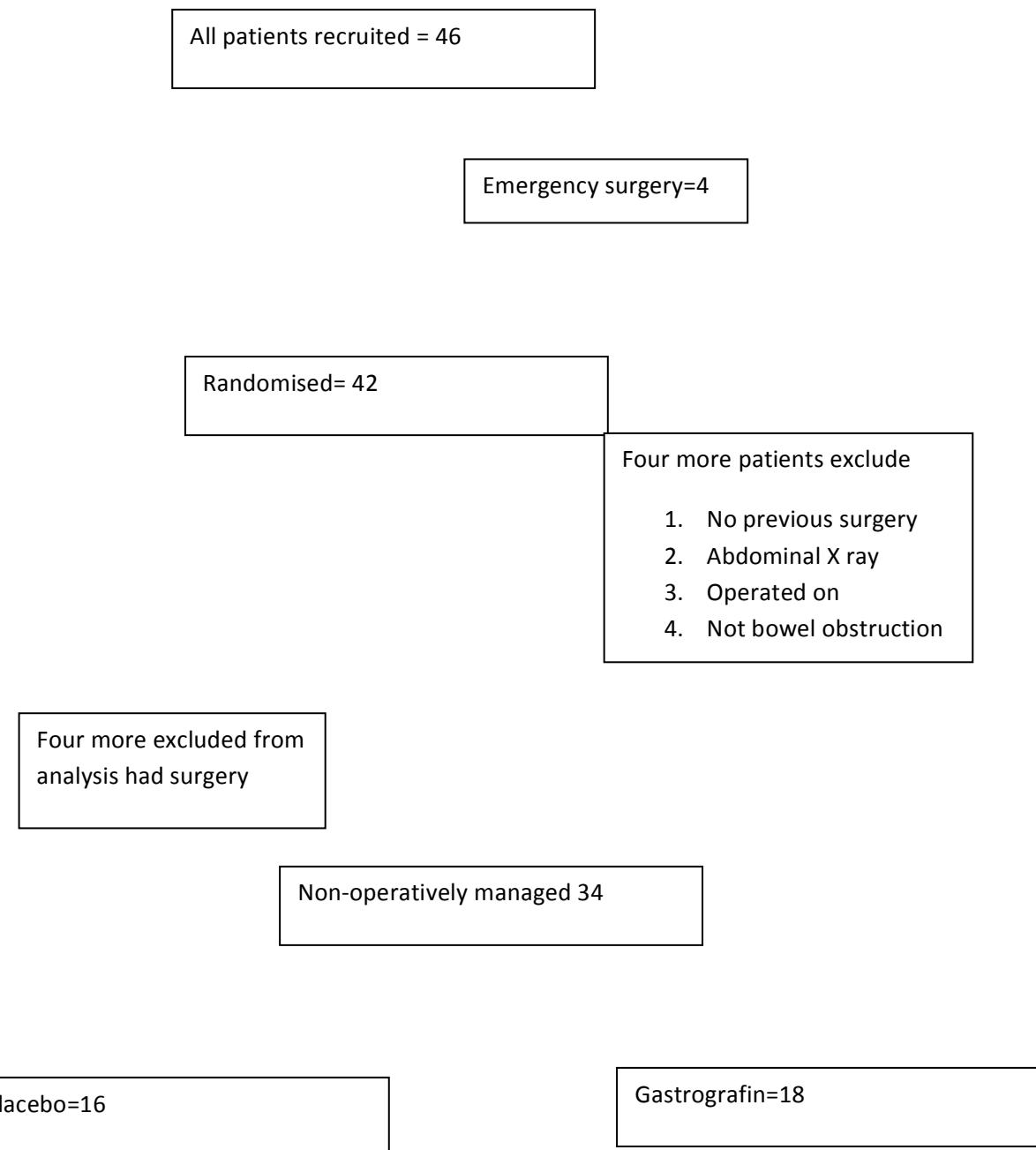
Management was planned according to clinical judgement on an individual basis. Patients were enrolled in the study if the admitting team chose to pursue non-operative management after obtaining a written consent. Patients did not undergo further radiological investigations on this hospital admission after all the surgical teams had been informed and agreed to include their patients in the study. Any

patient who underwent subsequent radiological intervention or surgery was excluded from analysis. Patients were also excluded if they had gastrointestinal cancer, large bowel obstruction, recent (within six weeks) abdominal surgery, ileus, were unable to give informed consent, required urgent (within 24 hours) surgery, or had peritonitis or inguinal hernia. Endpoints were time interval to resolution of SBO (flatus and bowel motion), length of hospital stay, operative interventions, and complications.

Seeking significance at the 5% level with 80% power, it was calculated that 25 patients in each group would be required to demonstrate a difference in duration of hospital stay of 1.6 days (this is the difference found in a previous study by the same research group).(244) The study was designed to allow interim analysis at intervals. Results are expressed as median (range), and the differences between groups were compared using the Mann-Whitney U test. A p value <0.05 was considered to be statistically significant.

Results

Forty-six patients were entered into the study. The study was stopped after 46 patients because an interim analysis demonstrated that Gastrografin had a therapeutic effect. Four patients, who were subsequently treated successfully without surgery, were excluded from the analysis. One patient was excluded because the bottle number was not entered on the information sheet. One patient was given placebo on the day of admission and when found to be failing to settle underwent a further abdominal radiograph after additional Gastrografin. One patient who had not undergone previous surgery and another patient who did not have a documented SBO were also excluded.

Figure 8. Patient allocation

The median number of previous operations was similar between the two groups.

Eight patients underwent surgery because they failed to settle. Four of these patients had received placebo and four had received Gastrograffin. One patient in each group died, for reasons unrelated to administration of Gastrograffin or placebo. Both these deaths were due to cardiovascular comorbidities.

The remaining 34 patients were successfully managed without surgery. As can be seen in Table 4, Gastrografin accelerated resolution of SBO and decreased length of hospital stay. A nonparametric test was used for comparison of groups because all patients with SBO failing to settle at four days after admission underwent surgical intervention, resulting in a skewed distribution.

Table 6. Time to complete resolution of SBO and hospital stay in patients given placebo or Gastrografin

	Placebo	Gastrografin	P value*
N	16	18	
Previous operations (n)	1 (1–5)	1 (1–3)	0.631
Resolution time (hours)	21 (9–96)	13 (6–96)	0.014
Hospital stay (days)	4 (2–8)	3 (1–8)	0.041

*Mann-Whitney U test. Results are given as median (range).

Of note, 16/22 (73%) of patients who received Gastrografin had complete resolution of their SBO within 24 hours of admission versus 11/20 (55%) of patients who received placebo. Of the six patients who failed to settle completely within 24 hours of Gastrografin administration, four subsequently underwent surgery.

Discussion

The findings of this study show that Gastrografin significantly shortens the time to resolution of SBO. Previous studies have suggested that this might be the case, but have used radiological investigations to identify patients who could be safely triaged to an early feeding regimen, thereby introducing the x-ray as a confounding variable by unblinding the study investigators. This study has answered the question of a therapeutic effect of Gastrografin in SBO by excluding patients who

underwent further radiological investigations, beyond those required to make the initial diagnosis of SBO.

Assalia et al. randomised 99 patients with 107 episodes of SBO to Gastrografin by nasogastric tube or to conventional treatment.(151) Importantly, patients were not blinded to treatment and no placebo was used. They found that patients given Gastrografin had much more rapid resolution of SBO than patients who were treated conventionally (6.2 hours versus 23.3 hours, respectively). In addition, the patients who received Gastrografin spent, on average, 2.2 fewer days in hospital. Operative mortality and complication rates were similar between the two groups. The results of this report are consistent with the findings of the present study.

Studies performed subsequent to the one by Assalia et al. (151) were complicated by the fact that patients were x-rayed several hours after administration of Gastrografin, and this almost certainly skewed their results in favour of Gastrografin, and certainly did not address the specific issue of a therapeutic role for Gastrografin. At best, these studies have demonstrated a useful triaging role for water-soluble contrast materials,(108, 144, 152, 162, 227, 243, 245) but have not addressed the issue of a therapeutic role for Gastrografin in hastening resolution of SBO.

The present placebo-controlled study shows that patients given Gastrografin have earlier resolution of SBO and this translates into earlier discharge from hospital. This improvement appears to be primarily due to a therapeutic effect of Gastrografin itself, rather than a triage effect due to its radiological properties. The mechanism of action of Gastrografin involves drawing of water into the intestinal

lumen via osmosis, as well as stimulation of peristalsis in the small bowel. These two actions combine to overcome SBO.

Interestingly, time to resolution of SBO was only eight hours faster in patients given Gastrografin, with a time saving in hospital stay of at least one day. This is probably because resolution of SBO with Gastrografin is seldom subtle, and patients can be fed early with confidence rather than the gradual return of bowel function usually observed with traditional conservative management of SBO. Nearly 75% of patients given Gastrografin had complete resolution of SBO within 24 hours versus 55% of placebo patients.

Although not powered for this end point, this study has not shown a difference in need for surgical intervention between placebo and Gastrografin, suggesting that Gastrografin is able to speed resolution in patients who will settle eventually, but cannot reduce the need for surgery in those who do not. In other words, if a patient is eventually going to require surgery for SBO there appears to be little that can be done to prevent this once SBO is established. However, it may be that an abdominal radiograph taken after administration of Gastrografin early in the hospital course can help to speed the decision to operate (144,151, 152).

These findings, as well as those of others, suggest that this x-ray should be done at 24 hours after Gastrografin administration because approximately 75% of patients will have settled and can be fed by this stage. In the remaining patients, a plain abdominal radiograph could help to distinguish between those who will resolve completely and can be fed early, and those who are unlikely to settle so can be offered early surgery. (108, 144, 152, 162, 227, 243, 245)

In summary this study has shown that Gastrografin does have a therapeutic effect in speeding resolution of adhesive SBO. A plain abdominal radiograph taken 24 hours after admission may shorten hospital stay by triaging patients to an operative or a non-operative course.

Chapter 5

Clinical impact of routine use of Gastrografin in management of adhesive SBO in a tertiary hospital

Introduction

As discussed in chapter 3 Gastrografin was initially used for diagnostic purposes in patients with SBO, and its passage was monitored using radiographs to determine whether it reached the caecum(136, 221). This approach helps to triage patients to operative or non-operative management. A randomised controlled trial (Chapter 4) showed that Gastrografin also has the therapeutic benefit of accelerating resolution of adhesive SBO and decreasing duration of hospital stay.(243, 246) Other studies have confirmed the same, although there is debate in the literature about whether use of Gastrografin decreases the need for surgery(141, 222). The body of evidence suggesting improved outcomes from Gastrografin is compelling and hence, in September 2003, a protocol was introduced at Middlemore Hospital for the routine use of Gastrografin as part of the initial management of adhesive SBO.

Whilst multiple clinical studies have demonstrated the value of Gastrografin for this indication, there is minimal literature evaluating the use of Gastrografin in clinical practice. Its impact outside a trial setting in a sample of sufficient size has not been adequately assessed. Therefore, this study investigates the impact of instituting a protocol of routine Gastrografin use in adhesive SBO, in particular examining whether use of Gastrografin would increase in clinical practice, as well as its impact on duration of hospital stay and operative rates. The purpose of this

study was to investigate whether implementation of a Gastrografin protocol in clinical practice reproduce the benefits reported in the trial setting.

Methods

An electronic database (Concerto 6.3) at Middlemore Hospital, New Zealand, was searched for patients discharged with a diagnosis of SBO from January 1997 to December 2007, using the ICD-10 code “small bowel obstruction”. Manual screening of records was then done to identify cases of adhesive SBO. Only patients presenting to the hospital with abdominal pain and subsequently diagnosed with adhesive SBO were included.

Diagnostic criteria for adhesive SBO were a history of previous abdominal surgery, confirmatory clinical features (e.g., abdominal pain, distension, vomiting, obstipation, high-pitched bowel sounds, empty rectum on digital rectal examination), and supporting radiological evidence (e.g., CT, abdominal radiograph). Patients with other causes of bowel obstruction were excluded.

Demographic data, type of treatment received (traditional conservative, Gastrografin, or operative) and length of hospital stay were recorded. Patients were categorised into two groups according to whether they were admitted before (period one) or after (period after) September 2003, and whether or not they received Gastrografin. September 2003 was used as a cut-off date for the two groups because a hospital protocol for use of Gastrografin was introduced at this time.

All data were recorded using SPSS 13.0 software (SPSS Inc., Chicago, IL). Statistical significance was determined using the Mann-Whitney U test for continuous data and the two-tailed Fisher's Exact test for categorical data.

Gastrografin protocol

The Middlemore Hospital protocol states that once the diagnosis of adhesive SBO has been established, a dose of Gastrografin 100mL should be given as soon as practicable, either orally or via a nasogastric tube. If the patient fails to pass flatus or a bowel motion after four hours, an abdominal radiograph should be obtained within the next 24 hours. If contrast has reached the caecum, oral intake of food is permitted. However, if contrast has not reached the large bowel, a clinical judgment should be made to determine whether conservative or operative management is required.

Results

Seven hundred and ten patients with adhesive SBO were identified from January 1997 to December 2007, comprising 415 (58.5%) females and 295 (41.5%) males, of mean age 59.8 years. In total, 57 patients required immediate surgery for adhesive small bowel obstruction in the study period. Six hundred and fifty-three patients were managed non-operatively, with 211 (31%) of these receiving Gastrografin and 499 (69%) not receiving Gastrografin. Non-passage of Gastrografin was observed in 22 patients, nine of whom required surgery. There were no significant differences in median length of hospital stay ($p=0.29$) or operative rate ($p=0.65$) between patients who received Gastrografin and those who did not (see Table 1).

Table 7. Median duration of hospital stay and operative rates in all patients

	GG +	GG-	Total	Mann- Whitney U test/ Fisher's Exact test
Period 1	n=16	n=360	n=376	
Median LOS (days, IQR)	4 (3–7)	4 (2–7)	4 (2–7)	p= 0.29
Operative (%)	6.3%	7.8%	7.7%	p=0.65
Period 2	n=195	n=139	n=334	
Median LOS (days), IQR	3 (2–5)	2 (1–5)	2 (1–5)	p=0.05
Operative (%)	5.1%	12.9%	8.4%	p=0.02
Total	n=211	n=499	n=710	
Median LOS (days), IQR	3 (2–5)	3 (2–6)		p=0.03
Operative (%)	5.2%	9.2%		p=0.10

Abbreviations: GG+, received Gastrografin; GG-, did not receive Gastrografin; LOS, length of stay; IQR, interquartile range

The median length of stay was not significantly different when only non-operative management was compared (p=0.19), as shown in Table 2.

Table 8. Median length of hospital stay in patients managed non-operatively

	GG +	GG-	Total	Mann- Whitney U Test
Period 1	n=15	n=332		
Median LOS (days), IQR	4 (3–7)	3 (2–6)	3 (2–6)	p=0.19
Period 2	n=185	n=121		
Median LOS (days), IQR	3 (2–4)	2 (1–3)	2 (1–4)	p=0.01
Total	n=200	n=453	n=653	
Median LOS (days), IQR	3 (2–4)	3 (2–5)	3 (2–5)	p=0.09

Abbreviations: GG+, received Gastrografin; GG-, did not receive Gastrografin; LOS, length of stay; IQR, interquartile range

In period two in total there were 334 admissions (of a grand total of 710 patients) with adhesive SBO, and 195(58.3%) of these patients received Gastrografin.

Following the introduction of the Gastrografin protocol in period 2, use of Gastrografin has been limited to between 58%–69% of all potentially eligible patients per year (see Table 3).

Table 9. Proportion of patients receiving Gastrografin

Time in period 2	9/03–8/04	9/04–8/05	9/05–8/06	9/06–8/07	9/07–10/07
Patients given Gastrografin	24/70	50/72	54/92	61/88	6/10
Percentage	34%	69%	58%	69%	60%

Patients receiving Gastrografin had a longer median length of hospital stay in period 2 (3 [2–5] versus 2 [1–5] days, p=0.05), even when only nonoperative management was compared (Table 8 (3 [2–4] versus 2 [1–3] days, p=0.01)). Forty-nine of 139 patients who did not receive Gastrografin had a length of stay of one day compared with 45/195 patients receiving Gastrografin (p= 0.02). Patients receiving Gastrografin had significantly lower operative rates than those who did not (5.1% versus 12.9%, p=0.02).

Table shows that the median length of hospital stay decreased over time (4 [2–7] versus 2 [1–5] days, p=0.01). Table 4 also reflects a decreased mean duration of stay when only non-operative management is compared across periods (3 [2–6] versus 2 [1–4] days, p=0.01). Patients who received Gastrografin had a slightly shorter median length of stay (3 [2–5] versus 3 [2–6], p=0.03). The median length of stay of patients managed non-operatively was not significantly different when Gastrografin administration was compared (3 [2–4] versus 3 [2–5] days, p=0.09). While there was a trend towards patients receiving Gastrografin having lower operative rates, this was not statistically significant (5.2% versus 9.2%, p=0.10).

The overall operative rates remained unchanged between the two time periods (7.7% versus 8.4%, p=0.42). Table 4

Table 10. Median length of stay and operative rate across both time periods

	Period 1	Period 2	Mann- Whitney U test/ Fisher's Exact test
Median LOS (days), IQR	4 (2–7)	2 (1–5)	p=0.01
Operative (%)	7.7	8.4	p=0.42

Abbreviations: LOS, length of stay; IQR, interquartile range

Discussion

Water-soluble contrast agents such as Gastrografin have added to the Surgeon's armamentarium in the non-operative management of adhesive SBO. Whilst initially thought to be of diagnostic value alone, as discussed in chapter 3 and 4 Gastrografin is now known to have a more significant role as a triaging and therapeutic agent (246, 247)^{163,165}. The benefits of Gastrografin have been demonstrated in multiple studies, and this agent has been gradually incorporated into clinical practice (141, 222, 244, 246, 247).

At Middlemore Hospital use of Gastrografin increased markedly after introduction of a protocol for its use in September 2003, but has remained at 58%–69% in subsequent years. The median length of stay has decreased over time but overall operative rates remain unchanged. However, in the present study, patients who received Gastrografin had a longer median length of hospital stay and lower operative rates when only period 2 is considered. Median length of hospital stay remained greater even when only nonoperative management was considered. These results suggest that period 1 and period 2 may be differentiated by factors

additional to introduction of the Gastrografin protocol, which influenced the results when the data are considered collectively.

These data show an increase in Gastrografin use from 4.3% in period 1 to 58.3% in period 2, which can be attributed to introduction of the protocol for its use at Middlemore Hospital. The low use of Gastrografin in period 1 is likely to be due to unfamiliarity with Gastrografin and its relative lack of availability. Whilst the increased use of Gastrografin in period 2 is encouraging, up to 42% of potentially eligible patients did not receive it. Furthermore, minimal improvement in protocol adherence has been observed following the initial increase.

The results identify non adherence to the protocol as an important reason for suboptimal management of patients with adhesive SBO. There are multiple potential causes for this non adherence. The 710 cases of adhesive SBO were identified on the basis of a discharge diagnosis of small bowel obstruction. Initial clinical uncertainty about the cause of SBO may have prevented timely administration of Gastrografin. The initial "therapeutic window" would thus remain underutilized. Late administration of Gastrografin may also affect length of hospital stay and the need for surgical intervention. Patients with mild adhesive SBO may not have received Gastrografin, and would have demonstrated marked clinical improvement upon repeat clinical review, which is another factor potentially influencing length of stay. Furthermore, due to high staff turnover, the initial attending doctor may have been unfamiliar with the hospital protocol for use of Gastrografin. Some patients may have been unsuitable for contrast administration whilst aspiration risk can often be a deterrent in the elderly. Although the increased use of Gastrografin following establishment of a protocol is encouraging, a greater

proportion of potentially eligible patients should be receiving Gastrografin to ensure the benefits observed in the trials are achieved.

Comparison of the two time periods in this study show that the median length of hospital stay decreased significantly following the implementation of a Gastrografin protocol. However, these findings are not replicated when patients receiving and not receiving Gastrografin are compared. In period 2, the median length of stay was greater in patients receiving Gastrografin, which is in contrast with the previously demonstrated triaging and therapeutic benefits of Gastrografin (244, 246-248). Data from period 1 could not be analysed for statistical significance due to the small number of patients receiving Gastrografin ($n= 16$). When the data for period 1 and period 2 are combined, the median length of stay for patients receiving Gastrografin was marginally lower than those not receiving it. However, the large number of patients not receiving Gastrografin in period 1 skews the data. When only non-operative management of adhesive SBO is compared, patients receiving Gastrografin also had a longer median length of stay in period 2, although no significant difference was observed when the combined data (period 1 and period 2) were analysed ($p=0.09$). Findings in this analysis may also be affected by skewing of data from period 1. The data thus suggest that whilst median length of stay has decreased over time, this may not be attributable to the introduction of Gastrografin. Other factors may have decreased the length of stay during the study period, including improvements in ward management, perioperative care, and access to radiology services.

The benefits of Gastrografin in reducing length of hospital stay, as demonstrated in clinical trials, have not been replicated in this study (151, 222, 244). This may be

due to Gastrografin being administered following an initial trial of conventional non-operative management rather than immediately on admission. This is a limitation of this study because accurate data regarding the timing of administration of Gastrografin were not available in this retrospective study. The addition of another diagnostic/therapeutic tool may have influenced clinical decision-making, because the treatment team may have had a higher threshold to persist with non-operative management in patients who received Gastrografin. This is reflected in the decreased operative rates in period 2 and the greater median length of stay when only non-operative management is compared. Furthermore, patients with mild adhesive SBO managed without Gastrografin had their length of stay recorded as one day, thereby skewing the results against the use of Gastrografin.

Previous studies have shown conflicting results with regard to decreased need for surgery following use of Gastrografin. Some studies that show a decreased need for surgery have used Gastrografin following a 48-hour period of unsuccessful conservative management and have been performed in an environment of low operative threshold (141, 249). Hence, when patients are trialled with Gastrografin, the additional length of time spent in pursuing nonoperative treatment may have benefited these patients, rather than Gastrografin per se.

A randomised controlled trial by Choi et al. also showed a markedly decreased need for surgery, but the randomisation of patients in this study was different to that in comparable studies (141). Some studies that have compared the efficacy of Gastrografin on admission versus conservative therapy have not shown a decreased need for surgery (151). The present study demonstrates that use of Gastrografin is associated with decreased operative rates in period 2, but with no

significant differences overall. The overall operative rate also remained unchanged, despite the greater proportion of patients receiving Gastrografin in period 2. Thus, it appears that a different subgroup of patients were being operated on, whilst a higher threshold for surgery appears to have persisted in patients who received Gastrografin, with the additional time perhaps allowing a greater proportion of adhesive SBO cases to resolve nonoperatively.

Patients who fail a trial of Gastrografin at Middlemore Hospital are not automatically assigned to an operative course. Non-operative management is often continued, depending on clinical assessment. Multiple studies have shown that up to 30% of patients with holdup of contrast in the small bowel at 24 hours can still be managed non-operatively(152, 239, 243). Patients who do not receive Gastrografin are operated on following a failed initial trial of "drip and suck" therapy. This trial period is at the discretion of the treatment team, and differences in operative threshold are likely to exist between clinicians.

The establishment of a protocol has increased the use of Gastrografin in adhesive SBO at Middlemore Hospital. However, previously demonstrated benefits from trials have not been replicated in the clinical setting.(244, 246-248) Factors other than Gastrografin use and protocol non adherence due to initial diagnostic uncertainty may have influenced patient management. Barriers to Gastrografin protocol adherence need to be addressed to replicate the previously demonstrated benefits of Gastrografin.

Chapter 6

Discussion

Formation of adhesions is an inevitable result of abdominal surgery, and is part of the complex healing process that starts with a localized inflammatory reaction and involves multiple growth mediators and coagulation factors causing deposition of fibrin and ends a few weeks later with fibrin deposits, which have undergone invasion by collagen producing fibroblasts and neovascularization, starting to remodel and form firm fibrous tissue. The extent of adhesion formation is related both to the extent of surgical dissection and the underlying disease process, with patients who have undergone surgery for established peritonitis and those who develop postoperative complications, such as anastomotic leakage or bleeding, being at higher risk of forming dense adhesions. Improvements in surgical technique, suture material, removal of powdered gloves, and possibly the introduction of laparoscopic surgery have reduced the risk of adhesions and consequent SBO. Despite this, SBO from adhesions remains a common cause for hospitalisation and operative intervention.

The diagnosis of SBO relies on typical symptoms of vomiting, constipation or obstipation, central colicky abdominal pain, and abdominal distension, with frequent high-pitched bowel sounds. Abdominal x-rays show dilated small bowel loops located centrally, and erect films show multiple central fluid levels. The sensitivity and specificity of plain abdominal film for small bowel obstruction ranges from 65-% to 85%. The abdominal x-ray may show some gas in the large bowel, which is suggestive but not diagnostic of partial SBO. This is important because

partial obstruction usually settles with non-operative treatment, whereas complete obstruction is very unlikely to settle without surgical intervention.

The majority of cases settle with non-operative treatment in the form of nasogastric aspiration, gut rest, pain control, and intravenous fluids. Some patients do require surgical intervention either at admission due to signs of peritonism or later because of failure to resolve on conservative measures. The use of a long intestinal tube does not seem to have any advantage over the ordinary nasogastric tube. The optimal timing for surgery in the latter situation is debatable, with a waiting period of 2–5 days. However, there is some evidence that early surgery may reduce the length of postoperative small bowel ileus. Of those patients who are managed non-operatively, 90% of those who resolve do so with the first 48 hours. Initial non-operative treatment, however, is suggested to continue for 72 hours, providing there are no new clinical signs that suggest bowel strangulation, after that if there are no signs of resolution and in particular when the output of the nasogastric tube is greater than 500ml over the last 24 hours, surgery is suggested to reduce the risk of complications. Longer period of observation may be advised in poor surgical risk patients.

There is a group of patients who on admission have clinical or radiological signs of strangulation and those patients require an emergency laparotomy on the day of admission after resuscitation with fluids, pain control and correction of electrolytes, which crucial to reduce the risk of complications. These patients are identified on clinical grounds usually relying on signs of peritonism with on-going abdominal pain supplemented by laboratory evidence of raised white cell count, raised creatine kinase or raised serum lactate levels. Occasionally the decision is not

straight forward. In that situation CT scan of the abdomen with oral and intravenous contrast is a beneficial tool, it detects small bowel strangulation with sensitivity and specificity of more than 90%. CT scan, however, should not be used routinely in adhesive small bowel obstruction. The specific signs that indicate small bowel strangulation are free fluid, mesenteric oedema, lack of faeces sign and bowel devascularisation. The current literature supports the use of a CT of the abdomen for all patients who had abdominal surgery within the last six weeks; this particular group of patients should not be managed similar to other adhesive small bowel obstruction. In patients with non-reducible abdominal wall hernia (incisional hernia) early operation is advised for obvious reasons.

Introduction of water-soluble contrast media in the form of Gastrografin has changed the management of adhesive SBO. It has proven to be safe, predicts the need for surgery and does not increase morbidity. It is given as 100mL via a nasogastric tube after emptying the stomach, and the tube is then blocked for at least one hour. A plain abdominal x-ray is taken 4–8 hours after introduction of the medium .Contrast is seen in the colon this confirms the diagnosis of partial SBO, which is very likely to resolve with non-operative treatment. Early studies found that routine use of this approach shortened hospital stay and hastened decisions about surgical treatment. Lack of contrast entering the large bowel confirms the diagnosis of complete obstruction, which is very unlikely to settle without surgical intervention. This test predicts the need for surgery or resolution with high sensitivity, specificity and negative predictive value. The benefit of this approach over the use of recently developed clinical models is the use of a single test whereas the predictive models require few clinical, laboratory and radiologic parameters, which means that every single patient gets a CT scan on admission; it

is more cumbersome and difficult to reproduce. Some those models also rely on subjective variable in the form of pain score on the visual analogue scale.

Data on SBO at Middlemore Hospital were reviewed. This study included 994 admissions of 648 patients with adhesive SBO during the study period. Median patient age was 64 years and 362 (56%) were female. There were 322 episodes of recurrence among 176 patients (27%). Sixty-eight patients (10%) required laparotomy. This shows that SBO is a common acute surgical admission and although the majority resolved with non-operative treatment, there was a high recurrence rate. Of the 176 patients who developed recurrence, 28 required laparotomy on readmission (15%). There were 50 deaths in this series (7%), with a complication rate of 12%. The median hospital stay was three (range 1–49) days. The median hospital stay for those who required surgery was 6.5 days and for those who resolved was three days. There was no factor identified that predicted recurrence of obstruction. Patients who had the index operation for cancer and those with the index operation complicated by sepsis, bleeding, and anastomotic leaks were likely to need laparotomy on the first admission.

A systematic review and meta-analysis of the role of Gastrografin in the diagnosis and the treatment of adhesive SBO was undertaken. The systematic review addressed two questions, the first being the diagnostic accuracy of Gastrografin, and the second being the possible therapeutic effect of Gastrografin

For the diagnostic part of the review, relevant articles were retrieved from the available literature and suitable studies were analysed for sensitivity, specificity, and positive and negative predictive values using the Cochrane method for meta-analysis of diagnostic studies. The results of the meta-analysis demonstrated that

Gastrografin is highly sensitive and very specific as a diagnostic test for the completeness of SBO or otherwise, with a high positive predictive value and a very low negative predictive value. In other words, patients in whom the Gastrografin is seen in the large bowel are very likely to resolve with no need for surgery, while patients in whom Gastrografin does not reach the large bowel are unlikely to settle without surgical relief of the obstructing adhesions, with sensitivity of 97% and specificity of 96%.

Some reports in the literature have suggested that Gastrografin may hasten resolution of SBO, and have reported a shortened hospital stay for patients treated non-operatively. Thus, a systematic review and meta-analysis of the role of Gastrografin as a therapeutic agent for bowel obstruction was undertaken. The review was conducted according to the Cochrane methodology guideline, which is highly sensitive and very specific for therapeutic studies. The theoretical basis for the therapeutic effect of Gastrografin is its high osmolarity, which is thought to work in two different ways, firstly by increasing the intraluminal pressure due to absorption of water from the bowel wall (this increase in pressure may induce vigorous peristalsis by the bowel wall) and, secondly, the process of water absorption from the bowel wall may actually enhance bowel motility by reducing oedema in the wall.

The result of the meta-analysis showed that there is a small but definite benefit from the use of water-soluble contrast as a therapeutic agent, in that it hastens resolution of SBO which is the time between admission and the first signs of clinical resolution. It shortens time from admission to the passage of a bowel motion, thereby decreasing the hospital stay; but there was no reduction in the

need for surgical intervention. The administration of water soluble contrast was not associated with increased complications or mortality. However, it was not possible in this review to separate a therapeutic role from a diagnostic role due to the use of an abdominal x ray. Based on this observation, a randomised, double-blind, controlled trial was carried out in patients admitted with adhesive SBO in order to assess the therapeutic role of Gastrografin in small bowel obstruction.

This trial was conducted at Auckland and Middlemore Hospitals. After confirming SBO (by clinical evaluation and plain abdominal x-rays), patients were randomised into two arms by computer-generated numbers. The treatment arm was given Gastrografin 100mL and the control arm was given an equal volume of placebo. Abdominal x-rays were not taken following entry into the study to keep the clinician blinded as to which arm the patient belonged to, and the management decision was made solely on clinical progress. Patients in whom there was clinical suspicion for bowel strangulation indicating a need for surgery were excluded.

The results of this trial showed a clear therapeutic benefit from use of Gastrografin in that patients in the treatment arm had earlier resolution and their hospital stay was shorter than in the control arm. However, the study was not powered adequately to assess whether Gastrografin was associated with a lesser need for surgical intervention. Mortality and morbidity were equal in both arms of the study, with no significant complications caused by the use of Gastrografin.

Based on the diagnostic and therapeutic effects observed in the published clinical studies, the use of Gastrografin became routine for patients admitted with SBO at Middlemore Hospital. Thus, the role of Gastrografin and its impact on management was able to be compared in terms of hospital stay before and after

the clinical introduction of Gastrografin. These results showed reasonable compliance with routine clinical administration of Gastrografin, with 68% of patients given this agent.

The advent of a routine clinical protocol for patients admitted with adhesive SBO has increased the use of Gastrografin at Middlemore Hospital. However, previously demonstrated benefits from the published trials were not replicated in the clinical setting (244, 246-248) . Factors other than Gastrografin use and protocol non adherence due to initial diagnostic uncertainty may have influenced patient management. Barriers to Gastrografin protocol adherence need to be addressed to replicate the previously demonstrated benefits of Gastrografin.

Chapter 7

Conclusions

There is very strong evidence that about 80% of patients admitted to hospital with an episode of subacute SBO caused by adhesions related to previous abdominal surgery will settle without the need for any operative intervention. Patients who have clinical evidence of small bowel strangulation on admission, such as severe ongoing pain, fever, raised white cell count, or generalised abdominal tenderness, are clearly better managed with emergency laparotomy to avoid perforation and consequent complications; this decision is a clinical one that relies on the expertise of the treating physician. Another subset of patients is more stable and does not need emergency laparotomy. A significant proportion of these patients will settle without surgery, and yet another group will require semi-urgent laparotomy within a few days of admission after an initial trial of non-operative management.

Water soluble contrast has been shown in this thesis to be a useful adjunct in the management of small bowel obstruction for both Diagnostic and therapeutic purposes. There is convincing evidence in the literature, as shown by the systematic review and meta-analysis that water-soluble contrast media administered to patients with SBO followed by abdominal x-ray within 4–8 hours can differentiate between partial and complete SBO, which helps to select the appropriate management strategy. At the time of the x-ray, presence of contrast in the colon predicts resolution of SBO without operation in 99% of patients. Patients in whom the contrast has not reached the colon should be scheduled for laparotomy. In this subset of patients, early surgery may be advantageous for

reducing hospital stay, duration of ileus, and risk of infectious complications. The routine use of Gastrografin at admission in patients proved to have small bowel obstruction on clinical grounds supported by evidence of bowel obstruction on plain abdominal X ray may obviate the need for CT scan.

The systematic review of the literature has shown that routine use of Gastrografin leads to shorter hospital stay by helping to triage patients to operative and non-operative management. This approach may help to save some resources.

The meta-analysis also showed that water-soluble contrast hastens resolution of adhesive SBO and reduces hospital stay. These findings suggest that Gastrografin may have a therapeutic value. Meta-analysis of studies addressing the therapeutic role of Gastrografin in SBO concluded that Gastrografin did not reduce the need for surgical intervention. Although there was significant reduction of hospital stays and faster time to resolution. The use of Gastrografin proved to be safe in this setting without any increase in overall complications rate or mortality.

The randomised controlled trial of the therapeutic role of Gastrografin concluded that there is faster resolution of SBO and a shorter hospital stay in patients who had Gastrografin, but with no reduction in the need for surgery. These findings have confirmed the therapeutic role of Gastrografin in small bowel obstruction.

Since the introduction of a protocol at Middlemore Hospital in September 2003, use of Gastrografin has dramatically increased, but has remained at 58%–69% in subsequent years. This rate of use is still relatively low that indicates poor compliance in the routine use of Gastrografin. The previously demonstrated benefits from trials discussed in the thesis have not been replicated in the clinical setting, and protocol non adherence seems the likely reason for this.

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