Assessment of Systemic Blood Flow in the Newborn Infant

Alan Martin Groves

A thesis submitted in fulfilment of the requirements for the degree of

Doctor of Medicine, The University of Auckland, 2006.

Abstract

Preterm infants are vulnerable to brain injury which is thought to be caused partly by abnormalities in cerebral perfusion. However the accurate assessment of cerebral and general systemic perfusion remains a challenge in the newborn infant. Commonly used clinical parameters such as blood pressure and blood lactate concentrations are imperfect predictors of blood flow. Cardiac output measurements used in older children do not reflect true systemic perfusion in the neonate due to shunting of blood through persisting fetal pathways. Echocardiographic measurements of descending aortic (DAo) and superior vena caval (SVC) blood flow may provide more reliable assessment of neonatal systemic perfusion. This thesis evaluates these techniques in the first days of postnatal life.

Measures of flow volume in the SVC and DAo were found to be feasible in the vast majority of infants, and were performed without significantly affecting cardiorespiratory status. Assessment of SVC flow volume showed similar repeatability to other measures of blood flow in neonates when assessed by a single observer, as did assessment of velocity of flow in the DAo.

We then used these techniques to further assess the transitional circulation, and found no evidence of a positive association between arterial blood pressure and volume of systemic perfusion. Contrary to previous assumptions that ductal shunting compromises systemic perfusion, we found that left ventricular output tended to increase with increasing shunt through the ductus arteriosus, thereby maintaining upper, though not necessarily lower, body perfusion.

There was an association between very low levels of flow in individuals and some adverse outcomes that had a strong circulatory component to their pathophysiology (periventricular haemorrhage and necrotising enterocolitis). However low blood flow in the SVC or DAo did not predict poor outcome within the entire cohort.

Assessments of SVC and DAo flow in the neonate are feasible, relatively repeatable and have already enhanced our understanding of the pathophysiology of the transitional circulation. These and other techniques to monitor systemic blood flow in the neonate may aid identification of circulatory failure, act as short-term endpoints in clinical trials of interventions supporting the circulation, and eventually improve neurodevelopmental outcome in preterm infants.

Acknowledgements

I am extremely grateful to my supervisors who provided invaluable support and guidance while writing this thesis. Carl Kuschel gave me the opportunity to come to Auckland, showed consistent enthusiasm for the project, and even allowed me free time by performing some of the echocardiograms. Professor Jane Harding showed boundless patience both in reading multiple drafts of this thesis and in steering me through my early statistical encounters; her wise words were always well chosen. Jon Skinner has an incredible understanding of haemodynamics, took interpretation of the data to a whole additional level, and was never shy in telling me when I was coming up short!

The staff at National Women's in Auckland were incredibly supportive throughout the duration of the study; recruitment would have been impossible without the input of the consultants, registrars and nurse practitioners, and my sanity would have been compromised without the friendship and support of Claire West. The unit nursing staff acted as strong advocates for the infants studied, but also showed great patience and good humour.

I am also most grateful to the infants who took part in the study, and to their parents for granting consent at what is always a very stressful time.

Financial support was provided by The Southern Trust, via the Starship Foundation, to whom I am deeply indebted. I hope they are pleased with the outcome of the project.

My sincere thanks go to all the staff at Sunderland Royal Hospital where I undertook my initial registrar training. My time on the neonatal unit there cemented my passion for neonatology. I would especially like to thank Majd Abu Harb whose outstanding

echocardiographic skills I have tried to emulate, and to Sam Richmond whose example as an inspiring, intelligent and complete neonatologist I will always try to follow.

This thesis is dedicated to my family and in particular to my parents who have always been there for me. Likewise to my brother, sister and my friends both in New Zealand and the UK, who helped me keep my ‘work life balance’.

Preface

The incidence of premature birth in industrialised nations shows no signs of decreasing(1). While survival rates have improved dramatically in recent decades there is little or no evidence for similar improvements in neurodevelopmental outcome(2). Many of the causes of adverse neurodevelopmental outcome are poorly understood. However there is increasing evidence that circulatory factors may play a critical role in the pathophysiology of brain injuries in preterm infants(3).

The circulation of the newborn infant undergoes a transition from the fetal to the adult pattern in early extra-uterine life. In the fetus the ductus arteriosus carries deoxygenated blood from the pulmonary artery away from the high resistance pulmonary circulation towards the placenta for oxygenation. Oxygenated blood returning to the right atrium from the placenta is diverted by the foramen ovale towards the brain and upper body via the left atrium, left ventricle and ascending aorta. The central features of the transitional circulation are the removal of the low resistance placental circulation by clamping of the umbilical cord, and an abrupt increase in pulmonary blood flow due to falling pulmonary artery pressure as the lungs take on the role of gaseous exchange. In term infants the fetal shunt pathways of the ductus arteriosus and foramen ovale are generally functionally closed within 24 hours of birth(4).

In term infants the changes occurring in the transitional circulation are rapid and lead to significant increases in cardiac output to match metabolic demand(4). In the extremely preterm infant the heart, like many other organs, may not be adequately prepared for the rigours of extra-uterine life. The immature myocardium may be less able to contract against the increase in vascular resistance produced by removal of the low resistance

placental bed(5). The fall in pulmonary vascular resistance is often delayed(6), as is functional closure of the fetal shunt pathways(4). Severe respiratory disease and the requirement for mechanical ventilation may further impair cardiac function in preterm infants(5).

Attempts to monitor cardiac function during this transitional period in preterm infants are hindered by the persistence of the fetal shunt pathways. Measurements of left and right ventricular output are useful in assessing systemic perfusion in older children and adults. However in the presence of shunting through the ductus arteriosus and foramen ovale, neither left nor right ventricular output assesses the volume of blood actually reaching the tissues.

In the absence of reliable guides to systemic perfusion, clinicians have limited ability to detect circulatory failure in preterm infants. Furthermore, even if circulatory failure was to be detected, the optimal treatment required to support the circulation is unclear, since adequacy of perfusion cannot easily be assessed as an outcome measure in clinical trials.

The work described in this thesis was prompted by a series of journal articles published in 2000-2001. These highlighted the vascular component of the pathophysiology of preterm brain injury(7), the importance of provision of appropriate cardiovascular monitoring and support to preterm infants(4, 8) and the potential for superior vena cava (SVC) flow to be measured as a marker of systemic perfusion that was unaffected by fetal shunt pathways(9) and that predicted subsequent brain injury(10).

We elected to use echocardiography to study a cohort of preterm infants born at the National Women's Hospital, Auckland, New Zealand. By studying a large cohort of

preterm infants we aimed to evaluate the feasibility of using echocardiography to make repeated haemodynamic measures in the early postnatal period in preterm infants.

A principle objective of the study was to further examine the utility of the technique of measurement of SVC flow volume. It was important to establish whether this measure was feasible and reproducible in the hands of a group of researchers distinct from those who first described the technique. As volume of descending aorta (DAo) flow is increasingly being monitored in paediatric(11) and adult(12) intensive care units, we also undertook the first systematic evaluation of this technique in preterm infants to assess its suitability as a further marker of systemic perfusion unaffected by fetal shunt pathways.

We aimed to assess the safety of these echocardiographic techniques, to establish reference ranges for SVC and DAo flow, and to carefully assess the repeatability of the measurements.

To allow interpretation of the patterns of SVC and DAo flow volume in the unique context of the transitional circulation we also quantified left and right ventricular outputs, assessed ductal and atrial shunt patterns and quantified arterial blood pressure. We were particularly interested in whether findings from our cohort of infants studied during the transition from the fetal to the adult circulations would provide further insights into the relationship between arterial blood pressure and systemic blood flow, and the impact of shunting through the fetal channels on adequacy of systemic perfusion during this critical time.

Finally, and perhaps most importantly, we hoped to further assess the association between markers of blood flow and outcome following preterm birth, particularly the association between early low SVC flow and subsequent brain injury. Specifically we

aimed to examine whether use of echocardiographic markers of perfusion in clinical practice could add to the information obtained through the currently routine practice of monitoring of arterial blood pressure.

The aim of the research described in this thesis is above all to increase awareness and understanding of the pathophysiology of the transitional circulation. In the future we hope to continue working to improve cardiovascular monitoring and support in preterm infants with the goal of improving long term neurodevelopmental outcome.

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