Implantable and Injectable Depot System for Sustained Release of Lidocaine to Address Post-operative Pain

Manisha Sharma[1], Kaushik Chandramouli[1], Andrew Hill[2], Simon Young[3], Darren Svirskis[1]

[1]School of Pharmacy, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand; [2]Department of Surgery, South Auckland Clinical Campus, Middlemore Hospital, Faculty of Medicine & Health Sciences, University of Auckland, New Zealand, [3]School of Medicine, Faculty of Medical & Health Sciences, University of Auckland, New Zealand

Background

Arthroplasty surgeries are associated with post-operative pain and significant resource consumption. Effective control of post-operative pain correlates with improved functional recovery, reduced complications, reduced hospital stay and reduced healthcare costs. Local anaesthetics such as lidocaine, have been found effective in treating post-operative pain (1). However the short duration of action of lidocaine requires frequent administration.

Aim

To deliver lidocaine to local tissues over an extended period of time following joint surgeries using biodegradable materials.

In-situ Gel Preparation

In-situ gelling depot systems were investigated to achieve the sustained delivery of lidocaine. A lidocaine loaded, in-situ gelling depot system was prepared by the cold method using the appropriate weight percentage of poloxamers (2), Polymer additives such as, polyvinyl pyrrolidone (PVP), hydroxypropyl methyl cellulose (HPMC) and carbopol were investigated to further sustain the drug release.

Results and Discussion

Table 1: Percentage of poloxamers, lidocaine and polymer additives (% w/w) used in different formulations. Sol-to-gel transition temperature of each formulation is also given as determined by the tube inversion method.

Composition	F4	F4+PVP	F4+HPMC	F4+ Carbopol
Poloxamer407	17	17	17	17
Poloxamer188	14	14	14	14
Lidocaine	1.5	1.5	1.5	1.5
Water	67.5	67.2	67.2	67.4
Polymer additive	0	0.3	0.3	0.1
Sol-to-gel transition temperature (°C) (mean± SD)	28.3± 0.6	26.3± 0.5	26.6± 1.1	27.1± 1.0

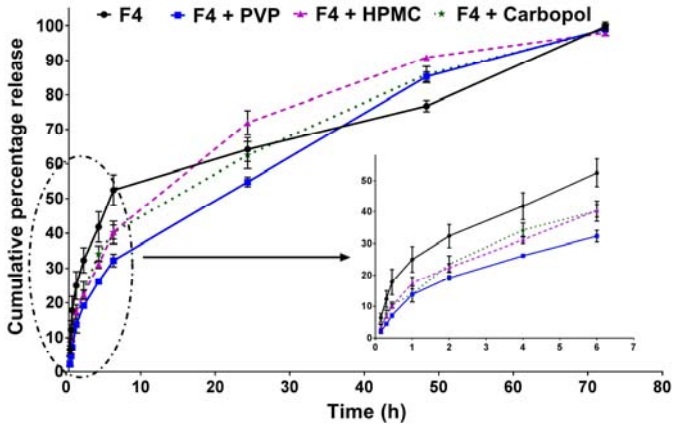

Figure 2. Cumulative release of lidocaine from different formulations. With the addition of polymer additives further reduction in the initial burst release was observed. Formulation with PVP (F4+PVP) demonstrated the lowest burst release, releasing 32.26 ± 1.82% of drug in first 6 h followed with steadily increase in release, 54.8 ± 1.4% released in 24 h, 85.3 ± 1.3% released in 48 h. Error bars represent standard deviation (n = 3).

Acknowledgement

M Sharma is thankful for financial support provided by the Faculty Research Development Fund (FRDF), FMHS, School of Pharmacy and an ECREA award, The University of Auckland.

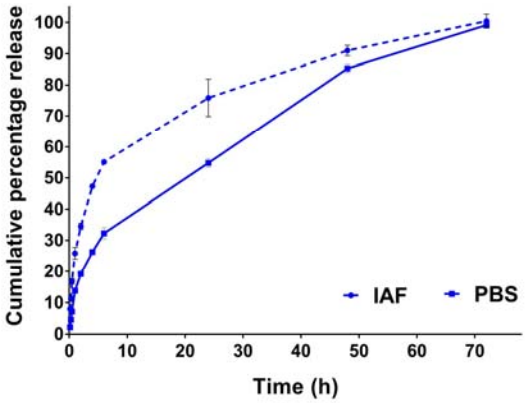

Figure 3. Comparative cumulative release of lidocaine from F4+PVP formulation in intra-articular fluid (IAF) demonstrated faster release into ex-vivo than PBS (pH 7.4). Error bars represent standard deviation (n = 3).

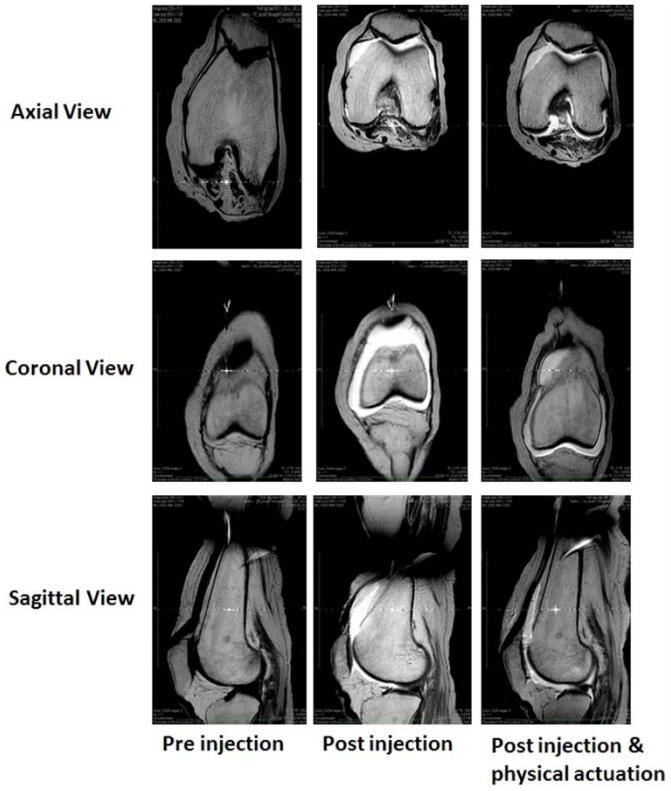

Figure 3. The gelling behaviour of the selected formulation was investigated in human fresh-frozen cadaver knees (under the acquisition of Human Tissue Act (NZ 2008)). MRI Scans were performed pre-injection, post-injection and following physical actuation of the knee joint. The images viewed in all 3 planes show the gel (white in the images) to have spread comprehensively throughout the knee joint.

Conclusion

The study demonstrated that injectable depot systems are ideal platforms to achieve sustained drug delivery of lidocaine and can be used to treat post-operative pain.

Reference:

1. Annals of Surgery. 2011;254(1):28-38;
2. Therapeutic Delivery, 2016, 7(4), 359–368 .

Manisha Sharma PhD, M Pharm, B Pharm
manisha.sharma@auckland.ac.nz