

Analysis of Flow Rate Through Elastomeric Local Infiltration Analgesia Pumps

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Abstract

Background: Local infiltration analgesia pumps have been increasingly used to provide postoperative pain relief. However, their flow rate over time may not be reliable and accurate which can pose concerns regarding the achievement of the desired therapeutic level. We sought to find out *in vitro* if the flow rate of two elastomeric infusion pumps when combined with two types of wound catheter is accurate and maintained over 48 hours which is the duration used at our clinical practice.

Methods: There were four combinations of pumps and catheter, and each were tested three times. For each test, three pump and catheter combinations were tested at the same time. Flow rate was determined by placing the pumps on digital scales and recording the mass loss of normal saline every 2 hours for 48 hours.

Results: None of the pump/catheter combinations achieved the desired 4ml/hr flow rate. There was no combination of pump and catheter that was significantly better than another. All pumps and catheter combinations lost approximately 1ml/hr of flow rate by 48 hours thus making them less reliable and robust in administering fluid accurately. Temperature did not appear to affect flow rate.

Conclusion: Elastomeric pumps tested do not achieve the desired flow rate and the flow rate drops over 48 hours.

Keywords: *Local Infiltration Analgesia; Elastomeric; Pumps; Arthroplasty; Wound Catheter*

Introduction

Local infiltration analgesia (LIA) involves infusion of a mixture of local anesthetic (e.g. ropivacaine), a non-steroidal anti-inflammatory drug (e.g. ketorolac) and epinephrine which causes local vasoconstriction thus minimising absorption of the drugs into the systemic circulation [1]. The beneficial effects of LIA wear off by 24 hours [2]. Continuous LIA (CLIA) has been developed to provide the LIA benefits for longer and this can be done with infusion pumps via intra-articular catheters. Infusion pumps can be electronic or elastomeric each with their own benefits and drawbacks.

Elastomeric infusion pumps have been used for over 25 years in delivering analgesia, chemotherapy and antibiotics. Some centres have used them to provide continuous local infiltration analgesia typically during a period of 24 - 48 hours but there have been some concerns regarding the accuracy and reliability of flow rate during that period.

Several recent meta-analysis have been reported in the literature comparing CLIA and LIA with each other and with placebo. However, the outcomes should be taken with some caution due to small samples and the heterogeneity in the methodology of the cited studies. A meta-analysis of randomised controlled trials comparing CLIA vs placebo following TKR found that CLIA provided better analgesia for the first 24 hours with rest and mobilization [3]. However, there was no significant difference for pain at 48hours with rest and at 72 hours with rest or mobilisation. Perhaps the flow rate is not maintained over the duration of infusion and thus analyzing this would help rule this out as a cause for the lack of clinically improved pain scores after 24 hours.

Elastomeric pumps generate fluid pressure in the region of 250 - 600 mm Hg, compared with 5-1200 mm Hg by electric pumps [4]. Electronic pumps are able to sustain the pressure over the infusion period however for elastomeric pumps there are numerous factors which affect flow rate thus causing them to be less reliable with the flow rate over time. Flow rate of elastomeric pumps is dependent primarily on pressure gradient across the fluid restrictor and fluid viscosity. The pressure gradient is itself affected by the smallest aperture through which the fluid passes through (determined by flow restrictor and wound catheter), initial filling volume [5], back pressure [6] (vertical displacement of the pump relative to infusion site), storage conditions and atmospheric pressure [5,7,8]. Fluid viscosity is itself affected by temperature and to a lesser extent by drug concentration [4]. Elastomeric pumps fluid flow accuracy is claimed to be $\pm 15\%$ on the proviso that manufacturers directions for use are adhered to so as to follow their method of calibration otherwise flow rate accuracy can be off by 40% or more [4].

The purpose of this study was to analyse the flow rate over 48 hours of two different elastomeric pumps and combine them with two different catheters and to determine whether the nominal flow rate is maintained and if different combinations altered the flow rate. The products chosen were ones that were currently used and those under consideration at the time of the study at Chapel Allerton Hospital, Leeds.

Materials and Methods

Flow rate over 48 hours of two elastomeric pumps (both distributed by Peak Medical) and two different catheters were analysed. One of the pumps was Nipro Surefuser™+ (Figure 1) and has been independently tested by the official French metrology laboratory (LNE, 2012) to ensure it passes the European safety standards, as set in the ISO-28620. The second elastomeric pump system was a new hexagonal pump (Figure 2).



Figure 1: The Nipro Surefuser™+ pump, supplied as part of the PainKwell™ infusion system.



Figure 2: Photograph of the new hexagonal pump, proposed to be supplied as part of the PainKwell™ infusion system.

The two types of catheter tested were a standard and a new catheter both of which were distributed by Peak Medical and came with the PainKwell™ infusion device. The new catheter has a wire coil spring within the lumen of the catheter along its whole length so that whilst it is still flexible it offers resistance to kinking. The catheter can be kinked when it is passed through the wound, when it is pushed into an adaptor so that it then connects to the fluid control unit, and by mistake when the surgeon is suturing the wound. Thus, it is important to not only resist kinking but if it does happen to recoil back to its original shape so as not to inadvertently increase the resistance to flow. The coil is embedded at the tip but does not protrude from it. The wire coils also serves to aid the flow of fluid through the catheter in a seeping action and so distribute the fluid more evenly through the fenestrations. One end of both catheters is open so as to be attached to the flow regulator unit whilst the other end is closed for both.

Each type of pump was tested with each type of catheter such that all four combinations of testing were performed. For each test, 3 pump/catheter combinations were tested simultaneously and repeated 3 times, thus giving a total of 9 sets of results for each test. This would ensure that the outcome of the results would be reliable and robust. Pumps used in the study were not designed to be reused by the manufacturer however studies have shown that elastomeric pumps maintain their flow rates at two [9] and three [10] repeated uses.

For each test, each pump system was filled with 250 ml of normal (0.9%) saline. Normal saline is a commonly used testing fluid as it has been shown to have the same flow profile when temperature is maintained as ropivacaine and bupivacaine since they belong to the same amino amide family and have the same densities [11].

The flow regulator was set to 4 ml/hr, which is the rate used clinically and considered to be safe with a wide margin of error. The pumps were placed on the scales and elevated so that the catheters would be above the beakers to collect the fluid in order to avoid submergence of the catheter into the dispensed saline, thus preventing increased resistance to flow.

The catheters were primed with normal saline using a 5 ml syringe. The digital mass balances were calibrated initially to determine

their accuracy, which was found to be 0.12%. A time drift test was then performed so as to establish the change in reading of a Surefuser™+ pump over 48 hours.

This test was carried out on each of the scales to be used and repeated three times. The average drift after 48 hours was 0.038%. This was considered to be insignificant when related to the proportion of the mass that will be lost during the infusion of saline and so will not be factored in as an error in the testing results.

The digital scales recorded the loss of mass from the pumps as the normal saline was infused through the catheter and onto the beakers. Normal saline contains 9 grams of sodium chloride (NaCl) in 1 litre of water. The mass of 1 ml of normal saline at 22°C is 1.0046g. It was thus assumed that 1g corresponds to 1 ml of fluid.

LabVIEW programme on a laptop was used to capture and record measurements from the scales automatically. Temperature during each test was logged using a USB thermometer air probe (USB ProbeLite). Like other studies [12], tests were performed at room temperature in order to simulate real conditions, and whilst not regulated, temperature was recorded throughout the experiments. Prior to each experiment LabView, USB ProbeLite and the digital scales were all restarted in order to reset and standardise.

Throughout testing only three of each type of component were used (i.e. 3 Surefuser™+ pumps, 3 new hexagonal pumps, 3 standards catheters and 3 new catheters). When experiments were repeated, each pump was connected to the same catheter and were recorded on the same mass balance, enabling analysis of each individual pump setup. In total, each pump/ catheter was refilled/ reused six times.

After 48 hours of infusion, tests were terminated irrespective of the amount of saline left to infuse. Catheters were detached from the pumps and the pumps were allowed to deflate naturally, taking approximately a total of 70 hours, whilst another test was set up using the alternative type of pump. This meant that the maximum time pumps were left unused was typically less than 24 hours.

Results

To recap there were four combinations of pump and catheter:

- Test 1: Surefuser™+ pump with standard catheter
- Test 2: Surefuser™+ pump with new catheter
- Test 3: New hexagonal pump with standard catheter
- Test 4: New hexagonal pump with new catheter

The mean combined pump flow rates of the four combinations of pump and catheter together with ± 1 standard deviation are shown graphically in Figures 3 A to D. Throughout testing there were five void results: two (one for Surefuser™+ pump with standard catheter and one for new pump and new catheter) where the automatic recording of the mass balance failed; two (one for Surefuser™+ pump with standard catheter, and one for new pump with standard catheter) due to a catheter connection breaking near the beginning of testing due to human error. Lastly, one pump was also knocked off the mass balance during testing (Surefuser™+ pump with standard catheter).

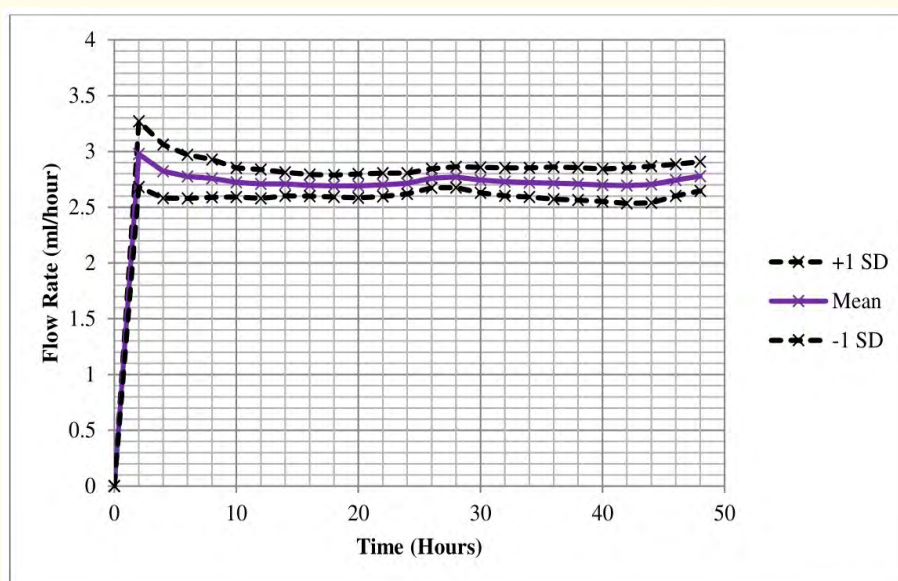


Figure 3A: Combined pump mean flow rate profile and ± 1 SD over 48 hours of Surefuser™+ pumps with the standard catheter.

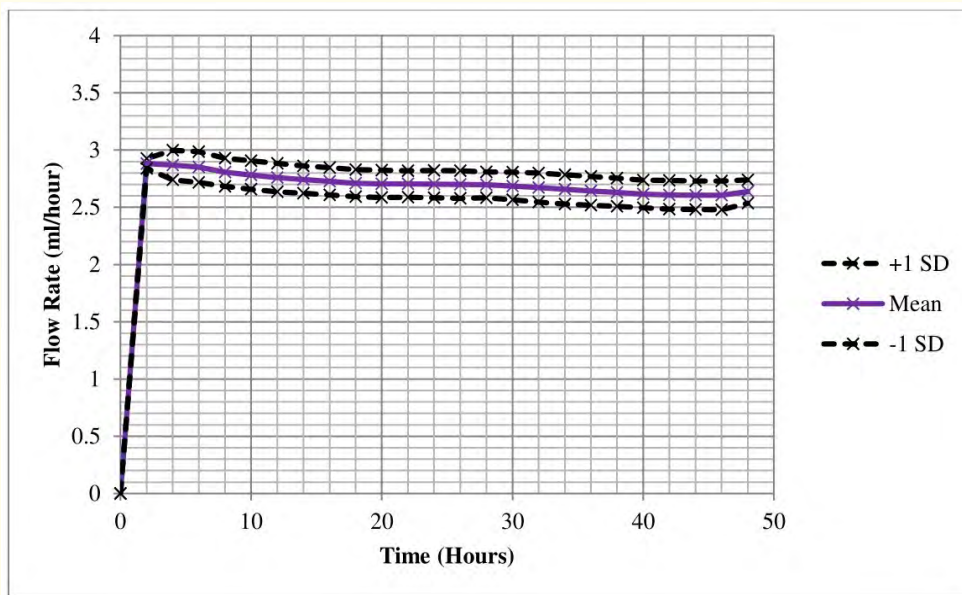


Figure 3B: Combined pump mean flow rate profile and ± 1 SD over 48 hours of Surefuser™+ pumps with the new catheter.

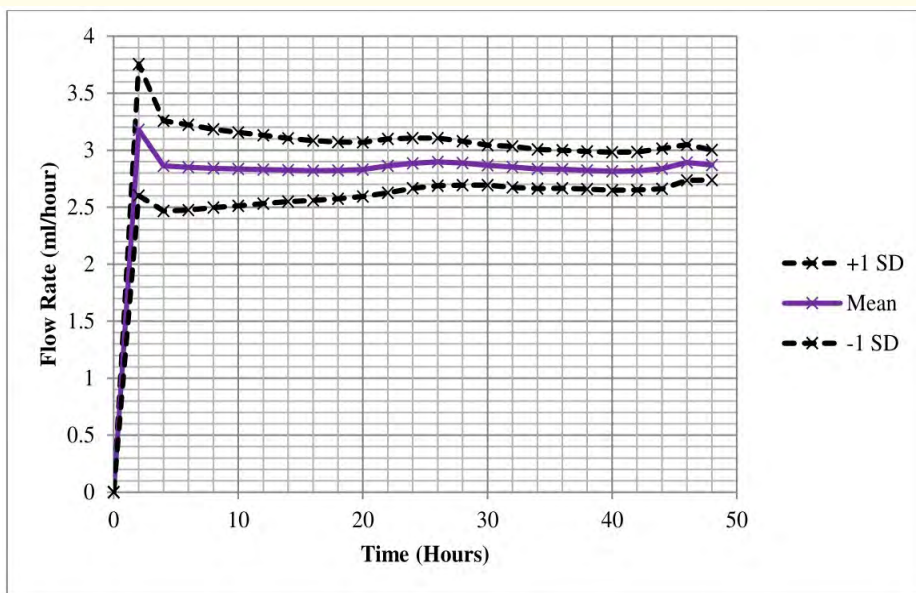


Figure 3C: Combined pump mean flow rate profile and ± 1 SD over 48 hours of new hexagonal pumps with the standard catheter.

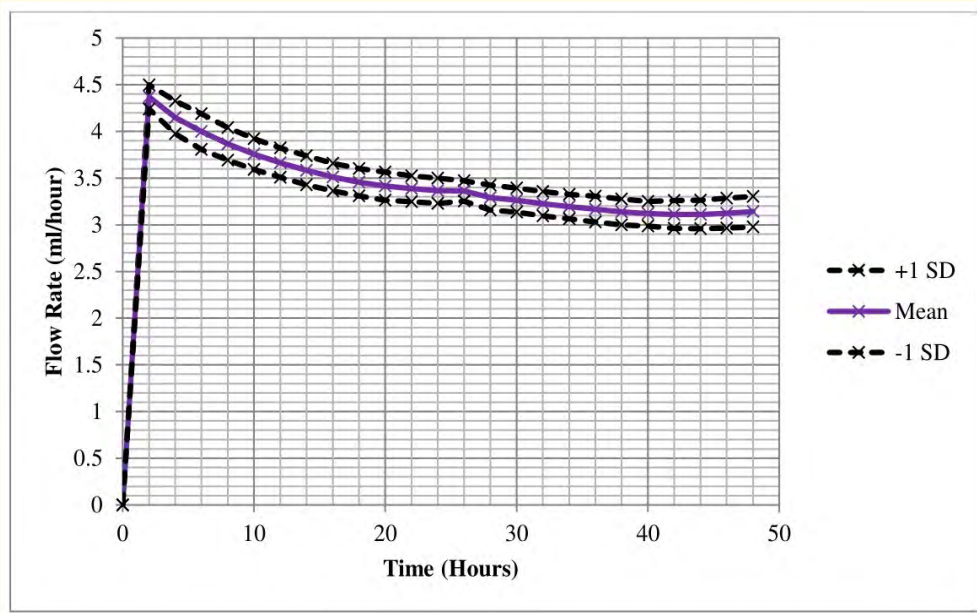


Figure 3D: Combined pump mean flow rate profile and ± 1 SD over 48 hours of the new hexagonal pumps with the new catheter.

Summary of all Four Tests

Figure 4A shows the overall mean flow rate over time of each of the four tests. It is therefore apparent that the new pump with the new catheter achieves the highest flow rate and even goes beyond the 4 ml/hr desired level. However, it loses approximately 1 ml/hr within 24 hours and plateaus very near the level of the other pump/catheter combinations. Figure 4B shows the overall mean flow rate of each test and ± 1 SD. The first three tests have very similar mean flow of around 2.7 ml/hr and test 4 reaches almost 3.5 ml/hr but has the largest variance compared to the other tests.

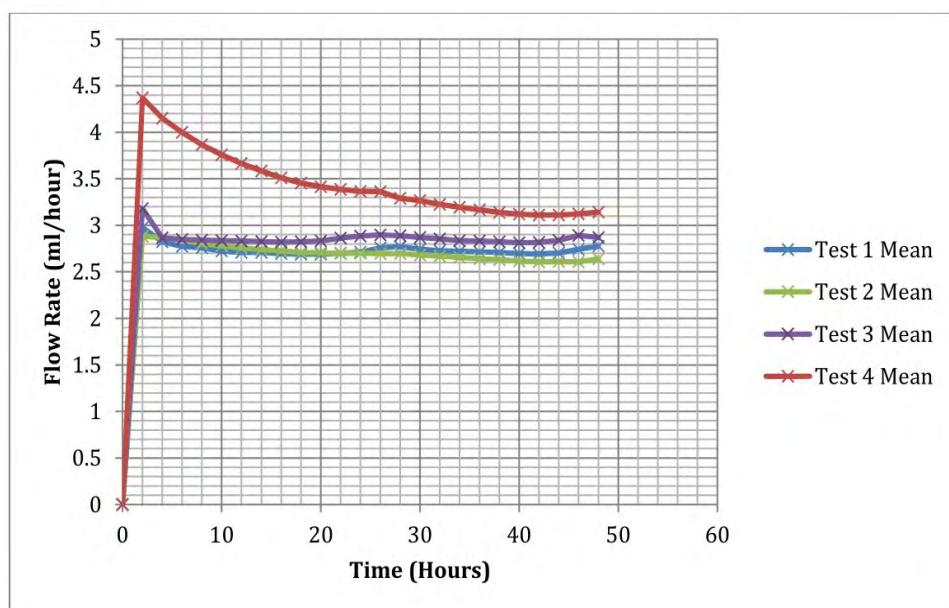


Figure 4A: Mean flow rate profiles of each test over 48 hours.

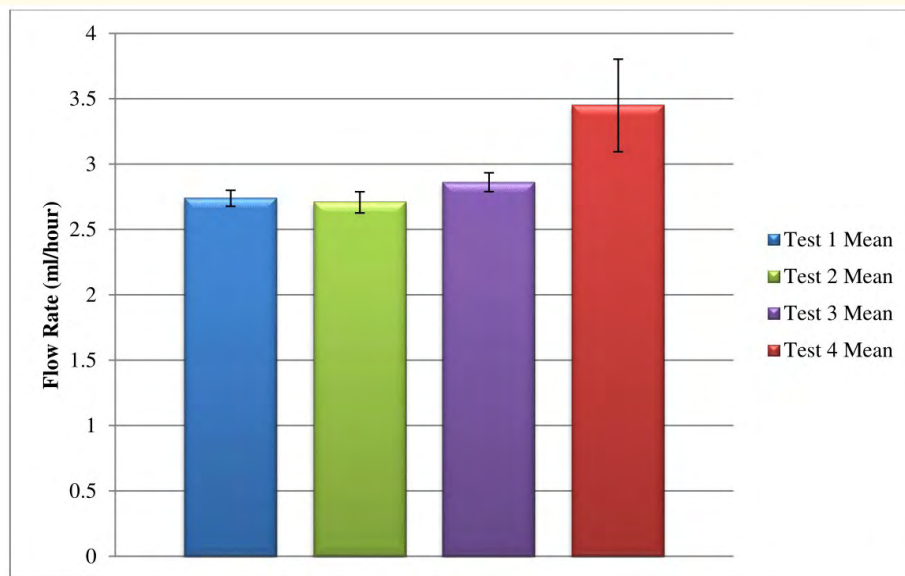


Figure 4B: Mean flow rates of each test with ± 1 SD.

Analysis of the influence of pump and catheter type on flow rate

Linear regression models were created separately for each individual experiment in which mass was the dependent variable, with time and temperature centred at their means (24 hours and 24.9°C respectively) and their interactions were independent variables. The coefficients for time (i.e. flow rate at mean temperature) and the interaction with temperature (i.e. the change in flow rate with temperature) were then used as the raw data for further analysis. Figure 5 summarises these results.

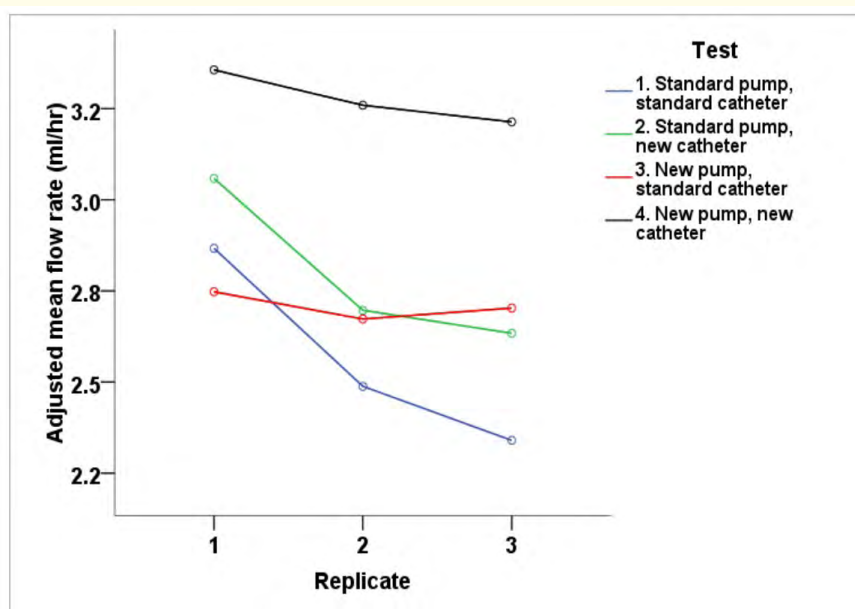


Figure 5: Adjusted mean flow rate for each replicate of pump and catheter combination.

Due to missing data, just two replicates per pump were selected; where they were both available the first and second replicates were used. Mixed between-within repeated measures ANOVA models were constructed with one between-subjects factor, pump type, and two within-subjects factors, catheter type and replicate.

Multivariate tests of within-subjects effects indicated that flow rate did not differ between the two replicates (Wilks' lambda = 0.819, F = 0.886, p = 0.400) and that the difference between replicates did not differ between the pump types (Wilks' lambda = 0.998, F = 0.007, p = 0.936), between the catheter types (Wilks' lambda = 0.987, F = 0.052, p = 0.831), or between pump and catheter combinations (Wilks' lambda = 0.958, F = 0.174, p = 0.698).

Flow rate was on average 0.459 ml/hr (95% CI 0.214 - 0.704) greater through the new catheters [mean flow rate standard catheter: 2.726 ml/hr (95% CI 2.630 - 2.822), mean flow rate new catheter: 3.185 ml/hr (2.931 - 3.439); Wilks' lambda = 0.129, F = 27.082, p = 0.006], and there was some indication that the extent of the difference between the catheters depended on the type of pump (Wilks' lambda = 0.397, F = 6.085, p = 0.069). Table 1 and Figure 6 show the results summary of each pump and catheter combination with two replicates taken into consideration. The increase in flow rate with the new catheter was larger for the new pumps. Flow rate was substantially higher for test 4 than for tests 1 and 3, but was not substantially higher than test 2, and there was not a substantive difference between tests 1 and 3.

There was no statistically significant difference between the pump types (F = 3.045, p = 0.156), however the presence of a borderline significant interaction with catheter type means the difference between the pumps depended to an extent on which catheter was being used; with the standard catheter there was little difference between the pumps; there was a larger difference between the pumps when the new catheters were used (Table 1, Figure 6).

Pump Type	Catheter Type	Test	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
Standard	Standard	1	2.742	.049	2.606	2.878
	New	2	2.983	.129	2.624	3.342
New	Standard	3	2.710	.049	2.574	2.846
	New	4	3.387	.129	3.027	3.746

Table 1: Summary of data with only two replicates considered.

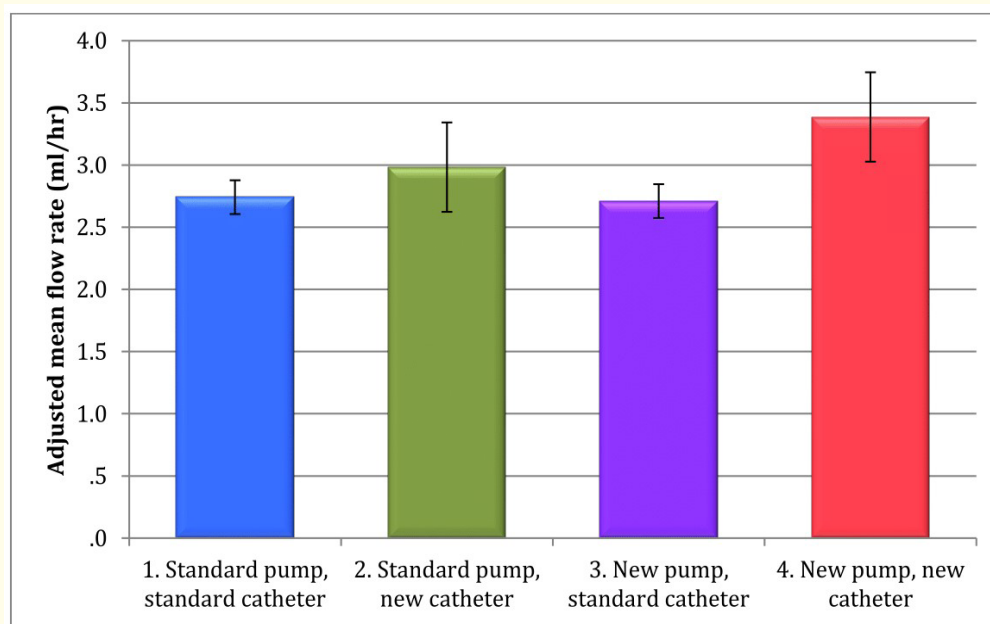


Figure 6: Adjusted mean flow rate for each pump and catheter combination after adjustment of two replicates with 95% confidence intervals.

Analysis of the influence of temperature on flow rate

Multivariate tests of within-subjects effects (Table 2) indicated that influence of temperature on flow rate did not differ between the two replicates (Wilks' lambda = 0.447, F = 4.952, p = 0.090) and that the difference between replicates did not differ between the pump

types (Wilks' lambda = 0.587, F = 2.817, p = 0.169), between the catheter types (Wilks' lambda = 0.692, F = 1.784, p = 0.253), or between pump and catheter combinations (Wilks' lambda = 0.996, F = 0.018, p = 0.901). There was also no difference between the catheter types (Wilks' lambda = 0.949, F = 0.215, p = 0.667) and no interaction between catheter type and pump type (Wilks' lambda = 0.996, F = 0.018, p = 0.901).

Effect	Value	F	Hypothesis df	Error df	Sig.
Replicate	.447	4.952a	1.000	4.000	.090
Replicate * PumpType	.587	2.817a	1.000	4.000	.169
CathType	.888	.506a	1.000	4.000	.516
CathType * PumpType	.949	.215a	1.000	4.000	.667
Replicate * CathType	.692	1.784a	1.000	4.000	.253
Replicate * CathType * PumpType	.996	.018a	1.000	4.000	.901

Table 2: Wilk's lambda multivariate analysis of variance of the interactions between replicate, pump and catheter type.

There was a borderline significant difference in the effect of temperature on flow rate between the pump types (F = 6.475, p = 0.064); whilst flow rate increased on average by 0.044 ml/hr (95% CI 0.027 - 0.062) with each degree rise in temperature. This effect was slightly greater for the new pumps [0.060 ml/hr (95% CI 0.036 - 0.085)] than for the standard pumps [0.029 ml/hr (95% CI 0.004 - 0.053)].

Discussion

Descriptive analysis

From the descriptive results it can be seen that peak flow in all tests occurred at 2 hours (Figure 4A). However, this is a single static reading and so this peak could be even higher. This is an inherent problem with the elastomeric pumps in that they do not provide a uniform flow output like electronic pumps. Clinically this could potentially pose a hazard that is why the 4ml/hr rate has been chosen which anaesthetists claim to have a wide safe margin. This sudden rise in flow rate also explains why the variance is highest initially. The elastomeric membrane has been stretched maximally at the start of the test and so the stress on the membrane that has built up forces the fluid out at maximal rate.

The new pump and catheter combination (test 4) produced the highest mean flow rate (Figure 4B) but the large variance of the data means that this increase should be taken with caution. Interestingly test 2 had slightly but insignificantly worse flow rate than test 1 so the increase in flow rate seen in test 4 can't be attributed solely to the new catheter. However, the effect of the new catheter is amplified with the new pump. The new pump cannot be said to be much better than the Surefuser™+ pump as test 3 has only a minimally better flow rate than test 1 or 2.

Accuracy of drug delivery not just static but over time as well is very important in medicine. In certain fields, it is even more important e.g. in chemotherapy where the therapeutic margin is small. In this scenario where the local anaesthetic is administered peripherally with epinephrine so as to minimise its systemic absorption accuracy may not be as important thus allowing some margin of error. However as can be seen from the tests by 24 - 48 hours the flow rate drops substantially by around 1 ml/hr. This shows poor accuracy over time and is an area for improvement. It may be that after 24 hours the flow rate should be increased by 1 ml/hr to take this drop into account.

Quantitative analysis

In the quantitative analysis, Figure 6 shows the results of the test when adjusted for time and temperature. It shows that the flow rate for the Surefuser™+ pumps reduced by each replicate more than the new pump hence this had a detrimental effect; the new pump showed more resilience to repeated use. It also shows that the Surefuser™+ pump and standard catheter was the worst combination and the new pump and new catheter was the best combination in terms of flow rate.

Statistical analysis was then carried out on two replicates due to missing data and this showed that indeed the flow rate did not differ between the two replicates, the difference between the replicates did not differ between the pump or catheter types or between pump and catheter combinations. This means that further analysis could be done as the data was more standardised by adjusting for time and temperature and considering only two replicates. The new catheter had an improved flow rate and the statistical analysis showed that this effect was more evident when the new pump was used. This is also shown in Figure 5. However, this increase by under 0.5 ml/hr may not be clinically significant.

The analysis shows that the new pump does not perform better than the Surefuser™+ pump but the new catheter may in fact be better than the standard one. The improved flow rate with the new catheter is seen more with the new pumps and is even more evident in the adjusted flow rate graph (Figure 6). This effect might be explained more by the way the elastomer of each pump can deal with the pressure required to push the fluid through the catheter. In other words, the standard catheter may pose a larger resistance to flow than the new catheter for which both pumps do not have strong enough elastomers to push the fluid through. The less resistance to flow in the new catheter (it is 225 mm shorter) might be enough for the slightly better but statistically insignificant elastomer of the new pump to push the fluid faster.

The statistical analysis did not detect a statistically significant effect of temperature on the flow rate. It may be that the temperature during the testing process did not vary enough to confirm a significant effect. The temperature in the tests did not vary more than 2°C. The manufacturer does recommend the strapping of the fluid controller to the skin (32°C) so as to optimise fluid flow. They assume that the slow flow of fluid from the pump through the catheter would allow enough time for the fluid to warm up to skin temperature.

Limitations

The pumps that were used in this study are not designed by the manufacturer to be reused as they cannot guarantee the flow rates. The study showed that despite reuse there was no significant difference in flow rates and this is supported by the literature [9,10].

The study was conducted at unregulated room temperature as opposed to the desired skin temperature of 32°C. The Surefuser™+ technical specification manual states that at temperatures of 25, 32 and 37°C the flow from the pump using normal saline is 8.8, 10.0 and 11.3 ml/hr respectively. Whilst the raised temperature may increase the flow through the pump the rate that is required in our clinical setting is 4 ml/hr and thus even at the colder room temperature the pump provides enough pressure to supersede the desired rate.

The elastomer reservoir in both pumps is made of synthetic rubber but the volume of the reservoir is different (250 ml for the Surefuser™+ and 300 ml for the new pump). The manufacturers do not specify whether the volume by which the reservoir is filled will affect flow rate. This effect of reservoir volume on flow rate was not investigated.

The rate of 4 ml/hr is the rate used at our clinical practice and was advised by anaesthesiologists for providing adequate analgesia whilst having a safe therapeutic window. With more resources and time, same testing could be carried out at different rates to evaluate whether this would have an additional effect.

This study was performed without a power analysis due to limited resources. Consequently, the results of the statistical analysis need to be taken with caution and interpreted together with the descriptive analysis. More work needs to be done to elucidate the effect of the numerous variables that can affect flow through the elastomeric infusion pumps such as vertical displacement, temperature, dimensions of the catheter, properties and distribution of the fenestrations, effect of kinking, accuracy of the flow regulators and monitoring flow whilst pumps are used on patients.

Conclusion

The Surefuser™+ and new pump with either catheter fail to achieve the desired 4 ml/hr flow rate. No pump/catheter combination was significantly better than another. The new catheter performed significantly better than the standard catheter and this improvement was greater with the new pump. The improved flow through the new catheter by just under 0.5 ml/hr is unlikely to be clinically significant. All pumps and catheter combinations lost approximately 1 ml/hr of flow rate by 48 hours thus making them less reliable and robust in administering fluid accurately over this period. Temperature did not appear to affect flow rate and for this testing process it did not appear to affect the results despite not being regulated.

Conflict of Interest

The author declares no conflict of interest.

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