Technical report

Performance of the Baxter Infusor LV10 under hyperbaric conditions

Iestyn Lewis, David Smart, Bebe Brown and Carol Baines

Abstract

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Introduction: Elastomeric drug delivery devices are a simple way to provide long-term IV therapy to patients in the outpatient setting. Patients receiving hyperbaric oxygen therapy occasionally need these devices. This study compared the performance of the Baxter infusor LV10 elastomeric device in repetitive conditions at pressures of 101.3 kPa and 243 kPa.

Methods: Ten Baxter infusor LV10 elastomeric devices were pressurised in a hyperbaric chamber to 243 kPa over a two-hour period consistent with a standard medical treatment run. This process was repeated 10 times for each device giving a total of 20 hours under pressure. The fluid delivered by each device was measured and the device weighed at the end of each pressurisation. Ten control devices containing identical drugs were tested in the same manner at 101.3 kPa over the same time period.

Results: No significant differences in output of the devices were observed between hyperbaric and control conditions. The flow rates measured in both study groups were 35% lower than the manufacturer's stated flow rate, possibly due to lower test environment temperature and outdated devices used in the tests.

Conclusion: Despite lower than expected flow rates, this study demonstrated no significant difference in the delivery rate of the Baxter infusor LV10 under 243 kPa hyperbaric conditions compared with room pressure.

Key words

Hyperbaric oxygen therapy, drugs, treatment, equipment, elastomers

Introduction

Elastomeric infusion pumps are disposable, non-electronic drug delivery devices. They provide an infusion of medication by deflation of a fluid-filled elastomeric balloon to drive solutions through intravenous (IV) tubing and into an IV catheter. Typical devices are stated to provide an infusion over 30 minutes to 12 days at +/- 10–20% of the desired flow rate.[1] Such pumps are small, lightweight, simple to use and enable ambulatory infusion therapy, particularly in the outpatient setting. They are used to deliver a wide variety of medication, such as antibiotics, analgesia and chemotherapy.

Hyperbaric oxygen treatment (HBOT) is the therapeutic use of oxygen at a pressure higher than one atmosphere absolute (101.3 kPa).[2] Given the nature of the conditions for which HBOT may be used, particularly infected deep wounds and osteomyelitis, patients often require long-term antimicrobial therapy, usually given orally, but IV antibiotics are sometimes required. Providing continuous infusions to a patient under hyperbaric conditions can be problematic using traditional electronic pumps.[3] Pumps require modification to function in the hyperbaric environment to prevent failure or damage from the increased pressure. In addition, batteries and electronics pose a fire risk within the chamber.[4] The majority of patients receiving HBOT are outpatients. In this setting, a cost-effective way to deliver IV antibiotics is via an elastomeric device over a 24-hour period.[5]

The Baxter LV10 infusor is the most commonly used elastomeric device in patients who require long-term IV antibiotics at the Royal Hobart Hospital. It is a large-volume, elastomeric device containing 240 ml of fluid. It has a stated flow rate of 10 $ml \cdot h^{-1}$ over a 24-hour period if the flow restrictor is kept at a temperature of $33^{O}C$.[6] The elastomer is made of polyisoprene. Mechanical testing of this material shows that a filled device generates a decreasing flow rate while it delivered the first third of the fluid contained within it; a steady state is then reached until the flow rate increased just before the balloon empties, after which the flow rate drops precipitously.[7] Figure 1 shows the flow rate as a function of time for a polyisoprene reservoir filled with different volumes.

The aim of this study was to prospectively compare the performance of the Baxter Infusor LV 10 under clinically relevant hyperbaric conditions of 243 kPa to that at room pressure (101.3 kPa).

Method

The Baxter infusor LV10 elastomeric delivery devices used for this study were supplied at no cost because they had reached their expiry dates and were to be discarded by the Royal Hobart Hospital Pharmacy. Fourteen devices contained antibiotics (tazocin, vancomycin & ceftriaxone) and were one month out of date. Six devices contained dopamine and were 18 months out of date. Saline (0.9%) was the diluent for all medications in the elastomeric devices.

Figure 1
Flow rate as a function of time for a polyisoprene reservoir filled with 240 ml for a 10 ml·h^{-1} claimed flow rate value (reproduced with permission[11])

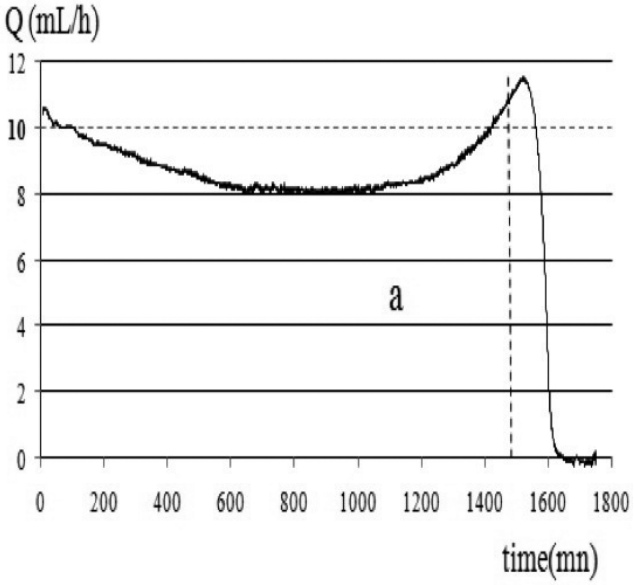
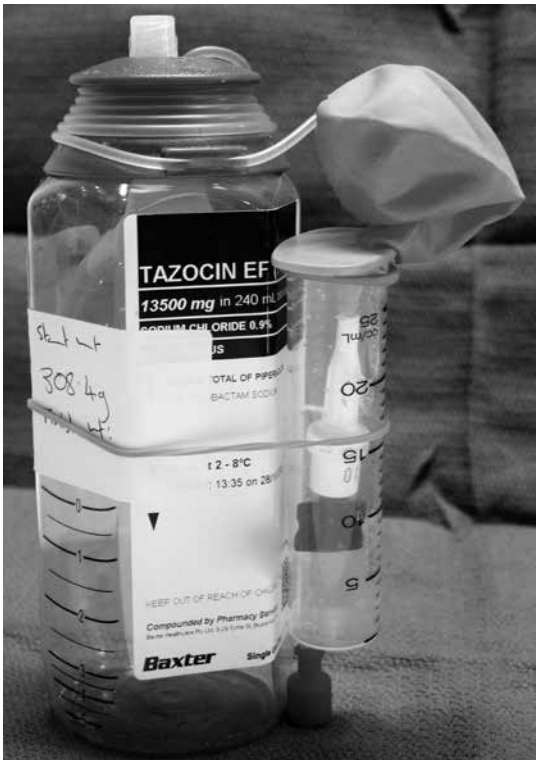


Figure 2
The Baxter Infusor LV 10 with syringe collection device and rubber syringe cover to prevent evaporation



The study apparatus is shown in Figure 2. The elastomeric devices were divided into two matched groups of 10 containing identical medications. Each group had four devices containing tazocin, three of dopamine, two ceftriaxone and one vancomycin. Ten elastomeric devices were placed inside the hyperbaric chamber and 10 were kept at room pressure outside the chamber. Both groups were then subject to 10 discrete two-hour sampling periods over 10 consecutive working days to a total of 20 hours of testing.

During sampling, fluid was run from the device via its infusion catheter into a 25-ml syringe. The syringe had the plunger removed and a luer-lock stopper to cover the tip, so it formed a closed collection reservoir. This was attached to the elastomeric device with an elastic band. A rubber balloon was used to cover the opening of the syringe to minimise evaporation of liquid. All the devices were weighed before the study and after every sampling period using laboratory scales. (ACB plus 600H, AE ADAM, Adam Equipment (SE Asia) PTY Ltd, Perth, Australia). These scales had been calibrated prior to the study to an accuracy of +/- 10 milligrams. Sample volumes were also measured using the 1 ml graduations on the side of the syringe to the nearest millilitre. Following sampling, a luer-lock stopper was used to contain the remaining contents of the elastomeric device between sampling periods, which corresponded to each hyperbaric pressurisation.

Hyperbaric samples were pressurised to 243 kPa and the control group maintained at 101.3 kPa. A twin-lock, multiplace hyperbaric chamber was used for the study (Hydro-Electric Commission Enterprises Corporation, Hobart, 1992). The hyperbaric protocol involved pressurising the chamber to 243 kPa over 10 minutes, remaining at pressure for 90 minutes, followed by 20 minutes of depressurisation; the standard clinical hyperbaric treatment at our facility. Ten consecutive measurements were collected from each device to assess flow rates across the devices' life cycle. This was considered clinically relevant as some patients may receive more than one treatment per day, or they may be receiving HBOT at any time across the 24-hour period of elastomeric device delivery. The control group was tested at 22^{O}C and the hyperbaric group at 23^{O}C; some variability in temperature was experienced in the hyperbaric group during compression and decompression.

At the start of each sampling period, the devices were unclamped and allowed to drain into the measuring syringe for two hours before being clamped off. As this was an open system there was no resistance to the discharge of fluid. At the end of each sampling period, the volume of discharged fluid was measured and the device weighed. Volumes and masses for each sampling period were then tabulated producing 10 measurements for each of the 10 devices in both groups.

Data are presented as the mean and 95% confidence intervals (95% CI). Differences in mass and volume between the hyperbaric and control groups were compared with an unpaired Student's *t*-test. A linear mixed model regression was also produced to account for the repeated results over

Figure 3
Total change in mass delivered by Baxter infusor LV10 over each two-hour sample period

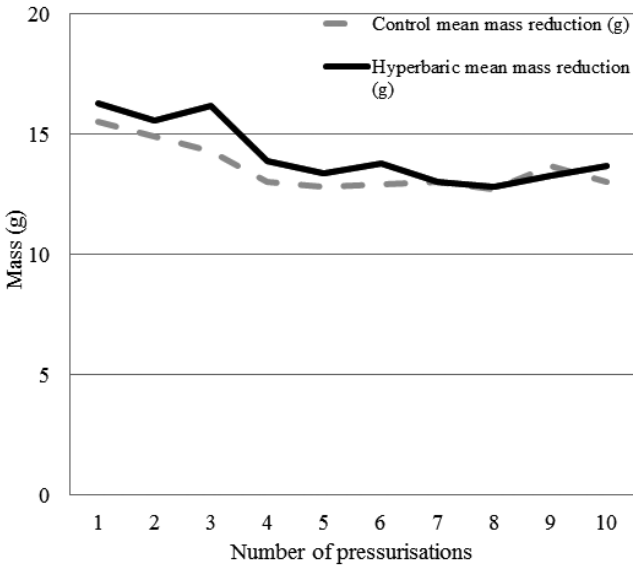
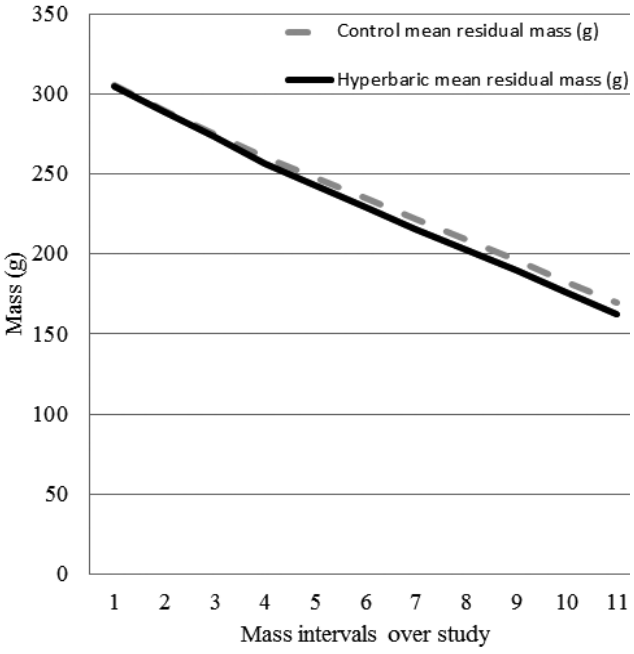


Figure 4
Mean residual mass in the Baxter infusors over 11 samples and 10 sampling periods for the hyperbaric (243 kPa) and control (101.3 kPa) groups



time and to allow for the variability of the different devices. Power analysis showed 20 infusion devices would have a power of 90% to predict a 15% difference in flow rate with an χvalue of 0.05. Two statistics programmes were used: Graphpad Prism 6, Graphpad Software Inc. version 6.0e 2014, La Jolla CA and Stata 12, Stata Corp 2011, Stata Statistical Software Release 12, College Station TX.

Results

The hyperbaric group delivered slightly larger volumes than the control group, 13.5 ml (95% CI 12.5–14.4) vs. 12.8 ml (11.9–13.5). Mean mass reduction per pressurisation was 14.22 g (13.28–15.17) hyperbaric vs. 13.57 g (12.86–14.28) control. Neither of these results was statistically significant. Analysis of the individual treatment runs showed no statistically significant difference between the hyperbaric group and the control group at any time. The mean mass reduction was 0.65 g less (-0.97 to 2.28) in the control group (13.57) compared to the hyperbaric group (14.22). The mean volume reduction was 0.7 ml (0.9–2.3) less in the control group compared to the hyperbaric group. Over the 10 sample periods all devices in both groups progressively delivered less fluid in each two-hour sample collection period. The mean mass reduction decreased by 0.30 g (-0.34 to -0.26 g) for both groups per successive two-hour period. The mean volume reduction fell by 0.3 ml (-0.4 to -0.3) for both groups per successive two-hour interval ($P < 0.001$). The linear mixed model regression showed that neither the mean mass reduction nor the mean volume reduction differed significantly ($P = 0.43$ and $P = 0.39$ respectively) between the control and hyperbaric groups when averaged over the 10 sample periods.

The delivery rate was slightly higher in the first three sample periods, when the devices were full. After this, both groups of devices settled into a relative steady state (Figure 3). Charting the total residual mass of the devices over the eleven mass measurements during the study showed there was no difference between the groups (Figure 4). When hourly flow rates were calculated, neither group achieved their stated nominal flow rate of 10 ml·h^{-1}; hyperbaric group 6.6 ml·h^{-1} (5.9–7.3) control group 6.3 ml·h^{-1} (5.6–6.9).

Further calculations were made in an attempt to control for the actual ambient temperatures in this study compared to the manufacturer's specified optimum temperature. Lower ambient temperatures were stated to produce lower flow rates. Using data from the manufacturer, flow rates are stated to fall by 2.3% for every 1^{O}C below 33^{O}C. Table 1 summarises the measured flow rates and the theoretical calculated flow rates if the ambient study temperatures of 22–23^{O}C were converted to 33^{O}C.

Subgroup analysis showed that the less out-of-date antibiotic devices delivered 15.2 ml (14.0–16.5) over two hours for the hyperbaric group and 14.4 ml (13.0–15.8) for the control group. The dopamine group delivered 11.9 ml (11.7–12.5) over two hours for the hyperbaric group and 11.6 ml (9.0–14.2) for the control group. There were no significant differences in flow rates between the hyperbaric and the control groups for either the antibiotic or dopamine samples, but the differences in flow rates between the newer antibiotic preparations and the older dopamine solutions

Table 1
Calculated volumes delivered over 60 min at the study temperature (22–23°C) and when converted to the manufacturer's specified optimum operating temperature of 33 °C and using their temperature change data (2.3% per 1°C)[6]; mean (95% CI)

	Hyperbaric group	Control group
Measured flow rate (ml·hr^{-1}) at 22-23°C	6.6 (5.9–7.3)	6.3 (5.6–6.9)
Calculated flow rate (ml·hr^{-1}) at 33°C	8.3 (7.4–9.2)	8.1 (7.2–8.9)

were statistically significant (P = 0.025 in the hyperbaric group and P = 0.005 in the control group).

Discussion

Previous studies have shown variable performance of elastomeric devices under hyper- and hypobaric conditions.[8–10] Nineteen On-Q pain infusion devices were tested under hyperbaric conditions against five atmospheric controls, all at room temperature. The devices in the hyperbaric group were subjected to six 104-minute treatment protocols; seven minutes to pressurise the chamber, 90 minutes at a test pressure of 101.3, 203, 243 or 304 kPa and seven minutes to depressurise. No differences in delivery performance were found at pressure, although there was a decrease in output over the 10 hours the devices were subject to testing. Initial output in the first 104-minute study period was 30% higher than the stated device output. By the sixth study period, after 10 hours of testing, the device was delivering 6% above the stated output. Testing was only carried out for 10 hours of the potential 28-hour lifespan of the device quoted by the manufacturer.[8]

The Baxter infusor LV10 device has been tested under a wide range of atmospheric conditions (81, 91, 101.3, 172 and 253 kPa for 21.5 hours at an ambient temperature of 30–32°C.[9] No significant difference in flow rates were discerned between different atmospheric pressures if the complete unit (reservoir and restrictor) were at the same pressure. Increased flow rates have been observed in an elastomeric patient-controlled analgesia (PCA) system under hyperbaric conditions, particularly with dextrose solutions.[10] These changes were more profound with higher concentration dextrose solutions, which are particularly viscous. Viscosity has an inverse relationship to flow rate and increasing concentrations of drug may affect a solution's viscosity.[1]

Our data on the Baxter Infusor LV10 are consistent with the materials science data available on polyisoprene elastomers, where at full stretch (when the elastomeric balloon is full), there is greater tension on the elastomer, and a non-linear steeper tension-versus-length curve results. The effect on the clinical device is to produce greater pressure on the contents and a higher flow rate in the first quartile of the device's functional time line. In the middle two quartiles, the tension versus length curve is relatively linear and even (Figure 1), delivering a relatively consistent flow rate, which is important clinically. In the last quartile of its functional time line, as the elastomer returns to its resting empty state, the tension falls rapidly as the volume falls and a reduced flow results.[7]

The devices were not tested until empty in our study, so we cannot comment on the performance in the last four hours of their 24-hour life. Based on our findings, each device would contain in excess of 70 ml of medication. A residual volume is clinically desirable, because it ensures some tension remains in the elastomer, thus ensuring that the flow (drug delivery) is maintained. The variability of flow rates across time was confirmed in this study, although it was not our primary aim.

We found no significant differences in flow rates between devices exposed to 243 kPa hyperbaric conditions and devices at room pressure. In the hyperbaric-exposed devices, pressure is exerted on the whole apparatus, and the elastomeric balloon was vented to the external pressure via holes in the protective casing. Hence, there are no areas of higher or lower pressure within the device.

Unlike the previous studies on the On-Q and Baxter devices,[8–10] the delivered flows in our study were consistently lower than the flow rates claimed by the manufacturer by up to 35%, but this was independent of pressure. Some of this underperformance could be attributed to the ambient temperatures under which our study was conducted. A second study on the On-Q pain infusion device exposed to temperature changes of 15–33°C above and below room temperature found that output varied by up to 50%.[11]

Baxter states that the ideal temperature for the use of the LV10 is 33°C, with a variability of +2.3% for every 1°C increase in temperature and -2.3% for every 1°C decrease in temperature.[6] The flow restrictor for this device is part of the leur-lock connector which, in clinical use, will be close to skin temperature. A potential flaw in this study is that the devices were tested at room temperature. Considering this, a reduction in drug delivery of approximately 20% could have been expected. We did attempt to correct for the temperature difference from the manufacturer's ideal by undertaking a theoretical calculation of flow rates using the above data. Even with this correction, the devices still underperformed.

Whether the manufacturer's 'optimal' temperature of 33°C is actually achieved in routine clinical use is unproven and requires investigation. Because the flow restrictor for this device is part of the leur-lock connector in clinical use, it is usually taped to the underlying skin. Skin temperature varies markedly with cardiovascular and hydration status, pyrexial infections and variations in ambient conditions, etc. Therefore, if the assumption is that the device is close to skin temperature, mounting the device on the skin may result in marked

variations in delivered flow rates. This has never been studied for these devices. Therefore, we chose to test the devices at a controlled ambient temperature environment of 22–23^{O}C.

Two additional factors may account for the lower flow rates observed in our study. These include the age of the elastomer and the viscosity of the solution. All the devices were out of date, but the oldest (dopamine, 18 months out of date) had significantly lower flow rates than the one-month out of date antibiotic-filled devices. It is likely that the aging process reduces the performance of the elastomer. Polyisoprene elastomer is similar to rubber in structure, and has similar potential to 'perish', thus reducing its elasticity. Differences in viscosity of the contents may also have affected the performance of the elastomers used in this study.[1,9] Baxter were unable to provide the viscosity figures for the different drugs, but it must be remembered that the diluent in each bottle was 0.9% saline (Baxter Healthcare Pty Ltd, personal communication, 2014). A further possible interaction could be the direct effect of the contents on the elastomer, accelerating its breakdown. It would seem that even in new devices there are variations in flow rate due to the characteristics of the contents that are not able to be applied in the daily clinical setting.

Variations in performance and the factors that affect elastomeric performance must be taken into account when treating patients with these devices. It is a concern that if patients had received treatment from the devices used in our study, they would have received a substantially lower dose of medication than expected. However, given the freedom of mobility provided for the patient and the cost effectiveness for long-term treatment using elastomeric devices, an under-performance of 20–30% may be acceptable for delivering antibiotics to patients with chronic infections.[5] If this is a consistent finding, drug doses could also be increased to compensate. Unfortunately, due to our use of out-dated elastomeric devices, and undertaking the study at lower than recommended temperatures, caution should be given to generalising from our data to patient populations. However, such underperformance is unlikely to be acceptable when analgesia, local anaesthesia and chemotherapy agents are being delivered. Ideally the study should be repeated with a total study period of 24 hours using in-date devices. Despite some limitations to this study, the important finding was that the devices performed the same at 243 kPa pressure in the chamber as they did at a normal atmospheric pressure of 101.3 kPa.

Conclusion

Our investigation demonstrates no significant difference in performance in the Baxter Infusor LV10 when used under clinically relevant hyperbaric conditions, providing the whole device is under pressure. On this basis we consider this device may be suitable for clinical use in the hyperbaric environment, but further validation is required.

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Iestyn Lewis[1], David Smart[1,2], Bebe Brown[1], Carol Baines[1]
[1] Department of Diving and Hyperbaric Medicine, Royal Hobart Hospital, Hobart, Tasmania
[2] Faculty of Health Sciences, University of Tasmania

Address for correspondence:
Iestyn Lewis
Department of Diving and Hyperbaric Medicine
Royal Hobart Hospital
Hobart, Tasmania 7000
Australia
Phone: *+61-(03)-6222-8193*
Fax: *+61-(03)-6222-7268*
E-mail: *<iestyn.lewis@dhhs.tas.gov.au>*