Technical reports

An assessment of the performance of the Baxter elastomeric (LV10) Infusor™ pump under hyperbaric conditions

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Abstract

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Introduction: There are limited data on the use of elastomeric infusion pumps during hyperbaric oxygen treatment.

Aim: This study evaluated the flow rate of the Baxter elastomeric LV10 Infusor™ pump under normobaric (101.3 kPa and three hyperbaric conditions of 203 kPa, 243 kPa and 284 kPa.

Methods: Elastomeric pumps were secured to participants in the same manner as for a typical patient, except that a container collected the delivered antibiotic solution. Pumps and tubing were weighed before and after the test period to determine volume delivered and to calculate flow rates at sea level and the three commonly used hyperbaric treatment pressures at two different time periods, 0–2 hours (h) and 19–21 h into the infusion.

Results: The mean flow rates in $ml \cdot hr^{-1}$ (SD) were: 9.5 (0.4), 10.3 (0.6), 10.4 (0.6), 10.4 (0.5) at 0–2 h and 10.5 (1.0), 12.2 (0.6), 9.4 (0.5), 10.3 (0.9) at 19–21 h for the normobaric, 203 kPa, 243 kPa and 284 kPa conditions respectively. There was no significant association between flow rate and time period ($P = 0.166$) but the 203 kPa flow rates were significantly faster than the other flow rates ($P = 0.008$). In retrospect, the 203 kPa experiments had all been conducted with the same antibiotic solution (ceftazidime 6 g). Repeating that experimental arm using flucloxacillin 8 g produced flow rates of 10.4 (0.8) $ml \cdot h^{-1}$, with no significant associations between flow rate and time period ($P = 0.652$) or pressure ($P = 0.705$).

Conclusion: In this study, the flow rate of the Baxter LV10 Infusor™ device was not significantly affected by increases in ambient pressure across the pressure range of 101.3 kPa to 284 kPa, and flow rates were generally within a clinically acceptable range of 9–12 $ml \cdot h^{-1}$. However, there was evidence that the specific antibiotic solution might affect flow rates and this requires further study.

Key words

Hyperbaric oxygen therapy; Infectious diseases; Drugs; Equipment; Treatment; Flow rate

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Introduction

Electronic medication infusion pumps are often used to deliver long-term intravenous (IV) antibiotic therapy to patients with infections such as necrotizing fasciitis, myonecrosis, refractory osteomyelitis and infected diabetic and venous foot ulcers; conditions which might also benefit from hyperbaric oxygen treatment (HBOT).[1,2] While some electronic medication infusion pumps have been modified to function in the hyperbaric environment,[3,4] others cannot be used during HBOT for a variety of reasons, most particularly the presence of lithium batteries which are a fire hazard under hyperoxic conditions. Therefore, non-electronic pumps, such as balloon-driven elastomeric infusion pumps, may be considered a safer alternative for the hyperbaric setting. These pumps typically have a medication-filled balloon reservoir that deflates at a consistent rate, pushing the antibiotic solution through a flow restrictor into the IV tubing and delivering it to the patient via a peripherally inserted central catheter (PICC) line.[5] Historically, elastomeric infusion devices have been disconnected from patients prior to entering a hyperbaric chamber due to concerns about the potential effects of the hyperbaric environment on the deflation rate of the balloon. This practice could result in two hours (h) or more of infusion time being lost each day, and requires additional manipulations of the PICC access increasing the risk of iatrogenic infections.

The purpose of this study was to assess the flow rates delivered by one type of elastomeric infusion pump, the Baxter elastomeric LV10 Infusor™, under various hyperbaric conditions. The two null hypotheses tested were:

- that the volume of solution delivered by the device during routine hyperbaric compression was the same as the volume of solution delivered under normobaric conditions; and
- that the volume delivered was within the appropriate clinical range.

Methods

Ethical approval for the study was obtained from the Townsville Hospital and Health Service Human Research Ethics Committee (HREC/15/QTHS/7).

Unused LV10 pumps filled with antibiotic solution were

Table 1
Antibiotic and dose for each time frame and pressure exposure; * primary analysis (Table 2); † secondary analysis (Table 3)

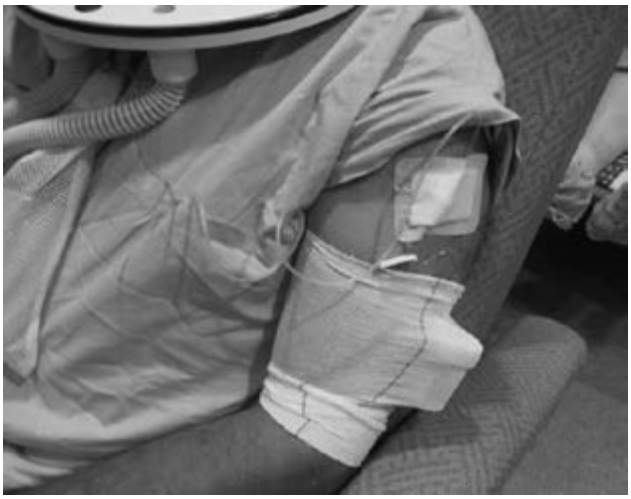
Time frame (h)	Pressure	Antibiotic	Dose (g)	no. of pumps
0–2	101.3 kPa	cefepime	3	3
		flucloxacillin	8	2
	203 kPa	cefepime	3	2
		flucloxacillin	8	3
	243 kPa	cefepime	3	5
	284 kPa	cefepime	3	3
		flucloxacillin	8	1
		cefoxitin	12	1
19–21	101.3 kPa	cefoxitin	6	2
		ceftazidime	6	1
		cephazolin	6	1
		piperacillin/ tazobactam	13/0.5	1
	203 kPa	ceftazidime*	6	5
		flucloxacillin†	8	5
	243 kPa	piperacillin/ tazobactam	13/0.5	1
		benzylpenicillin	10.8	4
	284 kPa	benzylpenicillin	10.8	3
		cefoxitin	6	2

sourced from the hospital pharmacy. Pumps were used within 14 days of the antibiotic expiration date and within the expiration date of the infusor device itself. Normal saline (NS) was the diluent for all antibiotics. The specific antibiotics and doses used in this study are listed in Table 1.

Pump flow rates were evaluated using mock infusions under both normobaric and hyperbaric conditions. Healthy volunteers were recruited for the normobaric tests, whilst hyperbaric staff, marine biology students and routine hyperbaric patients were recruited to participate in the compression tests which were conducted during clinical HBOT sessions. All participants were afebrile as measured on the forehead using an infrared thermometer (Thermofocus, Tecnimed Srl, Varese, Italy). Written informed consent was obtained from all participants. The study did not involve any deviation from the Hyperbaric Unit's normal clinical practice.

Pumps were warmed to room temperature for one hour and then attached to the research subject in a manner similar to that used for actual infusions. The luer-lock connecter of the infusion line was secured to the upper arm with an overlying single adhesive island dressing and a piece of Tubifast®. The flow restrictor is located just proximal to the luer-lock connection and is required to be secured to the patient at approximately 31°C to achieve the nominal flow rate.[5] Pilot data from five participants demonstrated the temperature (Vital Signs Monitor 300 Series, Welch Allyn, New York, USA) under the single island dressing was always near 31°C (SD 0.07), so no further effort was made to measure or control the temperature of the antibiotic solution at the flow restrictor. The pump was placed in a carry bag on the participant's chest so that the luer-lock connector and pump were secured at the same level. Finally, a short length of connecter tubing was attached to the luer-lock connector, with the other end draining into a small container strapped to the upper arm instead of infusing into the subject (Figure 1).

Figure 1
A short length of connecter tubing was attached to a luer-lock connector with the other end draining into a small container strapped to the upper arm instead of infusing into the patient



Pumps were tested at 101.3 kPa (sea level) and at 203, 243 and 284 kPa in a multiplace chamber to replicate commonly used hyperbaric treatment pressures. For each normobaric/ hyperbaric pressure, pumps were tested over two time intervals: at the beginning (0–2 hours, h) and near the end (19–21 h) of the 24-h infusion timeframe. The rate of the infusion fluctuates during the 24 h with the pump running slightly faster at the end of the infusion. Therefore, we used the 19–21 h time frame so that this increased flow rate would not impact on our results.[6] Separate pumps were used for each test to limit the compounding of any intrinsic error from a single pump; the pumps that were tested at 19–21 h were run for the first 19 hours in an incubator at 31.1°C.

The infusion pumps were weighed pre- and post-compression (Pelican® Digital Bench Scale: d = 0.01g, Class 3) to calculate the amount of solution delivered. Change in pump weight was used as a surrogate marker for volume delivered on a 1:1 ratio since the difference of weight and volume of NS, the primary diluent, is less than half of one percent (i.e., 1 mg of solution = 1 ml of solution). The duration of the compression was logged to enable calculation of the rate of the infusion as $ml \cdot h^{-1}$. The pre- and post- compression weight of collection containers was also determined to verify flow

Table 2

Flow rates from 0–2 hours and 19–21 h at differing treatment pressures (primary analysis) at an infusion rate of 10 ml·h^{-1}; the number of infusions that were outside the clinically acceptable range (9–12 ml·h^{-1}) were recorded

Time frame (h)	Pressure (kPa)	Flow rate (ml·h^{-1}) Mean	(SD)	Min	Max	95% CI	*n* <9 ml·h^{-1}	*n* >12 ml·h^{-1}
0–2	101.3	9.5	(0.4)	9.1	10.1	9.1–10	–	–
	203	10.4	(0.5)	9.7	10.9	9.7–11.2	–	–
	243	10.7	(0.4)	10.1	11.1	9.8–11.2	–	–
	284	10.5	(0.5)	9.7	11.1	9.9–11.2	–	–
19–21	101.3	10.5	(1.2)	8.4	11.3	9.4–11.8	1	–
	203	12.2	(0.6)	11.2	13.0	11.5–12.9	–	4
	243	9.4	(0.5)	8.6	9.8	8.9–10.1	1	–
	284	10.4	(1.0)	9.1	11.5	9.3–11.5	–	–

rate as determined by change in pump weight.

STATISTICAL ANALYSIS

According to Baxter, the elastomeric pump flow rate is expected to be 10 ml·h^{-1} ± 10% (nominal accuracy variation) using 5% dextrose as a diluent solution and may be 10% faster than the labelled rate (i.e., 11 ml·hr^{-1}) when NS is used as the diluent.[5] Therefore, we assumed a clinically acceptable range for infusion flow rates of 9 ml·h^{-1} (10 ml·h^{-1} - 10%) to 12 ml·h^{-1} (11 ml·h^{-1} + 10%).

A flow rate within 10% of expected is clinically acceptable, but a flow rate 20% less than recommended may mean that the patient would not receive the whole medication dose within the nominal delivery time, and a flow rate 20% higher than expected would result in the 24-hr pump running out prior to the intended completion time. Therefore, we powered the comparative component of this study to detect a 20% (2.2 ml·h^{-1}) difference in flow rate. We determined a sample size of five pumps in each group would provide a greater than 90% power (with $\alpha = 0.05$) to detect a 2.2 ml·h^{-1} difference in flow rates.

To compare flow rates across time periods and pressures, we first confirmed normal distribution of the data using the Shapiro-Wilk test and Q-Q plots.[7,8] We then compared mean flow rates for the two time periods and four pressure conditions using two-factor analysis of variance (ANOVA), with $P < 0.05$ used to establish statistical significance. All statistical analyses were performed using Stata release 11.2 (StataCorp, College Station, TX, USA).

Results

Forty mock infusions were completed. The room temperature for the study did not change as the hospital is an air-conditioned environment and remained at 22.5°C for all normobaric tests. The average chamber temperature during the administration was 24.6°C (SD 1.3), ranging from 15.0°C to 29.7°C. We did not prospectively measure or adjust for outside atmospheric pressure, but retrospective weather data available for ten of the 17 study days revealed generally stable barometric pressures ranging from 1011 to 1026 hPa (mean: 1019 (SD 4.4) hPa).[9]

The average volume delivered during the mock administrations was 19.7 (SD 2.0) ml, ranging from 15.8 to 23.8 ml. Compression times varied for the study due to treatment tables being different lengths of time; the mean duration of administration was 113 (SD 7.2) minutes, ranging from 100 to 121 minutes. The average calculated flow rate for all time periods and pressure groups was 10.5 (SD 1.0) ml·h^{-1}.

Table 2 shows the primary results for each time period and pressure. In the 0–2 h period, flow rates ranged between 9.1 and 11.1 ml·h^{-1}; in the 19–21 h time period, flow rates ranged between 8.6 ml·h^{-1} and 13.0 ml·h^{-1}. All of the 0–2 h observations were within the clinically acceptable window of 9 to 12 ml·h^{-1}, but six of the 19–21 h observations were outside that range: two observed flow rates (one at 101.3 kPa and one at 243 kPa) were less than 9 ml·h^{-1}, and four observed flow rates (all at 203 kPa) were greater than 12 ml·h^{-1}. Two-factor ANOVA revealed a statistically significant difference in flow rate among the four pressures ($F = 4.61$, $P = 0.008$), but not between the two time periods ($F = 2.00$, $P = 0.166$).

As can be seen in Table 2, the flow rates for the 9–21 h trials at 203 kPa were higher than for the remaining trials. Notably, all five of the 203 kPa 19–21 h trials were conducted with the same antibiotic and dose - ceftazidime 6 g - and four of the five observed flow rates were above 12 ml·h^{-1}. These results were not consistent with the rest of the data and could not be logically attributed to the increase in pressure.

To clarify this, the 19–21 h 203 kPa experiments were repeated using pumps filled with flucloxacillin 8 g, a drug and dosage commonly used in combination with HBOT. The mean (SD) flow rate for those trials was 10.4 (0.8) ml·h^{-1}, ranging from 9.6 to 11.5 ml·h^{-1} (Table 3). Repeat ANOVA (secondary analysis) performed

Table 3
Flow rates at 203 kPa at 19–21 h comparing ceftazidime and flucloxacillin

Antibiotic	Dose	Mean (SD)	Min	Max
Ceftazidime	6 g	12.2 (0.6)	11.2	13.0
Flucloxacillin	8 g	10.4 (0.8)	9.6	11.5

on the flucloxacillin data at 203 kPa at 19–21 h instead of ceftazidime found no significant differences between the flow rates among the pressures or time periods tested (pressure, F = 0.47, P = 0.705; time period, F = 0.21, P = 0.652).

A post-hoc comparison using Student t-test confirmed that the observed 19–21 h 203 kPa flow rates for the original five ceftazidime pumps (mean 12.2 ml·h^{-1}, SD 0.6) were greater than those for the replacement 203 kPa flucloxacillin pumps (mean 10.4 ml·h^{-1}, SD 0.7) (Table 3).

Discussion

Antibiotic infusions are often required for both inpatients and outpatients undergoing HBOT. Although technology continues to advance, early studies found substantial incompatibilities between electronic infusion pumps and HBOT, with both significant variations in pump flow rates and outright pump failures in hyperbaric settings.[10,11] Many newer generation electronic pumps perform well in hyperbaric conditions[3] but some electronic pumps used for monoplace chambers are no longer being manufactured.[4] Also, even modern pumps that use lithium batteries cannot be used during HBOT due to the risk of fire.[4]

Elastomeric infusion devices can deliver antibiotic infusions without any electronic elements, but there are limited data on their reliability in HBOT settings. Flow from elastomeric pumps filled with water was unaffected so long as the flow restrictor and the balloon reservoir were exposed to the same pressure conditions.[12] No difference in solution flow rates from LV10 pumps in normobaric and hyperbaric conditions were reported in another study but they observed flow rates that were 35% lower than expected in both conditions.[13] These findings might be explained by the use of long out-of-date solutions and not warming the flow restrictor to the recommended 31^{O}C.[13]

In our experiments, we used in-date infusion devices with antibiotic solutions within 14 days of their expiry date, and attached the flow restrictor to the mock patient's arm to achieve the necessary warming, as would be done during clinical care. The results of our study suggest that antibiotic delivery using LV10 pumps achieve flow rates within acceptable parameters during HBOT at 203, 243 and 284 kPa.

We did initially observe faster than expected flow rates in one arm of the study (203 kPa at 19–21 h), but there was no dose-response relationship in the data. That is, the flow rates returned to normal at even higher pressures. In retrospect, all of the initial experiments in that study arm were conducted with the same antibiotic solution: ceftazidime 6 g. At the time of this study, there was no literature suggesting that the type and/or dose of antibiotic solution could affect the flow rate through an elastomeric device; therefore, we simply used any available elastomeric pumps for our experiments. However, when we recreated that study arm using pumps containing flucloxacillin 8 g we found clinically acceptable flow rates that were not statistically different from those of the other study arms. Because of these divergent data we cannot dogmatically conclude that elastomeric infusion pumps are always safe in HBOT settings, and we encourage future research on the role of specific antibiotic (and other medication) solutions on elastomeric pump performance.

LIMITATIONS

For proper operation, the flow restrictor on the LV10 pump should be at 31.1^{O}C.[5] We did not mechanically control the temperature of the flow restrictor, but rather connected it to a participant using an island dressing in a manner similar to what would happen in clinical practice. Although pilot data indicated a temperature of approximately 31^{O}C under the dressing, we did not definitively measure the flow restrictor temperature in our study.

This study was performed using various available antibiotics at varying dosages, again as might occur in the clinical setting. Our data suggest there might be variations in the flow rates achieved with different antibiotic solutions, and further research exploring that issue would be valuable.

We only studied one specific elastomeric device, and did not compare the flow rates achieved with the Baxter LV10 Infusor™ to those achieved with other elastomeric devices, electronic pumps or other delivery technologies such as syringe pumps.

Finally, although this study closely replicated the clinical environment, it was not a clinical study per se. The pumps delivered solution into a collection container rather than intravenously, which might affect the observed flow rates. The methodology was consistent across all arms of the study, however, which should provide confidence in the comparative results. Future studies evaluating clinical use of elastomeric pumps during HBOT are warranted.

Conclusion

In this study, the flow rate of the Baxter elastomeric LV10 Infusor™ device was not significantly affected by increases in ambient pressure across the pressure range of 101.3 kPa to 284 kPa, and flow rates were generally within a clinically acceptable range of 9–12 ml·h^{-1}. However, there was some

evidence that the specific antibiotic solution might affect flow rates and this requires further study.

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Conflicts of interest: nil

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