Repeated hyperbaric exposure and glass ampoule safety

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Pharmacology; Equipment; Safety; Risk assessment; Pressure

Abstract
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Introduction: It has been our institution's policy to not place glass medication ampoules inside our hyperbaric chamber for fear of rupture. There is only a small and conflicting amount of data as to whether lass ampoules are safe for use under hyperbaric conditions.
Objectives: The primary objective of this study was to test the safety and usability of glass medication ampoules inside a hyperbaric chamber.
Methods: Repetitive, rapidly staged compressions and decompressions were performed on multiple different glass medication ampoules inside the medical lock of a medical hyperbaric chamber. Medication ampoules of varying sizes (1 ml to 10 ml) of medications that may be required in a hyperbaric emergency were assessed. The ampoules were rapidly compressed 100 times to pressures of 142 kPa, 183 kPa, 300 kPa, 405 kPa and 507 kPa. They were then dropped from a height of 30 cm while compressed at 507 kPa and then half the ampoules were opened while pressurized at 507 kPa.
Results: No ampoules were broken during compression or decompression. No ampoules broke when dropped from 30 cm onto the chamber floor. All ampoules opened at a pressure of 507 kPa functioned normally. No lids/ampoules shattered upon opening.
Conclusion: This study suggests that glass medication ampoules appear to be safe for use inside a medical hyperbaric chamber at routine treatment pressures.

Introduction

Glass ampoules are common ways of storing sterile medications, especially those medications that are for intravenous use. Many of the medications used in our hospital's emergency trolleys are contained in glass ampoules. This poses particular challenges in a hyperbaric environment as these ampoules are a fixed rigid container and contain a gas, usually carbon dioxide or nitrogen, together with the medication either as a liquid or solid. According to Boyle's law, as the ambient pressure increases during compression of the chamber the pressure is transferred onto the glass and as the gas is compressible no support of the glass is provided. If the pressure difference is too great the strain on the glass will cause the ampoule to shatter. For this reason, it is our local policy not to allow glass ampoules into our hyperbaric chambers. It is, however, well known among the diving community, especially the wreck diving community, that there are many ampoules which remain intact on sunken ships at depths exceeding our equivalent normal hyperbaric treatment pressures, e.g., *HMS Pandora*, which lies in 30+ metres' sea water.[1]

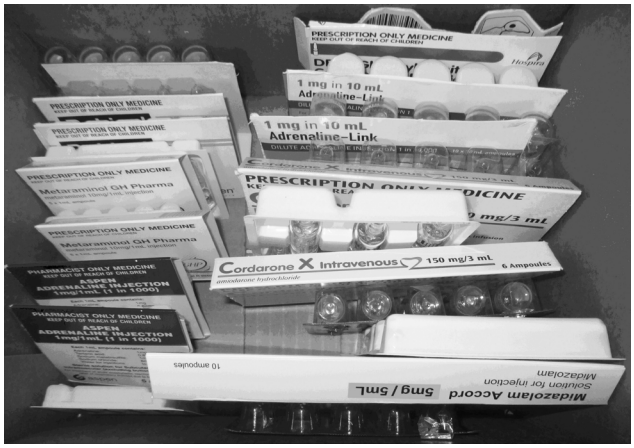
A literature review of Medline, the South Pacific Underwater Medicine Society (SPUMS) journal archives, The *Diving and Hyperbaric Medicine* Journal, the Rubicon Foundation database and Google Scholar revealed no articles on the breaking pressure and safety of glass medication ampoules. One article in 1964 commented that glass ampoules "*appear to withstand 5 to 6 atmospheres of pressure*".[2] However, recent literature, such as *Miller's textbook of anaesthesia*[3] and *Anaesthesia: a core review*[4], caution against the use of glass ampoules in a hyperbaric environment due to the risk of "*explosive rupture*". Neither Aspen Pharmaceuticals nor Pfizer Pharmaceuticals, the two largest suppliers of medications in glass ampoules to our institution, were able to advise whether there was a safe pressure to which such ampoules could be subjected, as they had no testing data for this (Lee K (Pfizer) and Thai M (Aspen), personal communications, 2017).

The current practice at our facility is to have medications outside the chamber and then if needed the outside attendant would draw up the medication into a syringe, making sure to expel any air, and then send it in through the medical lock. This method does delay the time taken for medications to be delivered to patients, especially in an emergency. It also utilises the outside attendant who is then unable to assist in other ways. There has also been a trend in high risk scenarios to pre-draw the medications into syringes and take

Table 1
Medication ampoules used in testing

Medication	**Dose** (mg)	**Volume** (ml)	**Batch/lot**	**Expiry date**	**Manufacturer**
Adrenaline 1:1000	1	1	AS711A1	07/2019	Aspen
Adrenaline 1:10,000	1	10	0085815	07/2018	Link Pharma
Metaraminol	10	1	7J0011C29	09/2020	Global Harvest
Noradrenaline	4	4	203931	09/2017	Mayne Pharma
Glycopyrrolate	0.2	1	AS704R1	04/2019	Aspen
Midazolam	5	5	W08873	05/2021	Accord Health
Amiodarone	150	3	7A032	04/2019	Sanofi
Glyceryl Trinitrate	50	10	709063 and 544058	03/2019 10/2017	Hospira

Figure 1
Drug ampoules in an open cardboard box ready to be placed in the medical lock of a hyperbaric chamber



them in with the patients; however, if unused these are then discarded. This has contributed to wastage of medications. Given the lack of evidence for ampoule pressure rating, a staged protocol was designed to test the strength of glass ampoules.

Methods

After appropriate ethics approval through the Townsville Hospital and Health Service Human Research Ethics Committee (HREC/17/QTHS/162), medications which were held in glass ampoules and used for predictable emergencies that might occur during a hyperbaric treatment were supplied by the hospital pharmacy (Table 1). Ten ampoules of each medication were tested to assess for any inter-ampoule differences. The ampoules had any plastic/foil covers removed and were kept in their plastic holders with cardboard dividers to simulate how they would be stored in the chamber. This also ensured that any ampoule breaking would not affect any other ampoule. All ampoules were placed inside an open cardboard container. The container was then placed into the medical lock of an empty chamber. The chamber was then pressurized to 142 kPa (the routine treatment pressure at our institution) and the medical lock containing the medications was repeatedly pressurized and depressurized 100 times. This was repeated at pressures of 183 kPa and 304 kPa. The ampoules were then compressed to 405 kPa and 507 kPa to assess the breaking strain of the ampoules at the maximum pressure of our hyperbaric chamber. The average rate of compression varied from 16 kPa·sec^{-1} at 142 kPa to 26 kPa·sec^{-1} at 507 kPa; the maximum rate exceeding 70 kPa·sec^{-1}. Ampoules were held at pressure for a minimum of five seconds for each compression.

Ampoules were checked regularly for breakage and data recorded. The protocol for any particular type of ampoule was to stop once 50% of that type had broken. If 50% of any type of ampoule had not broken at 507 kPa, the ampoules were removed from the lock into the chamber and dropped from a height of 30 cm to check for increased fragility.

Prior to the study, an ampoule of each type was dropped in 10 cm increments in height, at room pressure (approx. 101.3 kPa). The 10 ml glyceryl trinitrate ampoule broke when dropped from a height of 40 cm. Therefore, a height of 30 cm was used at which to drop these ampoules. None of the ampoules used in the drop test were utilised clinically. Half the remaining ampoules were then opened at depth to check usability and the remainder opened at the surface to again check usability. Broken ampoules were discarded into a sharps container and disposed of as per hospital policy. All testing was carried out by one researcher (SYT).

Results

No ampoules broke during any of the multiple recompression/decompression cycles.

The containers holding the ampoules were dropped from 30 cm without any ampoules breaking.

Ampoules were opened at 507 kPa pressure without the tops shattering.

Discussion

This experiment far exceeded the expected number, pressures and rates of compression and decompression in clinical hyperbaric practice to assess the safety and breaking strain of various glass ampoules inside a hyperbaric chamber. The usability of medications contained in glass ampoules in a hyperbaric environment was confirmed by opening half the ampoules at pressure. Despite the rapid compression/decompression pressure profiles there were no ampoule breakages and certainly no "*explosive ruptures*". That no ampoules broke when dropped in their storage box from a height of 30 cm onto the chamber floor at 507 kPa suggests that no increase in fragility of the ampoules occurred.

It appears that despite previous concerns regarding the safety of glass ampoules inside a hyperbaric chamber, the strength of currently manufactured ampoules appears to be quite robust and will tolerate repeated routine compression and decompression in a medical hyperbaric chamber at normal treatment pressures, remaining usable at pressure and can be opened as normal without incident.

LIMITATIONS

More testing would need to be carried out to test breaking strain at greater pressures which may be experienced in the commercial or military industries. Neither an exhaustive list of ampoules from different manufacturers nor multiple batches of ampoules were tested. Further testing of ampoules for microscopic fractures as well as for the stability and bioavailability of the contained medication was considered, especially given the temperature fluctuations that occur with rapid compression and decompression. After discussion with colleagues, it was felt that the first step should be to simply test whether ampoules were able to be repeatedly subjected to pressure and utilised in a high pressure environment. Since this necessitated opening the ampoules at depth, any further testing was void.

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Conflicts of interest: nil

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