

Glass particle contamination of parenteral preparations of intravenous drugs in anaesthetic practice

Zabir AF, MBChB
Choy CY, FANZCA
Rusbdan R, MMed UKM
Department of Anaesthesiology and Intensive Care
Hospital Universiti Kebangsaan, Malaysia

SAJAA 2008; 14(3): 17-19

Correspondence to: Prof Choy Yin Choy, e-mail: choyyinchoy@hotmail.com

ABSTRACT

This was a prospective, randomised, single-blinded comparative study to assess the amount of glass particle contamination in single-use drug ampoules, and to compare the differences between the filter straw (B Braun Filter Straw® 5 micron), 23G hypodermic needles and 18G drawing-up needles in reducing contamination. A total of 360 ampoules of expired drugs was collected and randomised into three groups. The content of each ampoule was syringed out using either a 23G needle, an 18G needle or a B Braun 5 micron Filter Straw®. The content was then emptied onto white filter paper, which was examined under microscopy. Glass particle contaminations were seen in 15 of the 360 ampoules (4.2%). The Filter Straw® group yielded no contaminants when compared with the 18G needle group ($p = 0.001$). The difference was not significant between the Filter Straw® and the 23G needle group ($p = 0.644$). The use of smaller gauge (23G) needles prevented glass particle contamination significantly when compared to bigger (18G) needles ($p = 0.021$). It can be concluded that larger ampoules (10 ml) produce significantly ($p = 0.01$) higher percentages of contaminants, even when compared to the smaller three ampoule groups combined (1 ml, 2 ml and 5 ml).

Introduction

The issue of glass particle contamination during parenteral drug administration has received little attention in the medical literature. Glass particle contamination is known to occur on opening single-dose drug ampoules.¹⁻⁷ It is not desirable to administer particulate contaminant to patients, and anaesthetists have cause for concern as they are frequently involved with drug preparation for parenteral administration in operating theatres and intensive care units. Pain and phlebitis have been shown to be associated with particulate contamination.^{8,9} In the case of chronic silicosis from occupational exposure, it takes an average of 10 years for the patient to develop symptoms. As a corollary, it is possible that the effects of glass-contaminated parenteral injections may develop over a certain period of time.¹⁻⁵

In experimental animal models, pulmonary manifestations (thrombi, micro-emboli and varying degrees of atelectasis) and chronic fibrotic or granulomatous lesions in the intestines, kidneys and liver are among the observed complications of parenteral glass particle injections.^{1,7} Progressive nodular liver cirrhosis from silicotic fibrosis has been reported.² Although supporting data are lacking, intrathecal drug administration during subarachnoid blocks and chemotherapy with glass particle contamination is potentially hazardous.

The glass ampoules are commonly made from Type 1 borosilicate glass.^{2,4} Borosilicate consists mainly of silica (70 to 80%) and boric oxide (7 to 13%), with smaller amounts of the alkalis (sodium and potassium oxides) and aluminium oxide. This type of glass has a relatively low content of alkali

and consequently has good chemical durability and thermal shock resistance.

Various types of filters (Millipore 19G, filter needles, in-line filters) have been used in different studies to reduce the incidence of glass particle contamination. The B Braun Filter Straw® 5 micron particulate ampoule filter was used in this study. The objectives of this study were to ascertain and assess the presence of glass particle contamination in commonly used glass ampoules in anaesthesia practice and to compare the amount of glass particles between the filter straw (B Braun Filter Straw® 5 micron), 23G hypodermic needles and 18G drawing-up needles in reducing glass particle contamination.

Methods

This study was designed as a prospective, randomised, single-blind comparative study to examine the extent of glass particle contamination of single-dose drug ampoules as evident from examination under a microscope. Approval by the Dissertation/Ethics Committee was obtained in July 2006.

Ampoules containing expired drugs were obtained through the liaison clinical pharmacist from the hospital pharmacy and various drug companies. Ninety 1 ml ampoules of atropine, neostigmine, ephedrine and adrenaline, 90 2 ml ampoules of fentanyl, suxamethonium, ranitidine, metoclopramide and frusemide, 90 5 ml ampoules of atracurium, dopamine and dobutamine and 90 10 ml ampoules of calcium chloride, glyceryl trinitrate and dextrose 50% were chosen. A total of 360 samples were collected. The number of samples was determined using

Power and Sample Size Calculations (Vanderbilt) version 2.1.31 software, based on an α value of 0.05 and power of 0.90.

A single operator broke each glass ampoule and aspirated the content into an appropriate syringe, either a 5 ml or 10 ml syringe connected to either a 23G hypodermic needle, an 18G drawing-up needle or the B Braun Filter Straw[®]. Each ampoule was assigned randomly to one of the following: 23G, 18G or Filter Straw[®], and numbered from one to 360.

Ampoules were broken in a standard manner. The operator held the top of the ampoule between the thumb and index finger of his one hand while holding the bottom part firmly with the other hand. The ampoule was then snapped open, hence avoiding scraping the opposing glass surfaces. When aspirating, the ampoule was tilted slightly and the needle end was placed at the dependent area of the ampoule. This was to ensure that the particles that may have settled would be drawn out as well.

The needle was discarded. The content of the syringe was then emptied rapidly onto white filter paper (Whatman No 93 circle 125 mm, 5 microns) placed in a funnel attached to a conical flask. Each filter paper was marked with the identifying number of the syringe. The filter paper was examined under a microscope (Olympus BX40) while still wet to determine the presence of glass particles. The microscope was equipped with grids and a calibrated ocular micrometer to enable demarcation and calculation of the particle sizes.

Microscopic examination was carried out by two pathologists from the Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia who had at least three years of working experience. They were blinded to the methods of drug aspiration in order to eliminate study bias.

The number of samples containing glass particles was expressed as a percentage of the total sample in each experimental arm. Statistical analysis was performed using SPSS for Windows (version 12.0). The data were analysed by one way analysis of variance (ANOVA). A p value of less than 0.05 was deemed significant.

Results

Out of the 360 glass ampoules that were examined, 15 samples (4.2%) were contaminated with glass particles (Table I). Twenty particles of different sizes were detected, ranging from 62.5 to 250 μm^2 (mean size $87.5 \pm 47.1 \mu\text{m}^2$). Particles smaller than 62.5 μm^2 were not quantified exactly, since the minimum grid size

Table I: Total number and size of glass particles by needle size/type

	23G n = 120	18G n = 120	Filter Straw [®] n = 120
Number of ampoules (percentage) with glass particles	4 (3.3%)	11 ⁺ (9.2%)	0 (0.0%)
Total number of particles	6	14	0

⁺ Significantly higher contamination compared to 23G ($p = 0.021$)

^{*} Significantly higher contamination compared to Filter Straw[®] ($p = 0.001$)

was 62.5 μm^2 . Of the 15 contaminated ampoules, 11 (73.3%) contained a single glass particle. Three samples had two glass particles and only one contained three glass particles.

No contaminant was found in the Filter Straw[®] group. Statistical validation gave a $p = 0.001$ when compared with the 18G drawing-up needle group. However, the comparison between the Filter Straw[®] group and the 23G needle group showed no statistical difference ($p = 0.644$). The difference in glass particle contamination between the 23G and 18G groups was significant ($p = 0.021$). There was no difference between the needle groups when scrutinised for the contaminant sizes (in μm^2) or in terms of the number of particles in each contaminated sample ($p > 0.05$).

Table II shows that 10 particles (50%) out of the total of 20 came from the 10 ml ampoules. Significant differences were found when we analysed the 10 ml ampoules in contrast to the combined total of all three smaller ampoules ($p = 0.01$). Larger ampoules produced more glass contamination.

Discussion

Heiss-Harris and Verklan and Preston and Hegadoren reported that glass particle contamination has been noted in broken glass ampoules since as early as 1947.^{1,3} Different arguments have been forwarded to determine the reasons why glass particles are present. Sabon, Cheng, Stommel and Hennen looked at different types of glass ampoules, such as transparent metal etched, transparent chemical scored, amber metal etched and amber chemical scored, and found that most glass contamination occurred in transparent metal-etched glass ampoules.² The same authors postulated that the force of aspiration and the aspiration of contents from the dependent areas of drug ampoules increased the chance of detecting particulate contamination.² Others

Table II: Glass particle contamination according to ampoule size; values expressed as number (percentage).

Ampoule size	23G needle	18G needle	Filter Straw [®]	Total
1 ml	0/30 (0)	1/30 (3.3)	0/30 (0)	1/90 (0.01)
2 ml	0/30 (0)	2/30 (6.6)	0/30 (0)	2/90 (0.02)
5 ml	1/30 (3.3)	3/30 (10)	0/30 (0)	4/90 (0.04)
10 ml	3/30 (10)	5/30 (16.6)	0/30 (0)	8/90 (0.08)
Total	4/120 (3.3)	11/120 (9.2)	0/120 (0)	15/90 (0.16)

detected more glass particle contamination when using bigger ampoules than when using smaller ampoules.³⁻⁵

Preston and Hegadoren showed a strong correlation between success in aspirating the contents of ampoules with larger needle sizes, independent of the amount of contamination.³ Lye and Hwang recommended aspiration through fine-bore needles to minimise the administration of glass particles to patients.⁴ Sabon et al and Preston and Hegadoren concluded that the use of filter devices reduce the amount of glass contamination.^{2,3} Carbone-Traber, however, showed that filters were only useful during laminar flow and were less effective in forceful flow situations, e.g. “intravenous push”.⁵

Extrapolating from the available animal and adult studies, Heiss-Harris and Verklan raised concerns about premature babies in neonatal intensive care units, who are particularly at risk of glass particulate contamination via central catheters during their lengthy hospital stay.¹ Their observations showed that none of the nurses used filtered needles when aspirating drugs from glass ampoules. In our intensive care unit, for example, patients on inotropic support via central lines are also potentially exposed to glass fragments for prolonged periods.

It is worth mentioning that, since the glass ampoules are not sterile, the risk of bacterial contamination from glass particles is certainly possible.⁵⁻⁸ Although the risk might not be significant in healthy individuals, it could represent a considerable threat to immunocompromised individuals, premature neonates and septicemic patients.^{1,6}

In our study, we examined 360 ampoules and had a contamination yield of only 4.2%. We found a total of 20 glass particles, which corresponds to 0.05 particles per ampoule. The earlier studies quoted much higher percentages of contamination (14 to 57%), albeit from smaller numbers of ampoules examined.¹⁻⁵ Our findings do not match those of Lye and Hwang, who found 0.22 particles per ampoules (112 particles from 510 samples).⁴ To a certain extent, the findings of this study have contradicted the findings of earlier studies in terms of the magnitude of contamination. When present, the examiners were able to identify these contaminations down to small particles of 62.5 μm^2 on the Rosenthal Grid from the glasses' birefringences.

The small percentage of glass particle contamination in this study could be attributed to several factors. One hundred and twenty of our ampoules were transparent and were examined on white filter paper. The other 240 ampoules were amber coloured. Interestingly, all 240 amber-coloured ampoules were smaller (1, 2 and 5 ml) ampoules. As shown in earlier studies, the innate characteristics of the ampoule itself determines the amount of glass particle contamination.² Larger, transparent, metal-etched ampoules produced more contaminants.²

The light sources of the available microscopes (Olympus BX40) beamed from underneath the filter paper. Preston and Hegadoren, in comparison, used microscopes with direct overhead lighting that easily reflected the glasses' luminescence.³ Other researchers have gone so far as to coat the ampoules' necks with methylene blue and then use a spectrophotometer for analysis.⁶ Therefore it was possible that suboptimal lighting conditions might have

caused the examiners to miss seeing the particles from the transparent ampoules, despite their being present on the white filter paper.

After a lengthy consultation with the clinical statistician, the small “yield” from this study necessitated a comparison between the results of the combined small ampoules (1 ml, 2 ml and 5 ml grouped together) and that of the 10 ml ampoules for statistical analysis.

In the subset of larger ampoules (10 ml), where most of the glass particle contamination was observed, we found a significant reduction as a result of using the B Braun 5 micron Filter Straw® ($p = 0.001$). We found that there was a high incidence of more contamination involving larger ampoules. This observation corresponds with the findings of earlier studies by Sabon et al and Lye and Hwang.^{2,4}

There was a reduction in the incidence of contamination as a result of using smaller needles (23G) to aspirate the contents of ampoules (regardless of ampoule size). Our study found a significant difference in glass particle contamination between the 23G versus 18G needle group ($p = 0.021$). In comparison, Preston and Hegadoren found 57% contamination in the larger needle group (18G) compared with 14% in the 21G needle group ($p = 0.01$).³

We hence recommend the judicious use of filters or the use of smaller-gauge needles when drawing drugs from larger glass ampoules (10 ml or bigger) for the treatment of high-risk populations such as premature neonates, immunocompromised patients and septicemic patients on inotropic support. **SAJAA**

Conclusion

In this study the extent of glass particle contamination was 4.2%. There was a significant reduction in glass particle contamination as a result of using B Braun 5 micron Filter Straw® and using the 23G hypodermic needle rather than using 18G drawing-up needles.

References

1. Heiss-Harris GM, Verklan MT. Maximizing patient safety: filter needle use with glass ampoules. *J Perinat Neonatal Nurs* 2005;19(1):74-81.
2. Sabon RL, Cheng EY, Stommel KA, Hennen CR. Glass particle contamination: influence of aspiration methods and ampoule types. *Anesthesiology* 1989;70:859-62.
3. Preston ST, Hegadoren K. Glass contamination in parenterally administered medication. *J Adv Nurs* 2004;48(3):266-70.
4. Lye ST, Hwang NC. Glass particle contamination: is it here to stay? *Anaesthesia* 2003;58(1):93-5.
5. Carbone-Traber K. Glass particle contamination in single-dose ampoules. *Anesth Analg* 1986;65:1361-3.
6. Kempen PM. Glass ampoules and associated hazards. *Critical Care Medicine* 1989;17(8):812-3.
7. Furgang F. Glass particles in ampoules. *Anesthesiology* 1974;41:525-6.
8. Turco S. Infusion phlebitis. *Hosp Pharm* 1974;9(11):422-5.
9. Falchuk KH. Micro-particulate-induced phlebitis: its prevention by in-line filtration. *New Engl J Med* 1985;Jan 10:78-82.
10. Shaw NJ, Lyall EGH. Hazards of glass ampoules. *BMJ* 1985;291:13-90.
11. Meister FL. Filter needles and glass ampoules. *AACCN* 1998;18(4).
12. Lusardi P. Research corner: myth versus reality: do we need to filter medication ampoules? *AACCN* 2002;19(4).