Reducing the risk of fatal and disabling hypoglycaemia: a comparison of arterial blood sampling systems

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Background. In 2008, the National Patient Safety Agency (NPSA) published a report after 42 incidents and two deaths where glucose-containing flush solutions were attached to the arterial line. The molar concentration of 5% glucose is 277 mmol litre\(^{-1}\). Only a tiny amount of sample contamination will lead to an artificially high glucose. As the NPSA sought a solution, a bench model was constructed to compare the performance of three open and three closed arterial line systems in limiting sample contamination.

Methods. All arterial line systems were set up in a standard manner and pressurized to 300 mm Hg with 5% glucose used as the flush solution. This was connected to the 'radial artery' using an 18 G needle representing the radial cannula. The radial artery was simulated using a wide-bore extension set with 'blood' flow at 60 ml min\(^{-1}\). Blood was simulated by the addition of red dye to Hartmann's solution. Increasing multiples of arterial line dead space were aspirated and discarded. Blood samples were then obtained and glucose concentration was measured.

Results. Significant glucose contamination (3 mmol litre\(^{-1}\) ± 3.4) was detected in all open arterial line systems up to an aspiration volume of five times the dead space. No samples from the closed systems recorded glucose concentration > 1 mmol litre\(^{-1}\).

Conclusions. Recommended minimal discard volumes are inadequate in the presence of glucose as the flush solution and can lead to high blood glucose readings, inappropriate insulin use, and iatrogenic neuroglycopaenia. Our study demonstrates that the closed-loop arterial sampling system could be the universal solution sought by the NPSA.

Br J Anaesth 2010; 104: 446–51

Keywords: complications, hypoglycaemia; monitoring, intensive care; safety, equipment; safety, techniques

Accepted for publication: January 20, 2010

In July 2008, the National Patient Safety Agency (NPSA) published a ‘Rapid Response Report’ after problems with indwelling arterial lines and the associated flush solutions.\(^1\) Over a 3 yr period (2005–8), the NPSA received reports of two deaths and 82 incidents where the wrong arterial line flush solution was attached to the arterial line.\(^2\) Forty-eight per cent of those incidents involved the use of glucose-containing (4–50%) flush solutions and a further 72 separate incidents related to faulty sampling techniques.

The molar concentration of glucose in 5% glucose is 277 mmol litre\(^{-1}\). A small volume of sample contamination with 5% glucose will, therefore, result in an artificial elevation of the measured glucose of the sample. The cases reported by the NPSA (Table 1) demonstrate that sample contamination has led to inappropriate insulin administration, severe hypoglycaemia, and neuroglycopaenia causing brain damage and death.

The NPSA suggested:

(i) The clear identification of arterial lines through a system of labelling such as a continuous coloured lines running through to prevent confusion with venous lines.

(ii) The production of a universal arterial flush solution that minimizes the risk of sample contamination.
A system to prevent sample contamination from an incorrect flush solution may already be available. Closed arterial line systems have two common features such as a permanently attached, volume-restricted blood aspiration syringe and a needle-free sampling-port septum.

The purpose of this study was to compare the performance of three closed system arterial line transducer sets (Edwards Lifesciences, CA, USA; Smiths Medical International, Watford, UK; Becton Dickinson, Oxford, UK) with their partner open systems when 5% glucose is used as the flush solution.

**Methods**

Six arterial line transducer systems were tested using a bench model: three ‘open’ and three ‘closed’. The ‘open’ systems tested were TruWave™ (Edwards Lifesciences), Logical™ (Smiths Medical International), and Gabarith™ (Becton Dickinson). The ‘closed’ systems (Fig. 1) were the VAMP™ (Edwards Lifesciences), Logical™ Closed (Smiths Medical), and Safedraw™ (Becton Dickinson).

The bench model reproduced the mechanics of arterial line sampling using a blood giving set (4 mm internal diameter, 120 cm long) and a wide bore (200 cm) extension set (Baxter, Newbury, Berkshire) representing the radial artery. Arterial blood was simulated by the addition of 2 ml of red vegetable dye to 1000 ml of Hartmann’s solution which was flushed through the ‘radial artery’ at a rate comparable with radial artery flow of 60 ml min⁻¹. The flow rate was determined by the use of a measured beaker and timer over 1 min.

All arterial transducer systems were set up in a standard manner. Purposefully, a 500 ml bag of 5% glucose solution was used as flush solution rather than the recommended 0.9% saline. This was connected to the arterial transducer giving set specific to each system. The system was primed and pressurized to 300 mm Hg using a standard pressure bag (as per manufacturer’s instructions). The radial ‘cannula’ was represented by an 18 G needle placed through the self-sealing port of the simulated ‘radial artery’ and connected to the distal (patient) end of the appropriate transducer flush system (Fig. 2).

**Open system**

The sample port of the transducer set was near the distal (patient) end. The measured dead space volume of the transducer set from the sample port to the distal, patient, end was 0.6 ml (Becton Dickinson) and 1.0 ml (Edwards Lifesciences and Smiths Medical). Discord volumes during sampling from the bench-top model were multiples of the arterial line system dead space. A discard volume was aspirated followed by a 1 ml test volume. A blood gas
analyser (Radiometer Copenhagen, ABL 700 series) provided a glucose measurement. Contamination of the sample was considered if the recorded glucose was $>0$ mmol litre$^{-1}$ and a clinically significant contamination if $>1$ mmol litre$^{-1}$. The discard volumes were 1, 2, 3, 4, and 5 multiples of the measured system dead space and each system was tested 10 times. This resulted in 50 measurements for each open system tested.

**Closed system**

The closed-loop transducer systems were all single line systems with a permanently attached syringe of varying capacity—2 ml (Safedraw), 12 ml (VAMP), and 10 ml (Logical). This volume was aspirated into the sampling system. Each system has a custom-made needle-safe sampling device from which a test sample of 1 ml was obtained. Otherwise, the closed system bench top arterial model was comparable with that used in the open system model. Each system was tested 10 times, but as there was no variable discard volume, 10 measurements were attained for each closed system.

All analyses were performed using the Statistical Package for Social Sciences (version 12, SPSS Inc., Chicago, IL, USA).

**Results**

Table 2 presents a summary of the glucose concentration from all open and closed arterial line sampling systems collectively. Glucose was detected in all the open arterial
line sampling systems tested, up to an aspiration volume of five times the system dead space.

The performance of the individual open and closed systems is represented graphically in Figure 3. Figure 3c highlights those samples recording a glucose concentration > 1 mmol litre\(^{-1}\). No samples from the closed systems recorded a glucose concentration > 1 mmol litre\(^{-1}\) (Fig. 3a).

Our data also demonstrated that the amount of sample contamination required to increase the measured blood glucose by 1 mmol litre\(^{-1}\) is very small at only 0.004 ml of 5% glucose (Fig. 4).

### Discussion

The disparity between the molar concentration of 5% glucose (277 mmol litre\(^{-1}\)) and the molar concentration of glucose in a typical arterial blood sample (<11 mmol...
litre\(^{-1}\)) will lead to a clinically significant elevation of measured blood glucose with contamination by only 0.004 ml of 5% glucose (Fig. 4). Where higher concentrations of glucose are inadvertently used as the flush solution (such as 50% glucose, Table 1), the volume required to contaminate the blood sample would be even smaller. For arterial line sampling, international guidelines recommend a minimal discard volume of blood equal to twice the dead space of the sampling line distal to the sample port. In our sample, this was 1.2, 2.0, and 2.0 ml for the BD, Smiths Medical, and Edwards Lifesciences systems, respectively. However, this presumes the flush solution to be 0.9% saline. This study has observed that where 5% glucose is the flush solution, a discard volume equal to five times the dead space did not prevent clinically significant sample contamination in the open systems tested.

The consequence of sample contamination is the inappropriate administration of insulin and risk of subsequent iatrogenic neuroglycopaenia. Our study has observed the efficacy of three closed arterial sampling systems in preventing iatrogenic sample contamination during simulated sampling when compared with their counterpart open systems.

Adverse events in the critical care environment are common, and the most common errors involve drug prescribing or administration. The American Institute of Healthcare Improvement, American College of Endocrinologists, and the NPSA\(^1\) have identified inappropriate insulin administration as being responsible for the most frequent cases of drug-related harm. Though the importance of glucose control in the intensive care environment is well recognized, both hyperglycaemia and hypoglycaemia are associated with increased morbidity\(^{10-15}\) and hypoglycaemia can easily go unnoticed in the sedated patient. Arterial line sampling is the recommended mainstay of blood glucose monitoring in the intensive care environment, with up to 46 000 blood gas analyses performed in a single intensive care unit in 1 yr.\(^{17}\) The numbers of arterial line sampling errors reported to the NPSA therefore appear low, but this will represent under-reporting of the true incidence that occurs.\(^{18-21}\) Factors involved in under-reporting include time constraints, unsatisfactory reporting processes, deficiencies in knowledge, cultural norms, inadequate feedback, beliefs about risk, and a perceived lack of value in the process.\(^{20,21}\)

The benefits of closed-loop sampling systems extend beyond that of minimizing sample contamination as reported. These include reduced iatrogenic anaemia from frequent sampling and loss of discard volume, reduced wrong route drug errors through the absence of luer ports, and the potential to limit line site infection through the use of closed sampling ports.

Human factors ensure that iatrogenic harm through incorrect arterial blood glucose sampling will persist without a systems-based solution, as recommended by the NPSA. Our study demonstrates a reliable and safe means of measuring blood glucose that accommodates the accidental use of 5% glucose as the flush solution. It demonstrates that the closed-loop arterial sampling system, already in existence and in routine use, could be the universal solution sought by the NPSA.

**Funding**

The arterial lines tested were donated by Edwards Lifesciences (CA, USA), Smiths Medical (Watford, UK), and Becton Dickinson (Oxford, UK). Other costs incurred were funded internally.
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