AAGBI SAFETY GUIDELINE

Arterial line blood sampling: preventing hypoglycaemic brain injury

Published by
The Association of Anaesthetists of Great Britain & Ireland

September 2014

This guideline was originally published in *Anaesthesia*. If you wish to refer to this guideline, please use the following reference:

Association of Anaesthetists of Great Britain and Ireland. Arterial line blood sampling: preventing hypoglycaemic brain injury 2014. *Anaesthesia* 2014, **69**: pages 380–385

This guideline can be viewed online via the following URL:
http://onlinelibrary.wiley.com/doi/10.1111/anae.12536/abstract

Guidelines

Arterial line blood sampling: preventing hypoglycaemic brain injury 2014

The Association of Anaesthetists of Great Britain and Ireland

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Summary

Drawing samples from an indwelling arterial line is the method of choice for frequent blood analysis in adult critical care areas. Sodium chloride 0.9% is the recommended flush solution for maintaining the patency of arterial catheters, but it is easy to confuse with glucose-containing bags on rapid visual examination. The unintentional use of a glucose-containing solution has resulted in artefactually high glucose concentrations in blood samples drawn from the arterial line, leading to insulin administration causing hypoglycaemia and fatal neuroglycopenic brain injury. Recent data show that it remains a common error for incorrect fluids to be administered as arterial line flush infusions. Adherence to the National Patient Safety Agency's 2008 Rapid Response Report on this topic may not be enough to prevent such errors. This guideline makes detailed recommendations on the prescription, checking and administration of arterial line infusions in adult practice. We also make recommendations about storage, arterial pressure monitoring and sampling systems and techniques. Finally, we make recommendations about glucose monitoring and insulin administration. It is intended that adherence to these guidelines will reduce the frequency of sample

contamination errors in arterial line use and capture events, when they do occur, before they cause patient harm.

This is a consensus document produced by expert members of a Sprint Working Party established by the Association of Anaesthetists of Great Britain and Ireland (AAGBI). It has been seen and approved by the AAGBI Board.
Accepted: 5 November 2013

- *What other guideline statements are available on this topic?*
  In July 2008, a National Patient Safety Agency (NPSA) Rapid Response Report was released [1], highlighting examples of patient harm resulting from glucose-containing flush infusions contaminating blood samples drawn from arterial lines [2, 3]. Subsequently, it was reported to the Safe Anaesthesia Liaison Group in 2011 that the NPSA had received 169 further incident reports, featuring 31 glucose monitoring errors (personal communication, Prof. D. Cousins, NHS England). The Medicines and Healthcare products Regulatory Authority (MHRA) issued a Drug Safety Update on the issue in 2012 [4].
- *Why was this guideline developed?*
  Experiment and experience show that compliance with the procedures required in the NPSA's 2008 Rapid Response Report, even with good sampling technique using a simple open arterial line system, is not sufficient to prevent injury or death arising from sample contamination error. In a series of 102 cases where a glucose-containing solution was incorrectly infused, sample contamination error occurred in 30 (personal communication, Prof. D. Cousins, NHS England). Recent data show that using incorrect arterial line fluid infusions is a common error, with an average of one such event reported to the National Reporting and Learning System every week [5]. More than 30% of intensive care units have reported recent arterial line errors, with a further 30% reporting errors from operating theatres or the emergency department [5]. In one case, neuroglycopenia contributed to the patient's death [6].
- *How and why does this statement differ from existing guidelines*?
  The Working Party identified three error-prone processes that can lead to iatrogenic hypoglycaemia. Our recommendations are

designed to address each of these processes and reduce the likelihood of active errors and latent risks leading to patient harm [7]. The error-prone processes are:

  - use of arterial flush solution (prescription, dispensing, checking and administration)
  - blood sampling technique for glucose concentration measurement
  - administration of insulin to treat apparent hyperglycaemia.
- For each error-prone procedure, the Working Party systematically considered whether it was possible or practicable to: eliminate the procedure; apply safeguard technology; use warning or alarm systems; specify training requirements for practitioners; and protect the patient from the consequences of occasional error.

  The evidence that informs these guidelines mostly concerns arterial blood sampling in adult patients. Our recommendations can also be applied to venous cannulae that are flushed and used for blood sampling. There may be additional considerations for paediatric practice that are outside our remit.

Basic knowledge for all practitioners

'Dextrose' and 'glucose' are interchangeable biological terms for dextrorotatory glucose ($C_6H_{12}O_6$). Figure 1 illustrates the arrangement of 'open' and 'closed' systems for maintaining patency and drawing blood samples from flushed vascular access systems. The open system has a single three-way tap, close to the vascular catheter, that is used for both removing residual flush solution and obtaining the blood sample. The volume of residual fluid between the sampling point and the bloodstream is referred to as the dead space. To prevent contamination of a blood sample with flush solution, it has been recommended that 3× dead space volume be withdrawn and discarded (or saved for return to the circulation) before a sample is taken [8]. However, bench-top experiments have shown that significant glucose contamination of the blood sample occurs even with 5× dead space removal when using an open arterial line sampling system with a glucose 5% flush solution [9]. A solution of glucose 5% contains approximately 280 $mmol.l^{-1}$, hence contamination of a 1-ml blood sample with just 0.03 ml flush solution would conceal true hypoglycaemia or make a normal sample hyperglycaemic, potentially leading to inappropriate insulin therapy. Erroneous administration of glucose 10% or 20% would result in even greater

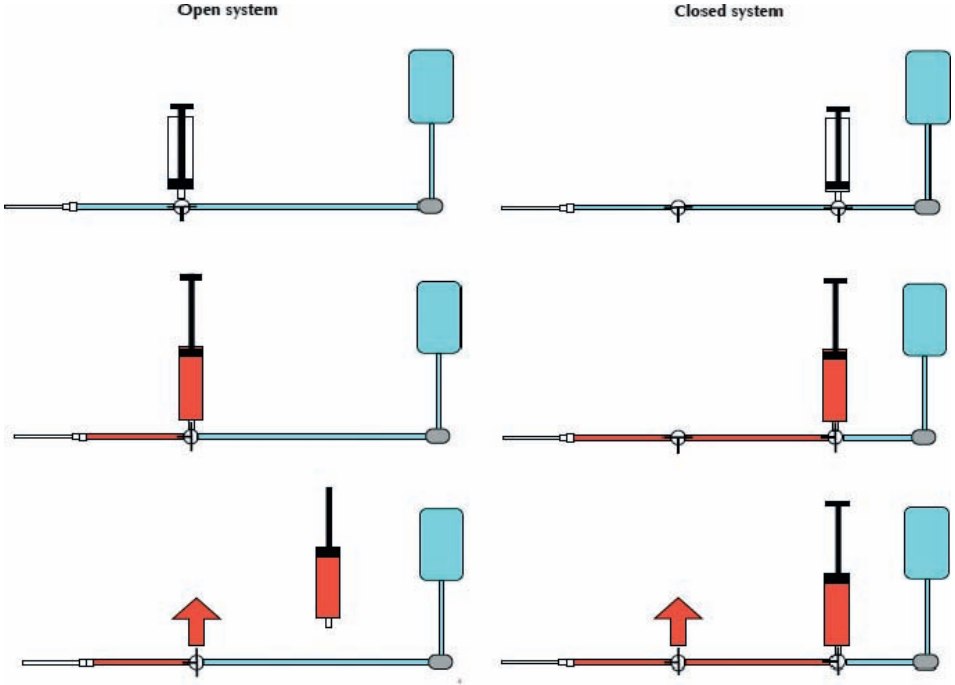

Figure 1 Open and closed systems for sampling from arterial lines. The syringe indicated is for removal of dead space volume and the red arrow indicates the sample drawing point.

contamination. With sodium chloride 0.9% flush, only gross sample contamination (e.g. due to incorrect sampling technique) will cause dangerous sampling errors. Contamination of a sample with heparinised saline also leads to artefactually increased phosphate concentrations. Erratic or highly varying sequential test results should heighten the suspicion of blood sample contamination error.

The closed system has a port for removal of dead space beyond a separate sampling point and, if used as intended by its designers, effectively eliminates the risk of significant contamination of the sample [9]. Moreover, it reduces the risk of bacteraemia and minimises wastage of blood because the withdrawn flush and blood can be returned to the circulation without opening the system.

Nervous tissue is not able to sustain functional or basal metabolic activity during hypoglycaemia, and prolonged neural glucose deprivation (neuroglycopenia) leads to permanent or fatal neural injury. Hypoglycaemia reduces conscious level and causes sympathetically mediated symptoms of anxiety, tachycardia, tachypnoea, pupillary dilation and sweating. Beta-blocker therapy blunts some of these symptoms. Hypoglycaemia is difficult to diagnose clinically in patients with an altered level of consciousness and in those treated with exogenous catecholamines. In these patients, practitioners should therefore check for hypoglycaemia in the presence of a new increase in heart rate or respiratory rate, sweating, convulsions, pupillary changes, or a fall in conscious level. Continuous electroencephalography has the potential to detect neuroglycopenia in monitored patients [10]. Fatal neuroglycopenic brain injury can occur within two hours of the onset of hypoglycaemia [2]. Neuroglycopenia is therefore not reliably prevented by routine checking of glucose levels (e.g. once per nursing shift) with blood from an alternative site.

Sodium chloride 0.9% with glucose 5% has been recommended as an intravenous fluid for use in paediatric practice [11]. Figure 2 illustrates how this fluid is particularly easy to confuse with sodium chloride 0.9%. Currently, at least twelve other fluids containing combinations of sodium chloride, glucose and potassium exist for use in a variety of clinical circumstances. They all carry increased risk of misidentification, accidental use as arterial line flush solution and glucose contamination of blood samples.

Peripheral glucose testing by pricking a finger or ear lobe may be inaccurate in patients with poor peripheral perfusion, on vasopressor therapy, or with severe peripheral oedema [12]. Continuous intravascular glucose

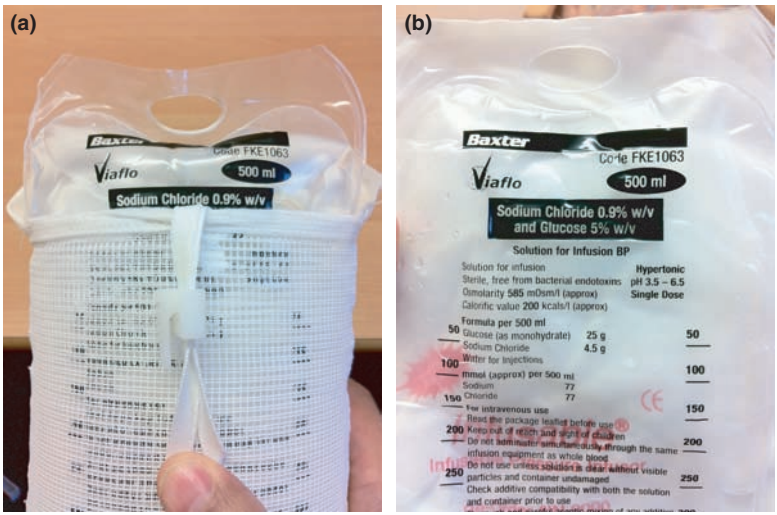

Figure 2 Appearance of sodium chloride 0.9% and glucose 5% fluid bag (a) when placed inside a pressure bag and (b) when removed, showing the ease of confusion with plain sodium chloride. Reproduced from [6], with permission.

monitoring is under development for introduction into clinical practice [13, 14], but until that technique is established, it is necessary to draw frequent blood samples for glucose analysis to guide insulin therapy in critically ill patients.

Recommendations

The Working Party's recommendations apply to any clinical areas where blood is sampled from arterial access devices and includes critical care areas, operating theatres and emergency departments.

Policy and training

Hospitals must raise awareness among relevant staff of the serious patient harm that can result from arterial line sample contamination errors and must have a policy that defines local procedures for arterial line use, including prescribing, administering and monitoring flush solutions and blood sampling technique.

Policies about the prescribing, administering and monitoring of intravenous infusions and policies about intravenous insulin therapy

should be cross-referenced to the arterial line and blood sampling policy.

All staff involved in the insertion of, management of, or sampling from, arterial lines must be appropriately trained and competent to deliver the standards set out in the policy, and performance against these standards should be regularly audited.

Fluids for flush infusions

Sodium chloride 0.9%, with or without heparin, should be the only solution to be used for arterial line infusion and flushing. Blood sampling from a cannula lumen that carries other solutions is not recommended.

Identifying arterial lines

Arterial infusion lines must be clearly identifiable. Labels and colour differentiation are appropriate measures to achieve this.

Fluid stock and storage

In clinical areas that use arterial lines, bags of sodium chloride 0.9% for use as arterial line flush should be stored away from fluids for intravenous use. Bags should be stored in a suitable receptacle and not scattered across a shelf.

Only those fluid solutions in regular use should be stored in a clinical area. For example, sodium chloride 0.9% with glucose 5%, which is recommended for use in paediatric practice, should not be stored in clinical areas where paediatric practice is unusual. If practicality dictates that such solutions must be stored, an additional risk assessment and management plan must be made to prevent their erroneous use.

Prescription and setting up

An arterial line flush solution must be documented by prescription or record of administration (e.g. anaesthetic chart) or standard operating procedure as defined in the hospital's arterial line policy.

The flush solution must be independently double-checked by a second practitioner before setting up and attaching to an arterial line. Also known as independent validation, an independent double-check of a high-alert medication is a procedure in which two clinicians separately check, alone and apart from each other, then compare results of each component of prescribing, dispensing and verifying the high-alert medication before administering it to the patient [15].

Pressurising devices

All pressurising devices must be designed to permit unimpaired inspection of the contained flush infusion bag while in use. A fully transparent front panel is strongly recommended.

Checking during use

The flush infusion bag must be independently double-checked at least once during each nursing shift and whenever nursing care of the patient is handed over. This double-check must include removal of the flush bag from its pressurising device (Fig. 2).

Sampling techniques

To avoid sample contamination with flush infusions, the use of 'closed' arterial line sampling systems is recommended.

Where an 'open' system is to be used for blood sampling, inevitable contamination must be kept to a minimum by making the dead space volume between the sampling port and the arterial lumen as small as practicable in the clinical situation. The syringe used for removal of dead space volume must be readily distinguishable from the sampling syringe. Throughout the sampling process and until the sample syringe is removed, the sampling technique must avoid flush solution's entering the dead space, the sample or any three-way tap at the sampling site.

Glucose concentration thresholds

When an arterial line is used to take blood samples for measurement of blood glucose concentrations, a value that is unexpectedly high must trigger a medical review and a check of the blood sampling system for possible sample contamination error. The source of the blood sample should be checked to ensure no possibility of sample contamination. If this is not possible, a confirmatory sample must be drawn from the most appropriate alternative site.

Initiating and increasing insulin infusions

Before commencing an insulin infusion in a patient not previously known to be an insulin-dependent diabetic and before increasing an insulin infusion rate above a policy-defined threshold (e.g. 6 $IU.h^{-1}$) on the basis of samples drawn from a flushed line, there must be a medical review. The source of the blood sample should be checked to ensure no possibility of sample contamination. If this is not possible, a confirmatory sample must be drawn from the most appropriate alternative site.

Abnormal blood tests

A blood test that shows an unexpected abnormality or unusual variation from previous results should prompt a check of the source of the blood sample to ensure no possibility of sample contamination. If this is not possible, a confirmatory sample must be drawn from the most appropriate alternative site.

Recording trends in measured glucose levels and physiological variables

Variations in blood chemistry and vital signs are easier to appreciate from a graphic trend display, which may facilitate earlier detection of hypoglycaemia. Graphic trend displays, particularly of glucose readings and of vital signs including heart rate and respiratory rate, are recommended.

Monitoring for signs of hypoglycaemia

Hypoglycaemia should be considered and specifically checked for in any sedated or unconscious patient receiving insulin therapy who exhibits a new increase in heart rate or respiratory rate, or sweating, pupillary changes or a fall in conscious level.

Incident reporting

Any incident causing potential or actual patient harm related to contamination of blood samples obtained from an arterial line should be reported to both local and national incident reporting systems. Any incident causing patient harm must be disclosed to the patient or his/her next of kin in accordance with local policy.

National monitoring of incidents

National patient safety organisations should monitor the occurrence of incidents relating to arterial line and flush infusion errors to determine whether further actions are needed to reduce their incidence.

Engineered solutions

Equipment manufacturers, pharmaceutical suppliers and clinicians should engage in a collaboration to develop safer systems for the prevention of arterial cannula clotting. Potential solutions to be considered will include:

- highly visible and easily distinguishable fluid bags for exclusive use with arterial pressure monitoring and sampling systems.

- special connections between the fluid bag and the arterial pressure monitoring and sampling system.
- integrated systems, possibly incorporating both the above solutions.

Supporting healthcare providers when errors occur

When errors occur, staff and organisations must "*promise to learn and commit to act*" [16]. It is often the systems, procedures, conditions, environment and constraints faced by healthcare providers that lead to patient safety problems. Rather than blame individuals, trust should be placed in the goodwill and good intentions of the staff and attention focused on learning from (and remembering) errors [16, 17].

Acknowledgements

We are grateful to all individuals and organisations who provided comments on the first draft of this guideline, and to the following people who attended a Consensus Conference for Stakeholders at 21 Portland Place on 10 October 2013: Chris Quinn (Beckton Dickson); Iswori Thakuri and Markku Ahtiainen (British Anaesthetic and Recovery Nurses Association); Catherine Plowright (British Association of Critical Care Nurses); Tim Lewis (College of Operating Department Practitioners); Jane Harper (Intensive Care Society); Caroline Wilson (Group of Anaesthetists in Training); Archie Naughton (AAGBI Lay Representative); Desmond Watson (Medical and Dental Defence Union of Scotland); Gary Duncum and Hayley Bird (Smiths Medical); Sharon Maris (Teleflex); Clare Crowley and Mark Tomlin (UK Clinical Pharmacy Association); Graham Milward (Vygon).

Competing interests

No external funding and no competing interests declared.

References

1. National Patient Safety Agency. Infusions and sampling from arterial lines. Rapid Response Report. NPSA/2008/RRR006. http://www.nrls.npsa.nhs.uk/resources/?EntryId45=59891 (accessed 01/08/2013).
2. Sinha S, Jayaram R, Hargreaves CG. Fatal neuroglycopaenia after accidental use of a glucose 5% solution in a peripheral arterial cannula flush system. *Anaesthesia* 2007; **62**: 615–20.
3. Panchagnula U, Thomas AN. The wrong arterial line flush solution. *Anaesthesia* 2007; **62**: 1077–8.
4. Medicines and Healthcare products Regulatory Authority. Glucose solutions: false blood glucose readings when used to flush arterial lines, leading to incorrect insulin

administration and potentially fatal hypoglycaemia. *Drug Safety Update* 2012; **5**: A2. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON175433 (accessed 01/08/2013).
5. Leslie R, Gouldson S, Habib N, et al. Management of arterial lines and blood sampling in intensive care: a threat to patient safety. *Anaesthesia* 2013; **68**: 1114–19.
6. Gupta KJ, Cook TM. Accidental hypoglycaemia caused by an arterial flush drug error: a case report and contributory causes analysis. *Anaesthesia* 2013; **68**: 1178–87.
7. Reason J. Human error: models and management. *British Medical Journal* 2000; **320**: 768–70.
8. Burnett RW, Covington AK, Fogh-Andersen N. Recommendations on whole blood sampling, transport, and storage for simultaneous determination of pH, blood gases, and electrolytes. International Federation of Clinical Chemistry Scientific Division. *Journal of the International Federation of Clinical Chemistry* 1994; **6**: 115–20.
9. Brennan KA, Eapen G, Turnbull D. Reducing the risk of fatal and disabling hypoglycaemia: a comparison of arterial blood sampling systems. *British Journal of Anaesthesia* 2010; **104**: 446–51.
10. Remvig LS, Elsborg R, Sejling AS, et al. Hypoglycemia-related electroencephalogram changes are independent of gender, age, duration of diabetes, and awareness status in type 1 diabetes. *Journal of Diabetes Science and Technology* 2012; **6**: 1337–44.
11. National Patient Safety Agency. Reducing the risk of hyponatraemia when administering intravenous infusions to children. Patient Safety Alert. NPSA/2007/22. http://www.nrls.npsa.nhs.uk/resources/?EntryId45=59809 (accessed 01/08/2013).
12. Jacobi J, Bircher N, Krinsley J, et al. Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. *Critical Care Medicine* 2012; **40**: 3251–76.
13. Beier B, Musick K, Matsumoto A, Panitch A, Nauman E, Irazoqui P. Toward a continuous intravascular glucose monitoring system. *Sensors (Basel)* 2011; **11**: 409–24.
14. Romey M, Jovanovic L, Bevier W, Markova K, Strasma P, Zisser H. Use of an intravascular fluorescent continuous glucose sensor in subjects with type 1 diabetes mellitus. *Journal of Diabetes Science and Technology* 2012; **6**: 1260–6.
15. ISMP Medication Safety Alert! Nurse Advize-ERR Volume 6 Edition 12 December 2008. http://www.ismp.org/Newsletters/nursing/Issues/NurseAdviseERR200812.pdf (accessed 13/10/2013).
16. National Advisory Group on the Safety of Patients in England. A promise to learn, a commitment to act – improving the safety of patients in England. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/226703/Berwick_Report.pdf (accessed 13/10/2013).
17. Smith A. Lest we forget: learning and remembering in clinical practice. *Anaesthesia* 2013; **68**: 1099–103.

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