

Context-sensitive fluid administration: what, when and how much?

MFM James^{a*}

^aDepartment of Anaesthesia, University of Cape Town, Cape Town

*Corresponding author: Michael James, e-mail: mike.james@uct.ac.za

Keywords: context-sensitive fluid administration, fluid therapy, benefits, harm

As with all drugs, fluid therapy must be regarded as context sensitive. If a drug is given in the wrong context to the wrong patient and without a proper indication, only the side-effects of the drug will be seen, with probable demonstrable harm. Fluids, as with all drugs, should only be administered in the proper context in which consideration is given to the pharmacological properties of the agent being administered, the condition for which the drug is being given, and the expected benefits and possible harm. Without clear consideration of the context, drug administration is negligent and harmful.

Intravenous fluids should only be administered in the context for which they are intended. If the context is the replenishment of intracellular fluid, a very different fluid composition will be needed compared to that used in the context in which the objective is the replenishment of extracellular fluid. In the context of plasma volume replacement, the context is again different, and a different fluid composition is needed.

The pathological circumstances in which fluids are administered thus forms the basic determinant of the context in which the fluids are to be administered, and ought to determine the composition, and dose and rate at which those fluids are to be administered. The current fluid debate has been seriously compromised by the failure of numerous authors to consider the context in which various fluid trials have been conducted.^{1,2} The context in which recent fluid trials have been conducted can be divided into three patient categories: the critically ill in the intensive care unit, and general surgical and cardiac surgical. A physiologically important difference between the critically ill patients and the others lies in the state of the endothelial glycocalyx.²

The endothelial glycocalyx is a complex structure that lines healthy blood vessel walls. It comprises sulphated proteoglycans, hyaluronic acid, heparan sulphate, glycoproteins and plasma proteins, and forms a surface layer that binds the plasma proteins, creating the functional oncotic pressure gradient across the vascular endothelium.³ If this layer is intact, the oncotic volume effect of the colloids far exceeds that of the crystalloids.⁴

The choice of solution in context-sensitive fluid therapy depends on the objective of the treatment. If the intention is to replace free water or intracellular water, a low-sodium, dextrose-containing solution is appropriate, with the volume administered being determined by a clinical judgement of the

degree of dehydration. If the objective is to replace extracellular fluid, the appropriate solution is a crystalloid with an electrolyte composition resembling extracellular fluid. The volume of such fluid is again context sensitive and should be calculated from any estimated deficit in the extracellular space, together with ongoing requirements for fluid replacement. Such a solution should not impose a metabolic load in terms of its ion composition, and should not induce major acid-base disturbances. Solutions such as "normal" saline consistently induce metabolic acidosis,⁵ and may result in an increased incidence of complications,⁶ and possibly increased mortality.⁷ However, the consistent demonstration that crystalloid overload is harmful is the clearest evidence that we have in the field of fluid therapy.⁸⁻¹⁰

In the context of pure hypovolaemia, large volumes of crystalloid solutions are required to replace lost blood volume.¹¹ In the context of acute intravascular hypovolaemia, logic dictates that the most appropriate fluid to be administered be one that should most resemble the lost volume, such as a blood, plasma or a colloid solution, to effectively re-expand the vascular compartment. It has been clearly demonstrated in animal models, which lack the unpredictable variability of the clinical situation, that colloid solutions are 3-4 times as effective as crystalloid in the face of hypovolaemic shock secondary to blood loss.¹¹ The synthetic colloids were developed as a possible solution to the combined problems of cost, lack of availability and risk associated with human-derived colloid solutions, such as albumin. Critical care studies performed on patients already stabilised in the intensive care unit were performed in an inappropriate context in which there was no clear evidence for hypovolaemia, no appropriate dosage regime and no clear protocol regarding important secondary end-points, such as the use of renal replacement therapy.^{12,13} In the latter study, the context was entirely one of sepsis, in which prior haemodynamic stabilisation had already been achieved, in many cases with colloid.

Current evidence supports the use of colloid solutions, such as modern hydroxyethyl starch, in the context of perioperative and trauma medicine, when acute plasma volume changes occur, if plasma volume expansion is appropriate and when haemodynamic stabilisation is undertaken in the acute phase.¹⁴⁻¹⁶

The question of the appropriate volumes of fluid to be administered in the perioperative period remains contentious. It has been suggested that the most logical approach to perioperative fluid therapy should be to target "zero balance"

in which the patient's weight from the first postoperative day is within a 2 kg range of the preoperative value.¹⁷ A recent review offers reasonable guidelines. Crystalloid should be administered, and guided by the concept of "zero balance", to patients with mild to moderate intercurrent disease undergoing moderate surgery. When the underlying disease state of the patient is more serious or the surgery more advanced, a mix of crystalloid and colloid fluid therapy is recommended, preferably guided by some form of goal-directed fluid therapy.¹⁸

References

- Weiskopf RB. Equivalent efficacy of hydroxyethyl starch 130/0.4 and human serum albumin: if nothing is the same, is everything different? The importance of context in clinical trials and statistics. *Anesthesiology*. 2013;119(6):1249-1254.
- Weiskopf RBMD. Hydroxyethyl starches: a tale of two contexts: the problem of knowledge. *Anesth Analg*. 2014;119(3):509-513.
- Weinbaum S, Tarbell JM, Damiano ER. The structure and function of the endothelial glycocalyx layer. *Annu Rev Biomed Eng*. 2007;9:121-167.
- Jacob M, Chappell D. Reappraising Starling: the physiology of the microcirculation. *Curr Opin Crit Care*. 2013;19(4):282-289.
- Orbegozo Cortés D, Rayo Bonor A, Vincent JL. Isotonic crystalloid solutions: a structured review of the literature. *Br J Anaesth*. 2014;112(6):968-981.
- Shaw AD, Bagshaw SM, Goldstein SL, et al. Major complications, mortality, and resource utilization after open abdominal surgery: 0.9% saline compared to Plasma-Lyte. *Ann Surg*. 2012;255(5):821-829.
- McCluskey SA, Karkouti K, Wijeyesundera D, et al. Hyperchloremia after noncardiac surgery is independently associated with increased morbidity and mortality: a propensity-matched cohort study. *Anesth Analg*. 2013;117(2):412-421.
- Brandstrup B, Tonnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg*. 2003;238(5):641-648.
- Nisanevich V, Felsenstein I, Almog G, et al. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology*. 2005;103(1):25-32.
- Boyd JH, Forbes J, Nakada TA, et al. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. *Crit Care Med*. 2011;39(2):259-265.
- Roger C, Muller L, Deras P, et al. Does the type of fluid affect rapidity of shock reversal in an anaesthetized-piglet model of near-fatal controlled haemorrhage? A randomized study. *Br J Anaesth*. 2014;112(6):1015-1023.
- Myburgh JA, Finfer S, Bellomo R, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med*. 2012;367(20):1901-1911.
- Perner A, Haase N, Guttormsen AB, et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. *N Engl J Med*. 2012;367(2):124-134.
- Van der Linden P, James M, Mythen M, Weiskopf RB. Safety of modern starches used during surgery. *Anesth Analg*. 2013;116(1):35-48.
- James MF, Michell WL, Joubert IA, et al. Resuscitation with hydroxyethyl starch improves renal function and lactate clearance in penetrating trauma in a randomized controlled study: the FIRST trial (Fluids in Resuscitation of Severe Trauma). *Br J Anaesth*. 2011;107(5):693-702.
- Annane D, Siami S, Jaber S, et al. Effects of fluid resuscitation with colloids vs crystalloids on mortality in critically ill patients presenting with hypovolemic shock: the CRISTAL randomized trial. *JAMA*. 2013;310(17):1809-1817.
- Brandstrup B, Svendsen PE, Rasmussen M, et al. Which goal for fluid therapy during colorectal surgery is followed by the best outcome: near-maximal stroke volume or zero fluid balance? *Br J Anaesth*. 2012;109(2):191-199.
- Miller TE, Roche AM, Mythen M. Fluid management and goal-directed therapy as an adjunct to Enhanced Recovery After Surgery (ERAS). *Can Journal Anaesth*. 2015;62(2):158-168.



Total Pain Solution



Moderate to moderately severe pain in adults¹

Rapidly-acting, longer duration, multi-modal, analgesic²

Oral administration²



Severe, chronic, intractable pain³

24-hour pain control⁴
Oral administration⁴
Once-daily dosing⁴



Chronic intractable pain⁵

Continuous 72-hour drug delivery⁵
Transdermal administration⁵
Lower incidence and impact of adverse effects vs. oral opioids⁵



TRAMACET® tablets. Composition: Each tablet contains 37.5 mg tramadol hydrochloride and 325 mg paracetamol. Reg. No. 35/2.9/0010. Full prescribing information refer to the package insert. (May 2008)

JURNISTA® 4 mg extended-release tablets. Each JURNISTA® 4 mg extended-release tablet contains 4.36 mg and delivers 4 mg hydromorphone hydrochloride, equivalent to 3.56 mg hydromorphone base. Reg. No. 41/2.9/1136. **JURNISTA**® 8 mg extended-release tablets. Each JURNISTA® 8 mg extended-release tablet contains 8.72 mg and delivers 8 mg hydromorphone hydrochloride, equivalent to 7.12 mg hydromorphone base. Reg. No. 41/2.9/1130. **JURNISTA**® 16 mg extended-release tablets. Each JURNISTA® 16 mg extended-release tablet contains 16.35 mg, and delivers 16 mg hydromorphone hydrochloride, equivalent to 14.24 mg hydromorphone base. Reg. No. 41/2.9/1131. Full prescribing information refer to the package insert. (October 2011)

DUROGESIC® 12 mcg/h transdermal patch. Each 5.25 cm² transdermal patch contains 2.1 mg fentanyl delivering 12.5 mcg fentanyl/h. Reg. No. A40/2.9/0203

DUROGESIC® 25 mcg/h transdermal patch. Each 10.5 cm² transdermal patch contains 4.2 mg fentanyl delivering 25 mcg fentanyl/h. Reg. No. 28/2.9/0288

DUROGESIC® 50 mcg/h transdermal patch. Each 21 cm² transdermal patch contains 8.4 mg fentanyl delivering 50 mcg fentanyl/h. Reg. No. 28/2.9/0289

DUROGESIC® 75 mcg/h transdermal patch. Each 31.5 cm² transdermal patch contains 12.6 mg fentanyl delivering 75 mcg fentanyl/h. Reg. No. 28/2.9/0290

DUROGESIC® 100 mcg/h transdermal patch. Each 42 cm² transdermal patch contains 16.8 mg fentanyl delivering 100 mcg fentanyl/h. Reg. No. 28/2.9/0291

For full prescribing information, refer to the latest package insert (March 2013).

References: 1. Tramacet® tablets package insert. May 2008. 2. Dhillon S. Tramadol/paracetamol fixed-dose combination. *Clin Drug Invest* 2010;30(10):711-738. 3. Jurnista® extended-release tablets package insert. Oct 2011. 4. Drover DR, Angst MS, Valle MS, et al. Input characteristics and bioavailability after administration of immediate and a new extended-release formulation of hydromorphone in healthy volunteers. *Anesthesiology* 2002; 97(4):827-836. 5. Durogesic® transdermal patches package insert. March 2013. 6. Kornick CA, Santiago-Palma J, Moryl N, et al. Benefit-risk assessment of transdermal fentanyl for the treatment of chronic pain. *Drug Safety* 2003;26(13):951-973.

JANSSEN PHARMACEUTICA (PTY) LTD/EDMS) BPK; (Reg. No./Regnr. 1980/011122/07); Building 6, Country Club Estate, 21 Woodlands Drive, Woodmead, 2191. www.janssen.co.za. Medical Info Line: 0860 11 11 17. Cert. no.: PHZA/PAI/0813/0001.