

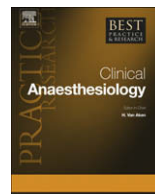


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Preface

Infusion therapy in anaesthesia and intensive care: Let's stop talking about 'wet' and 'dry'!

Topics related to fluid management are among the most controversially and intensively discussed ones in both research and daily clinical practice. In this issue of Best Practice & Research Clinical Anaesthesiology entitled 'VOLUME REPLACEMENT IN ANAESTHESIA AND INTENSIVE CARE', hot topics in this field are thoroughly outlined by internationally recognised experts in this field.

Whereas traditional infusion concepts often aimed at keeping the patient 'wet', newer studies indicated that a more restrictive infusion regimen may be preferable compared with liberal strategies. Motivated by the positive study results of Lobo et al.¹ and Brandstrup et al.², a kind of paradigm shift has recently been noticed in clinical practice. However, it should be taken into consideration that the terms 'restrictive', 'conservative', 'standard', 'liberal', etc., have no clear definitions, and sometimes imply the same, sometimes contradictory, approaches. Current evidence suggests that the patient should not be kept 'dry', but treated according to the principles of goal-directed therapies that compensate for individual needs.³ In this context, it appears to be essential that the primary objective of perioperative infusion therapy is maintenance of intravascular normovolaemia. To achieve this target, it is crucial to discriminate between fluid substitution (i.e., infusion of sensible and insensible fluid losses) and volume therapy (i.e., replacement of losses from the vascular compartment). Whereas fluid deficits can best be compensated by infusion of balanced electrolyte solutions, iso-oncotic colloids (in balanced carrier solutions) are suitable to replace intravascular volume losses, until the individual transfusion trigger is met. Pharmacokinetic models, such as those described by Prough and co-workers in this issue, may help to better estimate the peak effects and clearance of intravenously infused fluids and to predict kinetic responses to fluid therapy.

Closely related to the amount of fluid and volume to be administered in the perioperative setting is the debate concerning the right type of infusion. In this context, Bauer et al. emphasise that it is not the type of fluid *per se* (isotonic or hypertonic crystalloids, artificial or natural colloids) but rather the kind of surgery or individual condition of the patient that makes the difference. Whereas meta-analyses comparing hypertonic with isotonic crystalloids provided inconclusive results, isotonic crystalloids remain the cornerstone of fluid resuscitation.

However, since fluid overload and positive fluid balance are linked to bad outcome^{4,5}, infusion therapy should be rational (*quantum opus est et quantum satis est*) and endeavour prevention of oedema as well as preservation of micro-vascular blood flow and adequate tissue oxygenation. In this context, it has recently been shown that goal-directed administration of colloids is superior to restrictive or goal-directed therapy with crystalloids in view of tissue oxygen tension and micro-circulation in pigs with abdominal surgery and colonic anastomoses.^{6,7}

Conversely, there is an increasing evidence that administration of hyperoncotic colloids, such as 20% human albumin⁸ or 10% HES 200/0.5⁹ may impair renal function in haemodynamically unstable intensive care patients. These solutions should, therefore, be restricted or only used with great caution,

especially since alternatives with a better benefit/risk ratio (e.g., HES products of the third-generation tetrastarches) are currently available.

Although there has been a long tradition to infuse large amounts of fluids/volume to 'improve' vascular filling in patients with vasodilation, there is now impelling evidence at hand that this approach is not necessarily beneficial. In this context, it is likewise important to consider that all infusions are drugs with specific beneficial and potential adverse effects so that maximum allowed pharmaceutical doses have to be appreciated. The question why volume resuscitation with high doses may be ineffective has recently been elucidated by Rehm and co-workers.¹⁰ Interestingly, the latter authors demonstrated that a colloid bolus exerts a volume effect of approximately 100% in normovolaemic patients, but has only a 40% effect in the presence of hypervolaemia. Although appearing paradoxical at first glance, this effect can be explained by disruption of the endothelial glycocalyx, and ultimately leakage into the interstitial space. This points again to the fact that fluid overload (i.e., 'wet approach') needs to be avoided.

Although there is currently no evidence-based support for one type of fluid over another, colloids are more likely to remain within the intravascular compartment as compared with crystalloids. As mentioned in the guidelines of the Surviving Sepsis Campaign, volume of distribution is much larger for crystalloids than for colloids. Therefore, resuscitation with crystalloids requires more fluid to achieve the same end points and results in more oedema.¹¹

The role of natural and artificial colloids in perioperative medicine is critically elucidated by Vincent and Ertmer et al., respectively. In harmony with the results of the SAFE study, human albumin and saline should be considered clinically equivalent treatments for intravascular volume resuscitation. Subgroup analyses, however, suggested that albumin may worsen outcome in patients with traumatic brain injury, but may potentially be advantageous in septic patients. It was therefore concluded that "factors that may influence the choice of resuscitation fluid for a critically ill patient include the individual clinician's preference, the tolerability of the treatment, its safety, and its costs."¹² Since costs of synthetic colloids are markedly lower than for albumin, albumin is primarily used in patients with hypoalbuminaemia at risk of complications.

In view of their efficacy and safety, modern tetrastarches appear to be the most suitable synthetic colloids for volume therapy in anaesthesia and intensive care medicine. Since the effect of tetrastarches on overall morbidity and outcome has not yet been determined in prospective randomised trials, studies comparing crystalloids with third generation of starches are eagerly warranted. As such, the CRYSTMAS study is currently underway and addresses this clinically relevant issue.

Clinical side effects of (artificial) colloids include dose-dependent changes in coagulation. As elegantly summarised by Kozek-Langenecker, dextran, hetastarch and pentastarch have a more pronounced impact than tetrastarch, gelatine and albumin. However, it should also be taken into account that acidosis-induced changes in haemostasis may play a major role in this regard. From a physiological point of view, plasma-adapted carrier solutions may be preferred as compared with saline-based solutions.

Jacob and co-authors address one of the most persistent and at the same time least well-understood myths pertaining to the physiology of fluids in the human body: the so-called 'third space'. For decades, medical students and residents were acquainted with techniques for estimation of third space fluid losses, and recommendations for fluid management during major surgery and sepsis were based on the prerequisite to account for third spacing and to compensate this assumed primary loss by generous fluid administration. The practical consequence was an extremely positive fluid balance. In contrast, growing evidence points to the fact that fluid disappearing from the intravascular space accumulates interstitially, and that such shifting is related to a destruction of the endothelial glycocalyx secondary to inflammation and iatrogenic hypervolaemia.^{13,14} This new concept may thus have a major impact on our understanding of perioperative fluid balance and prompt a substantial change with respect to physicians' attitude towards fluid management. This draws attention to the problem of how to monitor fluid administration, in order to allow for an individually tailored and goal-directed regimen. A large body of evidence underscores that familiar and well-known variables based on filling pressures like central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) neither reflect an individual patient's preload, nor his capability to increase stroke volume after a volume challenge (Δ SVI).¹⁵

Whereas there are several studies showing that goal-directed protocols based on oesophageal Doppler-guided optimisation of stroke volume are effective in terms of improved outcome¹⁶, the Doppler technique itself has practical limitations and has not gained widespread use yet.¹⁷

In contrast, dynamic variables of fluid responsiveness, such as pulse pressure variability (PPV) and stroke volume variability (SVV) and volumetric variables of preload, such as global end-diastolic volume (GEDV) are easily derived from a bedside monitor and suitable for long-term use. They have been claimed to better reflect preload and fluid responsiveness than CVP and PCWP, and a recent study has fuelled enthusiasm with respect to these up-to-date variables in relation to outcome.¹⁸ However, to get the best information from these numbers, clinicians have to be aware of limitations inherently associated with these variables. Renner and co-workers present a variety of clinically relevant experimental scenarios, such as intra-abdominal hypertension, invasive ventilation pattern applying higher PEEP and vasopressor administration that each has a distinct impact of the ability of dynamic variables to predict fluid responsiveness.^{19,20} A sound and thorough knowledge of potential confounding factors allows for a more rational use of these new and promising variables to improve fluid management in critically ill patients.

Taken together, there is currently a need to question our traditional understandings and to re-evaluate both the amount and the type of fluid given to our patients. Since infusion therapy should be goal-directed, individualised and procedure specific³, it is time to stop talking about 'wet' and 'dry'!

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