Acetate-buffered crystalloid fluids: Current knowledge, a systematic review

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**A R T I C L E   I N F O**

**Keywords:**
Acetate
Acetate buffered
Crystalloid
Infusion therapy
Lactate buffered
Normal saline

**A B S T R A C T**

**Introduction:** The concept of fluid resuscitation with balanced solutions containing acetate is relatively new. The knowledge about acetate mostly originates from nephrological research, as acetate was primarily used as a dialysis buffer where much higher doses of acetate are infused. The aim of this review is to give an overview of the advantages and disadvantages of an acetate-buffered crystalloid fluid when compared with other crystalloid infusates.

**Methods:** We report trials with the primary object of comparing an acetate-buffered infusion solute to another crystalloid infusate. A systematic literature search of MEDLINE and the Cochrane Controlled Clinical trials register was conducted to identify suitable studies.

**Results:** The search strategy used produced 1205 potential titles. After eliminating doubles, 312 titles and abstracts were screened, and 31 references were retrieved for full-text analysis. A total of 27 scientific studies were included in the study.

**Conclusion:** Acetate-buffered crystalloid solutes do have a favorable influence on microcirculation. To what extent the acetate-buffered crystalloids influence kidney function is controversially discussed and not yet clear. Metabolic alkalosis did not occur in a single study in humans after an acetate-buffered infusion; potassium levels stayed stable in all studies. Cardiac output and contractility seem to be positively influenced; nonetheless, data on maintenance of a target blood pressure remain inconclusive. Whether acetate-buffered crystalloid fluids lead to lower rates of acute kidney injury and increased survival when compared with normal saline is yet unclear and may depend on the amount of fluid administered.

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1. Introduction

Intravenous infusion of crystalloid infusates is a key component in the treatment of shock and major surgical procedures [1–3]. It is aimed to restore intravascular volume, maintain cardiac output, and re-establish tissue oxygenation [2,4,5]. Nonetheless, crystalloid solutes have a variable composition and may therefore influence acid-base status, intra- and extracellular water content, and plasma electrolyte compositions [2]. They may have a major impact on organ function and outcome, especially in the critically ill where large volumes are required [3]. Despite continuing evaluation, no superiority of one particular type of fluid has been reached [1,6–8].

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Isotonic 0.9% saline is currently the most commonly used crystalloid in clinical practice, and it is the most frequently used choice for volume replacement [2,7,9–12]. Despite its name, the solution has a sodium and chloride content being 154 mmol/L compared with sodium 140 mmol/L and 109 mmol/L chloride in the extracellular fluid [9,13,14]. In recent years, several drawbacks of normal saline have been identified such as the appearance of hyperchloremic metabolic acidosis [7,9,10,13,15,16]. Despite the known disadvantages of 0.9% saline, balanced crystalloid fluids are much less commonly used [7,10]. The benefit of such infusion solutions was thought to be the ability to better compensate the ion fluctuations and buffering of the physiological acid-base status [1,2,17]. For an overview of the composition of the currently most often used infusates, see Table 1.

The concept of fluid resuscitation with balanced solutions containing acetate is relatively new [6,8]. The knowledge about acetate mostly originates from nephrological research in the 1970s where acetate was primarily used as a dialysis buffer [18,19]. There, it has been shown that acetate-containing solutes may cause cardiovascular instability by vasodilatation and impaired cardiac contractile response [8,19]. But it has to be noted that acetate dosage during dialysis was much higher than in conventional fluid therapy: the average acetate load was 262 mmol/(L h) of dialysis, respectively, 1048 mmol/L during a 4-hour dialysis
course when a 40 mmol/L acetate dialysate is used [20], whereas the average fluid load for a major abdominal surgical procedure of 4 hours is 3000 mL infusate resulting in a cumulative acetate load of 130-180 mmol/4 h dependent on the infusate used [19]. Therefore, the adverse events attributed to acetate infusion in these studies cannot be used to guide the choice for or against an acetate-buffered crystalloid fluid [19].

The aim of this review is to give an overview of the advantages and disadvantages of an acetate-buffered crystalloid fluid when compared with other crystalloid infusates.

2. Physiology

Acetate is the conjugated base of acetic acid [18]. Once it enters the blood, it is quickly taken up into the cells and there metabolized to acetyl-coenzyme A [19]. In contrast to the metabolism of lactate, this process can happen in every cell of the body that is able to perform an aerobic oxygen metabolism, with the highest metabolism rates in the heart, liver, skeletal muscle, and kidney [4,17,21,22]. Under aerobic conditions, acetyl-coenzyme A then enters the citric acid cycle with the final products of carbon dioxide and water or is consumed in anaplerotic pathways such as, for example, gluconeogenesis [17]. The generation of bicarbonate from acetate happens under normal circumstances in about 15 minutes compared with 1 hour when generated from lactate [4,8,23–27]. The conversion rate of acetate to bicarbonate is 90% under aerobic conditions [20]. How acetate metabolism is influenced by anaerobic-hypoxic states is yet unknown. One study by McCague et al [19] on sodium acetate infusion in critically ill found no adverse events and better buffer capacity in patients with major trauma in the sodium acetate group, but the way bicarbonate conversion rate of acetate is influenced needs to be evaluated by further research.

It has been shown that enzymatic processes are saturated when an acetate load of approximately 200 mmol/h (normal body weight) is reached [18,20]. The latter would equal 9-10 L of an acetate-buffered crystalloid infusate per hour, which is never reached in clinical practice and therefore irrelevant. For a comparison of acetate content of different infusion fluids, see Table 1.

How acetate influences the acid-base state is best understood by Stewart’s [18] approach: a solution that increases the body’s strong ion difference (strong cations — strong anions) will lead to an increase in pH [28,29]. In the case of an acetate-buffered crystalloid fluid, there is a net increase in cations as well as a net increase in anions, and therefore the strong ion difference stays stable. As the acetate anion is quickly metabolized away, the strong ion difference may slightly increase [3]. For an overview of how infusion fluids influence acid-base status, see Figs. 1 and 2.

3. Methods

3.1. Eligibility

We report only experimental and clinical trials with the primary objective of comparing an acetate-buffered infusion solute to another crystalloid infusate (eg, Ringer’s lactate or normal saline). The following studies were included in this review: clinical trials and observational studies on adults or experimental studies with the primary investigation target of comparing crystalloid fluid with crystalloid fluid. Studies investigating crystalloid vs colloid only were excluded from this study. Studies targeting crystalloid vs crystalloid and vs colloids were included in the study if all the study arms were analyzed independently. Studies on children, pregnant patients, cardiopulmonary bypass priming, or dialysis as well as studies in language other than English were also excluded from this review.

3.2. Information sources

A systematic literature search of MEDLINE and the Cochrane Controlled Clinical trials register was conducted to identify suitable studies. Only articles written in English were considered. Date restrictions were not applied to the searches.

3.3. Search strategy

We included the following search terms: acetate infusion fluid, acetate fluid therapy, acetate buffered crystalloid fluid, acetate solute, acetate crystalloid fluid, Ringer’s acetate, Plasmalyte, Elomel isoton, and Ringerfundin. No date restriction was applied. In addition to searching electronic databases, previous review articles on the subject were searched for further references.

3.4. Methodological quality of included studies

Methodological quality of included studies was assessed using criteria described by Jadad and colleagues for clinical trials [30]. The Jadad scale proposes methods used for randomization, blinding, and patient management in clinical trials. The range of possible scores is from 0 (lowest quality) to 5 (highest quality). Studies were not excluded based on Jadad scores.

4. Results

The search strategy used in this study produced 1205 potential titles (for Preferred Reporting Items of Systematic reviews and Meta-

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Table 1
Composition of current crystalloid fluids (either frequently used or mentioned in this review; all values in mOsm/L, respectively mmol/L)

<table>
<thead>
<tr>
<th></th>
<th>Nonbuffered</th>
<th>Lactate buffered</th>
<th>Acetate buffered</th>
<th>Bicarbonate buffered</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Isotonic saline</td>
<td>Ringer’s solution</td>
<td>Lactated Ringer’s</td>
<td>Hartmann’s solution</td>
</tr>
<tr>
<td>Osmolality</td>
<td>308</td>
<td>309</td>
<td>277</td>
<td>279</td>
</tr>
<tr>
<td>Na⁺</td>
<td>154</td>
<td>147</td>
<td>131</td>
<td>131</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>154</td>
<td>156</td>
<td>112</td>
<td>111</td>
</tr>
<tr>
<td>K⁺</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>2.3</td>
<td>2.3</td>
<td>1.8</td>
<td>2</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0</td>
</tr>
<tr>
<td>Lactate</td>
<td>28</td>
<td>29</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>Acetate</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Gluconate</td>
<td>—</td>
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<td>—</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Citrate</td>
<td>—</td>
<td>—</td>
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<td>—</td>
</tr>
</tbody>
</table>

* The list presented may not be complete.
* Not commercially available.
دانلود مقاله

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