NICE National Institute for Health and Care Excellence

Surveillance report 2017 - Intravenous fluid therapy in adults in hospital (2013) NICE guideline CG174

Surveillance report

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Surveillance decision

We will not update the guideline on intravenous fluid therapy in adults in hospital at this time.

Reason for the decision

Assessing the evidence

We found 90 studies through surveillance of this guideline.

This included evidence that supports current recommendations on:

- principles and protocols for intravenous fluid therapy
- assessment and monitoring
- resuscitation
- replacement and redistribution.

We found evidence on intravenous fluid therapy for adults under intensive care and perioperative care, which was not covered in the guideline. However, the evidence was insufficient to add new recommendations in these areas at this time.

We did not find any evidence related to routine maintenance and training and education.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the evidence and views of topic experts and stakeholders, we decided not to update NICE guideline CG174.

See how we made the decision for further information.

Commentary on selected evidence

With advice from topic experts we selected 3 studies for further commentary.

Principles and protocols for intravenous fluid therapy

We selected a randomised controlled trial by the ARISE Investigators and the ANZICS Clinical Trials Group (2014) for a full commentary because the results of this study support the original decision not to make any recommendations in relation to early goal-directed therapy (EGDT).

What the guideline recommends

NICE guideline CG174 recommends to offer intravenous (IV) fluid therapy as part of a protocol using the following algorithms:

- Assess patients' fluid and electrolyte needs following algorithm 1: assessment.
- If patients need IV fluids for fluid resuscitation, follow algorithm 2: fluid resuscitation.
- If patients need IV fluids for routine maintenance, follow algorithm 3: routine maintenance.
- If patients need IV fluids to address existing deficits or excesses, ongoing abnormal losses or abnormal fluid distribution, follow algorithm 4: replacement and redistribution.

Methods

The Australasian Resuscitation in Sepsis Evaluation (ARISE) investigators and the Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group (2014) conducted a randomised controlled trial (RCT) to test the hypothesis that EGDT, compared with usual care, would decrease 90-day mortality in people with early septic shock at the emergency department (n=1,600 participants). Adults were eligible if infection was suspected or confirmed, if they met 2 or more criteria for a systemic inflammatory

response, and if there was evidence of refractory hypotension or hypoperfusion. Exclusion criteria were contraindication to central venous catheter insertion in the superior vena cava or to receiving blood products; haemodynamic instability due to active bleeding; underlying disease process with a life expectancy <90 days; death deemed imminent and inevitable; documented limitation of therapy order restricting implementation of the study protocol or aggressive care deemed unsuitable by the treating clinician; in-patient transfer from another acute health care facility; confirmed or suspected pregnancy; inability to commence EGDT within 1 hour of randomisation or deliver EGDT for 6 hours. The study was conducted in 51 tertiary care and non-tertiary care hospitals in Australia, New Zealand, Finland, Hong Kong, and the Republic of Ireland. At time of selection, none of these hospitals had sepsis-resuscitation protocols or resuscitation guided by measurement of the central venous oxygen saturation ($ScvO_2$). The intervention was provided by a study team trained in EGDT delivery including the insertion of an arterial catheter and a central venous catheter capable of continuous $ScvO_2$ measurement within 1 hour after randomisation and a resuscitation algorithm followed until 6 hours after randomisation. The control (usual care) was provided by the treating clinical team. $ScvO_2$ measurement was not permitted in the control group during the 6 hours after randomisation. The primary outcome was death from any cause within 90 days after randomisation. All analyses were conducted according to the intention-to-treat principle.

Results

The intention-to-treat population included 793 participants in the EGDT group and 798 participants in the usual care group.

The primary outcome of death from any cause within 90 days after randomisation was:

- 147 participants died in the EGDT group (18.6%)
- 150 participants died in the usual care group (18.8%)
  - risk difference −0.3 (95% confidence interval [CI] −4.1 to 3.6, p=0.90)
  - relative risk 0.98 (95% CI 0.80 to 1.21, p=0.90).

Strengths and limitations

Strengths

The main strengths of this study were the low risk of bias and the focus on adults which make the results applicable to NICE guideline CG174.

Limitations

Although the study had low risk of bias, it would have been helpful to observe whether EDGT had an impact on other relevant outcomes considered in the guideline such as quality of life, renal complications and pulmonary oedema.

Impact on guideline

This RCT provided evidence that EDGT does not seem to be better than usual care for resuscitation in people with early septic shock. EGDT was reviewed during guideline development but no recommendations were developed regarding EGDT. This new evidence was considered to be unlikely to impact on the guideline because EGDT does not seem to have any benefit on the management of intravenous fluid therapy in hospitalised adult patients. Guideline committee members commented during this surveillance review that EGDT was discussed by the committee at the time of the initial development of the guideline. The conclusion at that time was that EGDT did not seem to have any benefit on the management of IV fluid therapy. They also said that this RCT appeared to support that discussion and offered no evidence to refute that assertion. It was highlighted that this RCT did not consider some of the measures that were considered as potential factors or complications with this approach and further evidence to explore EGDT's effect in relation to further complications would be beneficial before revising this element of the guideline.

Resuscitation

We selected a systematic review and network meta-analysis by Rochwerg et al. (2014) for a full commentary because the results of this study fit with evidence reviewed for the guideline in terms of population and outcomes. The results also support recommendations 1.3.1 to 1.3.3 for the use of crystalloids and human albumin for intravenous fluid resuscitation and that tetrastarch should not be used for fluid resuscitation.

What the guideline recommends

NICE guideline CG174 recommends using crystalloids that contain sodium in the range 130 mmol/litre to154 mmol/litre, with a bolus of 500 ml over less than 15 minutes if patients need IV fluid resuscitation. NICE guideline CG174 also recommends that tetrastarch for fluid resuscitation should not be used and to consider human albumin solution 4% to 5% for fluid resuscitation only in patients with severe sepsis.

Methods

Rochwerg et al. (2014) conducted a systematic review and network meta-analysis of 14 RCTs (n=18,916 participants) to assess the effect of fluid resuscitation on mortality in people with severe sepsis and septic shock. Parallel-group and factorial RCTs were eligible for inclusion. Quasi-randomised and crossover trials were excluded. The authors also noted that all studies published by Dr Joachim Boldt were excluded because of suspected lack of integrity. Further exclusions were studies in which most participants had the systemic inflammatory response syndrome secondary to other causes, without a clear sepsis subgroup and those focusing on people after elective surgery. There were no restrictions on language or date of publication. The inclusion criteria for participants in the RCTs were critically ill people with severe sepsis or septic shock (aged 16 years or older). Studies were included if there was available data on people with sepsis when mixed critically ill populations were studied. Any fluid or fluid strategy for resuscitation compared with other fluid or fluid strategy were the interventions. The primary outcome was 90-day mortality. If this outcome was not available, the longest mortality was taken as the outcome either 30-day, intensive care unit, or hospital mortality. Fluids were classified for analysis as:

- crystalloids (balanced or unbalanced solutions)
- colloids (albumin, gelatin, and low- and high-molecular-weight hydroxyethyl starch [HES]).

There were 2 network meta-analyses (NMA) and a direct fixed-effects meta-analysis:

- 4-node NMA comparing crystalloids, albumin, HES, and gelatin
- 6-node NMA comparing balanced crystalloids, unbalanced crystalloids (saline), low-molecular weight HES (L-HES), high-molecular-weight HES (H-HES), albumin, and gelatin

- fixed-effects meta-analysis comparing all crystalloids with all colloids.

Results

Fourteen RCTs were included. In 4 of these, people with sepsis were studied as part of a subgroup analysis. The main results are shown below.

4-node NMA

- HES compared to crystalloid
  - direct estimate (odds ratio [OR] 1.14, 95% confidence interval [CI] 0.99 to 1.30; 10 studies)
  - indirect estimate (OR 0.81, 95% credible interval [CrI] 0.13 to 5.14)
  - NMA estimate (OR 1.13, 95% CrI 0.99 to 1.30).
- Albumin compared to crystalloid
  - direct estimate (OR 0.81, 95% CI 0.64 to 1.03; 2 studies)
  - indirect estimate (OR 1.13, 95% CrI 0.18 to 7.32)
  - NMA estimate (OR 0.83, 95% CrI 0.65 to 1.04).
- Gelatin compared to crystalloid
  - direct estimate (no studies)
  - indirect estimate (OR 1.24, 95% CrI 0.61 to 2.55)
  - NMA estimate (OR 1.24, 95% CrI 0.61 to 2.55).
- Albumin compared to HES
  - direct estimate (OR 1.40, 95% CI 0.35 to 5.56; 2 studies)
  - indirect estimate (OR 0.71, 95% CrI 0.54 to 0.94)
  - NMA estimate (OR 0.73, 95% CrI 0.56 to 0.95).

- Gelatin compared to HES
  - direct estimate (OR 1.09, 95% CI 0.55 to 2.19; 1 study)
  - indirect estimate (none reported)
  - NMA estimate (OR 1.10, 95% CrI 0.54 to 2.22).
- Gelatin compared to albumin
  - direct estimate (no studies)
  - indirect estimate (OR 1.51, 95% CrI 0.71 to 3.20)
  - NMA estimate (OR 1.51, 95% CrI 0.71 to 3.20).

6-node NMA

- L-HES compared to saline
  - direct estimate (OR 1.07, 95% CI 0.89 to 1.29; 4 studies)
  - indirect estimate (OR 0.59, 95% CrI 0.25 to 1.35)
  - NMA estimate (OR 1.04, 95% CrI 0.87 to 1.25).
- H-HES compared to saline
  - direct estimate (OR 0.64, 95% CI 0.30 to 1.37; 3 studies)
  - indirect estimate (OR 1.13, 95% CrI 0.71 to 1.80)
  - NMA estimate (OR 0.95, 95% CrI 0.64 to 1.41).
- Albumin compared to saline
  - direct estimate (OR 0.81, 95% CI 0.64 to 1.03; 2 studies)
  - indirect estimate (OR 0.96, 95% CrI 0.14 to 6.31)
  - NMA estimate (OR 0.82, 95% CrI 0.65 to 1.04).

- Balance crystalloid compared to saline
  - direct estimate (no studies)
  - indirect estimate (OR 0.78, 95% CrI 0.58 to 1.05)
  - NMA estimate (OR 0.78, 95% CrI 0.58 to 1.05).
- Gelatin compared to saline
  - direct estimate (no studies)
  - indirect estimate (OR 1.04, 95% CrI 0.46 to 2.32)
  - NMA estimate (OR 1.04, 95% CrI 0.46 to 2.32).
- H-HES compared to L-HES
  - direct estimate (no studies)
  - indirect estimate (OR 0.91, 95% CrI 0.63 to 1.33)
  - NMA estimate (OR 0.91, 95% CrI 0.63 to 1.33).
- Albumin compared to L-HES
  - direct estimate (no studies)
  - indirect estimate (OR 0.79, 95% CrI 0.59 to 1.06)
  - NMA estimate (OR 0.79, 95% CrI 0.59 to 1.06).
- Balanced crystalloid compared to L-HES
  - direct estimate (OR 0.80, 95% CI 0.61 to 1.04; 2 studies)
  - indirect estimate (OR 0.44, 95% CrI 0.19 to 0.97)
  - NMA estimate (OR 0.75, 95% CrI 0.58 to 0.97).

- Gelatin compared to L-HES
  - direct estimate (no studies)
  - indirect estimate (OR 1.00, 95% CrI 0.44 to 2.21)
  - NMA estimate (OR 1.00, 95% CrI 0.44 to 2.21).
- Albumin compared to H-HES
  - direct estimate (OR 1.40, 95% CI 0.34 to 5.56; 2 studies)
  - indirect estimate (OR 0.83, 95% CrI 0.52 to 1.33)
  - NMA estimate (OR 0.87, 95% CrI 0.55 to 1.36).
- Balanced crystalloid compared to H-HES
  - direct estimate (OR 0.74, 95% CI 0.52 to 1.05; 1 study)
  - indirect estimate (OR 1.35, 95% CrI 0.63 to 2.92)
  - NMA estimate (OR 0.82, 95% CrI 0.60 to 1.13).
- Gelatin compared to H-HES
  - direct estimate (OR 1.09, 95% CI 0.55 to 2.19; 1 study)
  - indirect estimate (none reported)
  - NMA estimate (OR 1.10, 95% CrI 0.54 to 2.21).
- Balanced crystalloid compared to albumin
  - direct estimate (no studies)
  - indirect estimate (OR 0.95, 95% CrI 0.65 to 1.38)
  - NMA estimate (OR 0.95, 95% CrI 0.65 to 1.38).

- Gelatin compared to albumin
  - direct estimate (no studies)
  - indirect estimate (OR 1.26, 95% CrI 0.55 to 2.90)
  - NMA estimate (OR 1.26, 95% CrI 0.55 to 2.90).
- Gelatin compared to balanced crystalloid
  - direct estimate (no studies)
  - indirect estimate (OR 1.34, 95% CrI 0.61 to 2.89)
  - NMA estimate (OR 1.34, 95% CrI 0.61 to 2.89).

Fixed-effects meta-analysis

- All crystalloids compared to all colloids (OR 0.99, 95% CI 0.89 to 1.10, p=0.85; 12 studies, n=6,644).

Strengths and limitations

Strengths

The main strength of this NMA was the focus on RCTs evaluating direct and indirect comparisons of all types of fluids for resuscitation in people with severe sepsis and septic shock with the primary outcome of mortality.

Limitations

This NMA had some methodological limitations such as the lack of reporting of the search strategy and excluded studies, the variability in the dose of each type of fluid, and the variability in the primary outcome with different follow-up times for mortality.

Impact on guideline

This evidence supports recommendations 1.3.1 to 1.3.3 for the use of crystalloids and human albumin for intravenous fluid resuscitation and that tetrastarch should not be used for fluid resuscitation. Topic experts highlighted that the NMA included a discussion about

the use of balanced crystalloids compared to unbalanced crystalloids but without a definitive conclusion to suggest a change to the original recommendations in NICE guideline CG174.

Intravenous fluid therapy at the intensive care unit

We selected a double-crossover RCT by Young et al. (2015) for a full commentary because some of the topic experts suggested extending the scope of the guideline to include critical care and highlighted this RCT.

What the guideline recommends

During guideline development, the scope of the guideline was limited by excluding patients with more specialised fluid prescription needs. One of the exclusions was intensive monitoring in patients under intensive care.

Methods

Young et al. (2015) conducted a 28-week double-crossover RCT (n=2,278 participants) to compare the effectiveness of 2 types of fluid therapies: a buffered crystalloid and a saline crystalloid at the intensive care unit (ICU). Eligible participants were all ICU patients receiving crystalloid fluid therapy as clinically indicated. Patients were excluded if they were on renal replacement therapy (RRT), or expected to require RRT within 6 hours, or if they were admitted to the ICU only for organ donation, or for palliative care, or those who were previously enrolled in the study. The participant ICUs were adult or mixed (adult and paediatric) general medical and surgical ICUs (3 ICUs). A fourth ICU had a predominance of cardiothoracic and vascular surgical patients. The interventions were 0.9% saline crystalloid (saline) and Plasma-Lyte 148 (PL-148) which was the buffered crystalloid. Interventions were used in alternating treatment blocks of 7 weeks. The double-crossover occurred in each ICU using each study fluid twice over the 28 weeks of the study. The primary outcome was the proportion of patients with acute kidney injury (AKI).

Results

The primary outcome of AKI was reported within 90 days after enrolment:

- Buffered crystalloid group (9.6%).

- Saline group (9.2%)
  - Absolute difference 0.4%, 95 % CI −2.1% to 2.9%; relative risk 1.04, 95% CI 0.80 to 1.36, p=0.77.

Strengths and limitations

Strengths

The main strength of this study was the low risk of selection, performance, and reporting bias.

Limitations

A limitation of this study was the unclear risk of detection bias and the high risk of attrition bias. Trained staff from intensive care units collected outcome data but it is unclear whether they had knowledge of the allocated interventions. Authors calculated the percentage of missing data taking the number of patients who completed the study as the total rather than the number of patients enrolled in the study.

Impact on guideline

This RCT was considered to be relevant because acute kidney injury (primary outcome) was one of the outcomes considered in NICE guideline CG174. However, the scope of NICE guideline CG174 does not cover intravenous fluid therapy for patients in intensive care units. This new evidence was considered to be unlikely to impact on the guideline because none of the fluids demonstrated superiority. Topic experts highlighted that this RCT would have been considered as indirect evidence during guideline development and also referred to an editorial by Kellum and Shaw (2015) highlighting several shortcomings of this RCT.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of NICE's guideline on intravenous fluid therapy in adults in hospital (CG174) in 2013.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence

We found 89 studies in a search for systematic reviews and randomised controlled trials published between 12 March 2013 and 29 October 2016. We also considered 1 additional study identified by members of the guideline committee who originally worked on this guideline.

From all sources, we considered 90 studies to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: summary of evidence from surveillance for details of all evidence considered, and references.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

Views of stakeholders

Stakeholders commented on the decision not to update the guideline. See appendix B for stakeholders' comments and our responses.

Five stakeholders responded to the consultation not to update the guideline with 2 stakeholders providing comments.

Of the 2 stakeholders who commented on the proposal not to update the guideline: 1 agreed with the decision and 1 disagreed with the decision. The remaining 3 stakeholders did not have any comments to submit. One of the stakeholders suggested that there should be a dedicated lead in hospitals rather than this being additional to a clinician's existing role. However, NICE guideline CG174 already recommends that hospitals should have an intravenous (IV) fluids lead, responsible for training, clinical governance, audit and review of IV fluid prescribing and patient outcomes.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

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