



Surveillance report (exceptional review) 2017 – Acute kidney injury: prevention, detection and management (2013) NICE guideline CG169

Surveillance report

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Surveillance decision

We propose a partial update of [acute kidney injury](#). This should include the following review question:

- What is the clinical and cost effectiveness of N-acetylcysteine and/or intravenous fluids in preventing contrast-induced acute kidney injury in at-risk patients?

Reason for the decision

Assessing the evidence

The purpose of this exceptional review was to examine any impact on the acute kidney injury guideline following the publication of new evidence. This evidence was highlighted to NICE by a topic expert following publication of the 2017 surveillance review of this guideline. No additional evidence published since the [last surveillance review of the acute kidney injury guideline](#) in April 2017 was considered by the exceptional review.

Methods

The [AMACING study](#) compared the effectiveness of no prophylaxis to intravenous volume expansion with 0.9% sodium chloride (NaCl hydration), in 660 people referred for an elective procedure requiring intravascular-iodinated contrast material who were at high risk of contrast-induced acute kidney injury (CI-AKI). People at high risk of CI-AKI included had: an estimated glomerular filtration rate (eGFR) between 45 ml and 59 ml per min/1.73 m² combined with either diabetes, or at least 2 predefined risk factors; eGFR between 30 and 45 ml per min/1.73 m²; multiple myeloma; or lymphoplasmacytic lymphoma with small chain proteinuria.

Serum creatinine measurements were made between 2 to 6 days and between 26 to 35 days following contrast exposure, and compared to baseline measurements made immediately before start of treatment. Incidence of contrast-induced nephropathy was defined as an increase in serum creatinine by more than 25% or 44 µmol/litre within 2 to 6 days. Other outcome measures were collected through hospital records and questionnaires in a 35-day follow-up.

Due to the unavailability of historical evidence comparing NaCl hydration to placebo, a non-inferiority margin of 2.1% was estimated from the reported contrast-induced nephropathy incidence rate of 2.4% in people who had received prophylactic hydration.

Results

Outcomes were compared in people who had received NaCl hydration prior to receiving iodinated contrast with people who had received no hydration. The results showed non-inferiority of either treatment. Mean 2 to 6 days change in serum creatinine was 0.31 µmol/litre in the NaCl hydration group (standard deviation [SD] 13.79) and 1.30 µmol/litre in the no-hydration group (SD 15.09; $p=0.4049$). The absolute difference in proportions of people in each group with contrast-induced nephropathy was -0.10% (one-sided 95% CI -2.25 to 2.06%; $p=0.4710$). Hospitalisation rates were lower in those not receiving hydration treatment, with 50% of people in this group not being hospitalised at all, compared to 100% of people receiving NaCl hydration being hospitalised for at least daycare treatment, resulting in significant cost savings for the no-hydration group. No instances of renal failure or need for dialysis were recorded within 35 days; instances of renal decline of more than 10 eGFR units or instances of decline to below 30 ml per min/1.73 m² were not statistically significantly different in either treatment group ($p=0.3512$ and $p=0.7881$ respectively). Three deaths were recorded, all occurring in participants receiving no hydration, however these causes were unrelated to treatment.

Overall, 5.5% of people in the NaCl hydration group experienced adverse events as a result of treatment. This included 4.0% of participants experiencing symptomatic heart failure, 0.3% experiencing hyponatraemia and 1.2% experiencing arrhythmia. No similar events were recorded in the no-hydration group.

2017 surveillance review

The recent [surveillance review](#) of NICE guideline CG169 considered the full guideline, including the review question considered in the current exceptional surveillance review:

- What is the clinical and cost effectiveness of N-acetylcysteine and/or intravenous fluids in preventing CI-AKI in at-risk patients?

Evidence was identified reporting mixed results in this area. The results of some studies indicated that there is no difference between the use of sodium chloride and sodium bicarbonate hydration, some evidence suggesting there is no difference between sodium

bicarbonate hydration and no hydration or placebo and evidence suggesting sodium bicarbonate hydration is more effective than placebo. Therefore, it was concluded that the evidence was insufficient to prompt an update of this review question. However, no evidence was identified during surveillance on the comparison of NaCl hydration with no hydration.

Guideline development

Two studies were evaluated during guideline development relevant to this intervention, in which evidence of low to very low quality was reported. However oral hydration was provided as a comparator in 1 of these studies and it was unclear whether oral hydration was used as the comparator treatment in the second study. Therefore, the evidence described in this review is the first identified to compare NaCl hydration with no treatment before iodinated contrast administration in this population. In addition, the participant number in the study being considered in this review (n=660) is larger than the numbers included in the 2 studies considered during development (n=300 and n=102).

Views of topic experts

We engaged with 3 topic experts who were also members of the guideline committee involved in the development of NICE guideline CG169. It was noted that this is an evidence poor area, which contributed to uncertainties when developing the recommendations around CI-AKI. Therefore, the study considered in this review may be more informative than other evidence in this area. It was highlighted that there may be a number of reasons as to why the risks of CI-AKI might be decreasing, including greater awareness of the risk factors and universal use of safer contrast agents. As such, the risks of routine use of intravenous fluid, especially sodium chloride, are becoming more apparent. It was suggested that consideration should be made as to whether intravenous NaCl hydration should always be used in people at high risk of AKI. It was also highlighted that the study under consideration denotes a specific high risk population which may not be able to be extrapolated to all people undergoing contrast agent administration.

Impact

Recommendation 1.2.7 currently states that intravenous volume expansion should be offered to adults having iodinated contrast agents if they are at increased risk of CI-AKI or they have an acute illness. It is recommended that sodium bicarbonate or 0.9% sodium chloride is used for this.

The absolute difference in the incidence rate of contrast-induced nephropathy between treatment groups was below the non-inferiority margin of 2.1% at -10% (-2.25 to 2.06). Therefore, it is indicated that NaCl hydration does not provide clinical benefit compared to no hydration, for protection from CI-AKI.

The evidence considered also reports that 5.5% of people undergoing NaCl hydration experienced adverse events related to this treatment, and shows that no hydration is cost saving compared to NaCl hydration, due to both reduced treatment and hospitalisation costs. Therefore, consideration of this evidence as part of an update to this area of the guideline may result in the avoidance of harm as well as cost savings.

It should be noted that while a high risk population was included in the evidence evaluated in this exceptional review, people with an eGFR lower than 30 ml per min/1.73 m² were excluded from the study due to safety considerations, as were emergency cases and intensive care patients. Therefore, the evidence presented in this review may not be directly applicable to this specific population. However, the evidence is directly relevant to others within the high risk population covered in the guideline, and therefore there is potential impact on the recommendation to offer all people at increased risk of CI-AKI NaCl hydration.

The current recommendation (1.2.7) to offer NaCl hydration for the prevention of CI-AKI was written based on limited, low quality evidence. Following consideration of the results published in the AMACING trial, as well as topic expert views that this may provide stronger evidence in this area than previously available, there may be an impact on the current recommendation.

Health economic modelling was conducted for this review question, comparing different types of fluid regimens for the prevention of CI-AKI, including NaCl hydration. Therefore, the evidence considered in this exceptional review may also need to be considered for its impact on this model during the update.

Other clinical areas

This exceptional surveillance review did not search for new evidence relating to other clinical areas in the guideline.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

See [how we made the decision](#) for further information.

How we made the decision

Exceptionally, significant new evidence may mean an update of a guideline is agreed before the next scheduled check of the need for an update. The evidence might be a single piece of evidence, an accumulation of evidence or other published NICE guidance.

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

This surveillance report provides an overview of 1 study published since the end of the search period for the guideline (October 2016). The results of this study were considered in detail to determine if there is an impact on guideline recommendations.

No additional evidence published since the last surveillance review in April 2017 was considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was an exceptional surveillance review we did not consult on the decision.

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