UNCERTAINTIES

What is the role of clinically assisted hydration in the last days of life?

Andrew Davies, 1 Caroline Barry, 2 Stephen Barclay 3

What you need to know

- Decisions about the provision of clinically assisted hydration to patients in their last days of life are complex and should always be individualised.
- Evidence is lacking about the potential benefits and harms of clinically assisted hydration in the last days of life.
- Clinical guidelines are available to support decision making and need to be used in conjunction with relevant national ethical and legal frameworks.

Clinically assisted hydration, also known as medically assisted hydration, is the process by which “fluids” are given parenterally via a cannula (either intravenously or subcutaneously) or enterally via a tube (into the stomach or small bowel or, less commonly, into the rectum). Decisions about the role of clinically assisted hydration in the last days of life are often complex and can have a major impact on the dying patient, as well as their loved ones and clinical staff. These challenging clinical decisions must be made with high degrees of uncertainty due to a paucity of evidence. This article summarises the evidence base for clinically assisted hydration in the last days of life and offers suggestions for clinical practice in light of these uncertainties.

Possible benefits and harms of clinically assisted hydration in the last days of life are varied. Proposed benefits include patient comfort (such as prevention of thirst and dry mouth) and the maintenance of renal perfusion with prevention of accumulation of toxins and drugs (prevention of delirium and opioid toxicity). Delirium is a common problem at the end of life and is the cause of much distress to patients, their loved ones, and clinical staff. Possible harms of hydration include fluid overload (such as worsening of peripheral oedema and cardiac failure), fluid related complications (such as worsening of vomiting and respiratory secretions), and medicalisation of the normal dying process. Some commentators even suggest that ketones and other byproducts of dehydration may have positive effects on patients’ condition and symptom control (analgesic and sedative effects), but, as with all of these proposed benefits and harms, there is no robust evidence for them.

The provision of clinically assisted hydration in the last days of life is contentious in all groups of patients regardless of demographics or diagnosis, and its use is highly variable. One systematic review of studies involving cancer patients reported that provision ranged from 12% to 88%, with the intervention being more often used in hospitals than in hospices. Cumulative evidence from qualitative and quantitative studies suggests that many patients and families favour the provision of clinically assisted hydration when the patient is unable to maintain hydration at the end of life, and believe that withholding or withdrawing fluids would accelerate the process of dying. However, there are a wide range of views, and these may be influenced by factors such as ethnicity, culture, religion, and personal experience. Healthcare professionals also have a range of opinions, including believing that clinically assisted hydration may improve or worsen symptom control or prolong survival or the dying process. Additionally, healthcare professionals often believe that there are specific indications or contraindications to the use of this medical intervention despite the lack of evidence.

What is the evidence of uncertainty?

The 2014 Cochrane review of medically assisted hydration for adult palliative care patients identified six studies, three randomised controlled trials (RCTs) and three prospective controlled trials. The primary outcome measure was quality of life, and the secondary outcome measures were survival and adverse events. The three RCTs involved inpatients with advanced (terminal) cancer (one from Argentina, and two from the US) and evaluated the use of clinically assisted hydration to manage dehydration, rather than to maintain hydration. All three trials used “low” volumes of fluid (1 L/day) even though all patients were dehydrated. One trial was considered low quality and reported a statistically significant improvement in nausea at 48 hours (end of study) (P=0.027) but no other effects of clinically assisted hydration (that is, thirst, delirium). One high quality RCT reported a statistically significant improvement in sedation and myoclonus (but not hallucinations and fatigue) at 48 hours (end of study) (P=0.035 and P=0.005 respectively) in patients allocated to receive clinically assisted hydration. Another high quality RCT reported no difference in symptoms, quality of life, or survival at seven days (end of study). Survival was not assessed in the earlier RCTs. The Cochrane review concluded that the benefits and harms of clinically assisted hydration could not be determined because of insufficient good quality evidence.

A 2021 systematic review identified three new studies: one RCT (CHELsea I), a retrospective case-control study, and a prospective observational study. The
RCT was a cluster randomised (feasibility) trial, involving 120 adult cancer inpatients (from cancer centres and hospice units in the UK), who were deemed to be in the last week of life and unable to maintain hydration through drinking. Patients who were dehydrated or who had an indication for, or a contraindication to, clinically assisted hydration were excluded from the study. Sites were randomised to either usual end-of-life care or to usual end-of-life care with clinically assisted hydration: the clinically assisted hydration was given in line with NICE clinical guidance on intravenous fluid therapy in adults, and treatment continued until death. The RCT achieved its predetermined criteria for success (that is, participant recruitment, participant retention, adherence to study procedures, safety of study interventions) but, being a feasibility study, was underpowered. There are no analogous RCTs involving patients with non-malignant disease or children with malignant or non-malignant disease. A contemporaneous (July 2022) review of Medline OVID, CINAHL, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials revealed no other relevant RCTs.

Is ongoing research likely to provide relevant evidence?

An NIHR funded cluster randomised trial (CHELsea II) is enrolling 1600 non-dehydrated patients across 80 centres who will be treated until death according to the NICE clinical guidance on intravenous fluid therapy in adults. The trial will recruit patients deemed to be in the last week of life (patients with cancer or non-malignant disease) who are unable to maintain hydration by drinking, have no clinical indication for, or contraindication to, the use of clinically assisted hydration, and have not experienced delirium (primary outcome) or audible upper airway secretions in the previous 24 hours. The study sites will be randomised to either intervention A (oral fluids, regular mouth care, and usual symptom control) or intervention B (oral fluids, regular mouth care, usual symptom control, and clinically assisted hydration). The clinically assisted hydration with dextrose saline may be given either intravenously or subcutaneously with the volume of fluid based on NICE clinical guidance (and specifically on the patient’s weight). The primary outcome is the prevalence of delirium according to the Nursing Delirium Screening Scale (Nu-DESC); other study outcomes are the incidence of other end-of-life care problems (such as shortness of breath, audible upper airway secretions), overall survival (from randomisation to time until death), and adverse events.

We searched the WHO International Clinical Trials Registry Platform for active or planned trials or other studies. No other relevant active or planned RCTs or other studies were identified.

What should we do in light of the uncertainty?

In some cases there will be a clear indication for clinically assisted hydration (for example, symptomatic dehydration, malignant hypercalcaemia), whereas in others there will be a clear contraindication (such as symptomatic fluid overload, syndrome of inappropriate antidiuretic hormone secretion). Where there is no clear indication or contraindication, clinicians should openly discuss with patients and/or their loved ones the uncertainties relating to benefits and risks of clinically assisted hydration. We suggest using a personalised, holistic approach to decision making which considers not just the physical, but also psychological, spiritual, and social factors important to the patient and their family.

Box 1 provides a suggested approach to support decision making concerning clinically assisted hydration, including advice about assessment, management (that is, individualised care, therapeutic trials), and reassessment. This pragmatic advice is based on expert opinion in the absence of robust research evidence. This approach should be relevant in many jurisdictions, but readers need to be aware of their national or regional clinical or ethical guidelines and their national legislation relating to the withholding and withdrawing of medical interventions (specifically clinically assisted hydration).

### Box 1: Example of an approach to decision making concerning clinically assisted hydration

- When possible, conduct daily assessments of the patient’s hydration status. Review the need to start clinically assisted hydration, respecting the person’s wishes and preferences
- Discuss the risks and benefits of clinically assisted hydration with the patient and those important to them
- Ensure that any concerns raised by the patient or those important to them are addressed before starting clinically assisted hydration
- Use a personalised approach with patients and consider:
  - Cultural, spiritual, and religious beliefs that may affect their preferences
  - Level of consciousness
  - Any swallowing difficulties
  - Level of thirst
  - Risk of pulmonary oedema
- Consider a therapeutic trial of clinically assisted hydration if the person has distressing symptoms or signs that could be associated with dehydration (such as thirst or delirium) or oral hydration is inadequate
- For people being started on clinically assisted hydration:
  - Monitor at least every 12 hours for changes in the symptoms or signs of dehydration and for any evidence of benefit or harm
  - Continue with clinically assisted hydration if there are signs of clinical benefit
  - Reduce or stop clinically assisted hydration if there are signs of possible harm to the dying person, such as fluid overload, or if they no longer want it
- For people already dependent on clinically assisted hydration (enteral or parenteral) before the last days of life:
  - Review the risks and benefits of continuing clinically assisted hydration with the person and those important to them
  - Consider whether to continue, reduce, or stop clinically assisted hydration as the person nears death

### Recommendations for future research

Future research should consider:

- Evaluation of different populations such as gerontology patients, paediatric patients, patients with specific comorbidities (such as heart failure, renal failure), and those in other settings (such as home or nursing home)
- Interventions that include the use of different fluid regimens (that is, fluid type, volume), and different routes of administration (intravenous, subcutaneous). These should be compared with standard end-of-life care (including help to drink, and mouth care)
- Assessments of outcome endpoints include development of end-of-life care problems (such as delirium, shortness of breath), overall survival, adverse effects of clinically assisted hydration, health economic impact of clinically assisted hydration

---

[BMJ: first published as 10.1136/bmj-2022-072116 on 17 March 2023. Downloaded from http://www.bmj.com, on 29 March 2023 at Cambridge University Library. Protected by copyright.]
How patients were involved in the creation of this article

No patients or their family carers were involved in the creation of this article.

Education into practice

• Is your clinical team’s use of clinically assisted hydration at the end of life individualised?
• If so, how do you make the decision to initiate or discontinue this treatment, and is this decision making process supported by national guidance?

How this article was created

This article was written in response to NIHR awarding funding for the CHELsea II study.

We searched the following databases for supporting information: Medline OVID, CINAHL, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials. We searched the following registry for supporting information: World Health Organization International Clinical Trials Registry Platform (which includes ClinicalTrials.gov, EU Clinical Trials Register, and ISRCTN).

Contributors: AD wrote the first draft, and all authors contributed to redrafting. All authors approved the final version. AD is the guarantor for the article.

Competing interests: The BMJ has judged that there are no disqualifying ties to commercial companies. The authors declare the following other interests: AD is the chief investigator on the CHELsea II trial study. SB is supported by the National Institute for Health and Care Research Applied Research Collaboration East of England (NIHR-ARC EoE) at Cambridge and Peterborough NHS Foundation Trust.

The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Provenance and peer review: Commissioned, externally peer reviewed.