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Laboratory Investigation

LABORATORY INVESTIGATION

Could patient-controlled thirst-driven fluid administration lead to more rapid rehydration than clinician-directed fluid management? An early feasibility study

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Abstract

Background: Fluid management is a major factor determining perioperative outcome, yet in reality, fluid administration practice is variable. Thirst however, is a highly sensitive and reliable indicator of fluid deficits. We explored the use of thirst sensation to trigger i.v. fluid boluses to guide individualized fluid management.
Methods: We performed a randomized double crossover trial on 16 healthy male volunteers, of mean age 31 yr and BMI 24.4 kg m^{-2}. Twice, after administrations of oral furosemide (40 mg) and 12 h of oral fluid restriction, participants received a 4-h i.v. fluid infusion. In the experimental arm, participants pressed a trigger to relieve their thirst, administering a 200 ml bolus. In the control arm, i.v. fluid was infused following National Institute for Health and Clinical Excellence (NICE) guidelines at 1.25 ml kg^{-1} h^{-1} with a clinician delivered 500 ml i.v. bolus in response to clinical signs of dehydration. Plasma osmolality (pOsm) and urine specific gravity were measured before and after each infusion.
Results: More fluid was infused in response to thirst than by adherence to NICE guidelines, with a mean difference of 743 ml (P=0.0005). Thirst-driven fluid administration was fitted to an exponential function of time, plateauing after a mean half-life of 98.8 min. In the experimental arm there was a greater reduction in urine specific gravity and thirst score with mean differences 0.0053 g cm^{-3} (P=0.002) and 3.3 (P=0.003), respectively. pOsm demonstrated no fluid overload.
Conclusions: A system delivering i.v. fluid in response to subjective thirst corrects fluid deficits in healthy participants. A clinical feasibility study will assess the potential use of this system in the perioperative setting.
Clinical trial registration: NCT 03176043.

Keywords: dehydration; perioperative period; thirst

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Editor's key points

- In a randomized crossover trial on volunteers, the authors assessed whether or not fluid administration based on thirst sensation would be better than the conventional method recommended by NICE guidelines.
- A system delivering i.v. fluid in response to subjective thirst was better than the conventional method in correcting fluid deficits, without causing fluid overload, in healthy participants.

Dehydration is associated with an increased risk of suffering acute kidney injury,[1] myocardial infarction,[2] venous thromboembolism,[3] and delirium.[4] By contrast, iatrogenic fluid overload is associated with an array of clinical risks including pulmonary and gut wall oedema, intestinal ileus, impaired coagulation, urinary retention, and impaired stroke volume.[5] Thus, both excessively restrictive and liberal fluid administration may be associated with harm.[6,7] Careful fluid management, which maintains euvolaemia throughout the perioperative period minimizes gut injury, facilitating early oral fluid intake, and mobilization in line with enhanced recovery pathways.[8,9]

Goal directed fluid therapy, guided by measurements of stroke volume variation, cardiac output, and pulse contour analysis, can reduce both postoperative morbidity and length of stay.[7,10] This intensive monitoring is mostly reserved for the highly-regulated environment of the operating theatre or high-dependency unit, while at other points in the perioperative period, no single gold standard test exists that accurately indicates hydration status.[11] The commonly used clinical features of dehydration represent a poor guide to fluid administration, only appearing when fluid losses exceed 4–5%.[12,13] The diagnosis of dehydration based on clinical signs is therefore unreliable, with very low sensitivity of between 0 and 44%, and poor specificity.[14] Consequently, perioperative fluid management is often highly variable and suboptimal,[15] often delegated to junior staff while physical access to oral fluids is limited.[16] While there is substantial literature regarding perioperative goal directed therapy, the same meticulous investigation has not been applied to broader ward-based settings.

Elevated plasma osmolality (pOsm) may represent the best objective index of dehydration in hospitalized patients,[17] with a value >295 mOsm kg^{-1} increasingly selected as a defining reference for dehydration.[18] In adults across all ages, and in both sexes, there exists a specific threshold value of pOsm, above which central osmoreceptors linearly increase the sensation of thirst.[19–24] The thirst response is also stimulated by reductions in intravascular volume. The reduced renal artery baroreceptor activity stimulates thirst by increasing serum angiotensin II,[25] while reduced atrial and pulmonary arterial baroreceptor activity stimulates thirst either through reductions in tonic atrial natriuretic peptide release[26] or through a shared vagal and glossopharyngeal pathway.[27] This baroreceptor pathway converges with afferents from central osmoreceptors on the hypothalamic thirst centre. Reductions in intravascular volume interact synergistically with increase in pOsm to drive thirst.[28] The stimulation of thirst occurs in response to an integration of physiological parameters and could provide valuable feedback pertaining to a patient's overall fluid balance.

Patient-controlled analgesia systems have successfully demonstrated the effectiveness of utilizing subjective discomfort to titrate an i.v. analgesic therapy.[29] Therefore, we hypothesize that the sensation of thirst could similarly be used as a guide to titrate i.v. fluid therapy within strict upper limits. As the first step in testing this hypothesis, we performed a randomized controlled double crossover study on healthy adult volunteers. This laboratory-based early feasibility study serves as a precursor to a clinical feasibility study in perioperative setting.

Methods

The study was completed with local institutional (University College London, UCL) research Ethics Committee approval (Ref. 9339-001). All participants provided written, informed consent before the study. Inclusion criteria were: males aged 18–65 yr, ASA physical status I, body mass between 55 and 100 kg and not on regular medication.

Dehydration protocol

Participants avoided strenuous exercise for 48 h before each trial. Participants were instructed to take 40 mg of the oral loop diuretic, furosemide at 20:00 h the evening before the study, and then to abstain from all fluid, food, and caffeine intake until the end of study. Participants completed this dehydration protocol on two occasions, 7–14 days apart (Fig. 1). Participants were requested to record their pre-diuresis body mass where possible.

Rehydration protocol

Participants attended our laboratory at 08:00 h on the morning after their diuresis and fluid restriction. On arrival, participants provided an initial urine sample, and their height and weight were documented. Having lain recumbent for 15 min, an 18 G cannula was placed in a large forearm vein, from which a 5 ml blood sample was drawn.[19] A balanced electrolyte solution (4% glucose in 0.18% sodium chloride) was then administered via an Infusomat® Space volumetric pump (B Braun, Melsungen, Germany) over 4 h. At the start of the infusion, and at 60 min intervals thereafter, participants were weighed and asked to mark a 125 mm visual analogue subjective thirst scale (ranging from 'not thirsty' to 'extremely thirsty')[19]: dividing the distance marked by 12.5 mm gave a thirst score out of 10. At the end of the 4-h trial, a second 5 ml blood sample was obtained. Participants voided their bladder 30 min before the end of trial and a final urine sample was obtained at the end of the trial. Urine samples were immediately analysed for specific gravity with Multistix Reagent Strips (Siemens, Berlin, Germany). Blood samples from the beginning and end of the trial were collected into serum separating tubes and immediately centrifuged; 1.5 ml of serum were obtained and frozen at −82°C, and later analysed for pOsm by a blinded investigator using freezing point depression (3320 Osmometer: Advanced Instruments, Northwood, MA, USA).

In an unblinded, randomized double crossover design trial, one of two infusion protocols was used at each visit, the order being determined by block randomization using the R 'blockrand' package.[30]