Letters

To Relieve the Patient's Thirst, Refresh the Mouth First: A Pilot Study Using Mini Mint Ice Cubes in Severely Dehydrated Patients

Key Words
Thirst, hypernatremia, sodium, critical illness, water deprivation, symptom

To the Editor:

Thirst refers to the urge to drink and it is consistently reported as one of the top five stressful symptoms by critically ill patients.[1] It can also become a real torment for terminally ill patients[2] or severely dehydrated individuals.[3] However, thirst is often overlooked, poorly understood, and underrecognized in the hospital.[4] For a long time, it was thought to be closely related to changes in the blood volume or plasma osmolarity and to the regulation of blood sodium concentration (Na+).[5,6] Rehydration usually aims at normalizing biological targets like Na+ or plasma osmolarity, and the preferred routes for rehydration in the hospital are intravenous fluid administration and nasogastric tube feeding.[7] For many reasons, oral intake is not advised in the critically ill patient and the mouth is commonly not taken into account when severe dehydration occurs. Water, cold, and mint can independently modulate the sensation of thirst by their effects on thermoreceptors and osmoreceptors in the mouth.[8] A recent animal study supported the critical role of thirst-promoting neurons of the subfornical organ that both receive input from the mouth and integrate blood composition to anticipate the variations in plasma homeostasis.[9] In accordance with these physiological observations and recent animal findings, the aims of this physiological study were 1) to investigate whether thirst can be efficiently relieved by the simple application of mini mint ice cubes in the mouth of critically ill profoundly dehydrated subjects suffering from craving thirst and significant hypernatremia; 2) to give a refreshing insight into the understanding of the relationship between thirst, osmolarity, Na^+, water intake, and the route used for rehydration in severely dehydrated subjects.

Methods

This prospective interventional study was approved by the national ethics committee (approval number ID-RCB: 2017-A03559-44 - Ref CPP: 2018.03.05) and received the ClinicalTrial.gov identifier NCT03610074. Signed informed consent was obtained from all participants. Twenty-one patients were needed to demonstrate a 1.5-point reduction in the thirst intensity score with a standard deviation of 2, within five minutes following mini mint ice cubes application in the mouth, with a power of 90% and an alpha risk of 0.05 (paired Student t-test). Taking into account the possibility of technical problems in 15% of cases, 26 consecutive severely dehydrated patients exhibiting either $Na^+ \geq 150$ mmol/L or >145 mmol/L with a water deficit >3 L—water deficit (L) = $(Na^+ - 140)/140 \times$ weight (kg) $\times$ 0.6—were prospectively included in two ICUs over a one-year period.[7] Patients unable to understand study outcome and to answer basic questions, delirious patients, pregnant women, dying subjects, and those refusing to sign the informed consent form were ruled out from the study. Thirst was assessed using a 0–10 Numeric Rating Scale of thirst intensity and a five-point-Likert

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Comfort Scale (both detailed in the Appendix), before (H0) and within five minutes, then repeatedly until 24 hours following the application of three mini mint ice cubes in the mouth. They were made by mixing still natural mineral water (Cristaline®) with concentrated mint syrup (Teisseire®) to obtain a 20% mint concentration. The resulted liquid was kept in a freezer in silicone mini ice cube trays to obtain mini mint ice cubes of 1 cm^3. A blood sample was taken at H0 for the measurement of Na^+ and calculation of osmolarity as follows: $Osm = 2 \times Na^+ + urea + glucose$.[5] Within five minutes and at 24 hours following the application of the mini mint ice cubes, new laboratory tests were

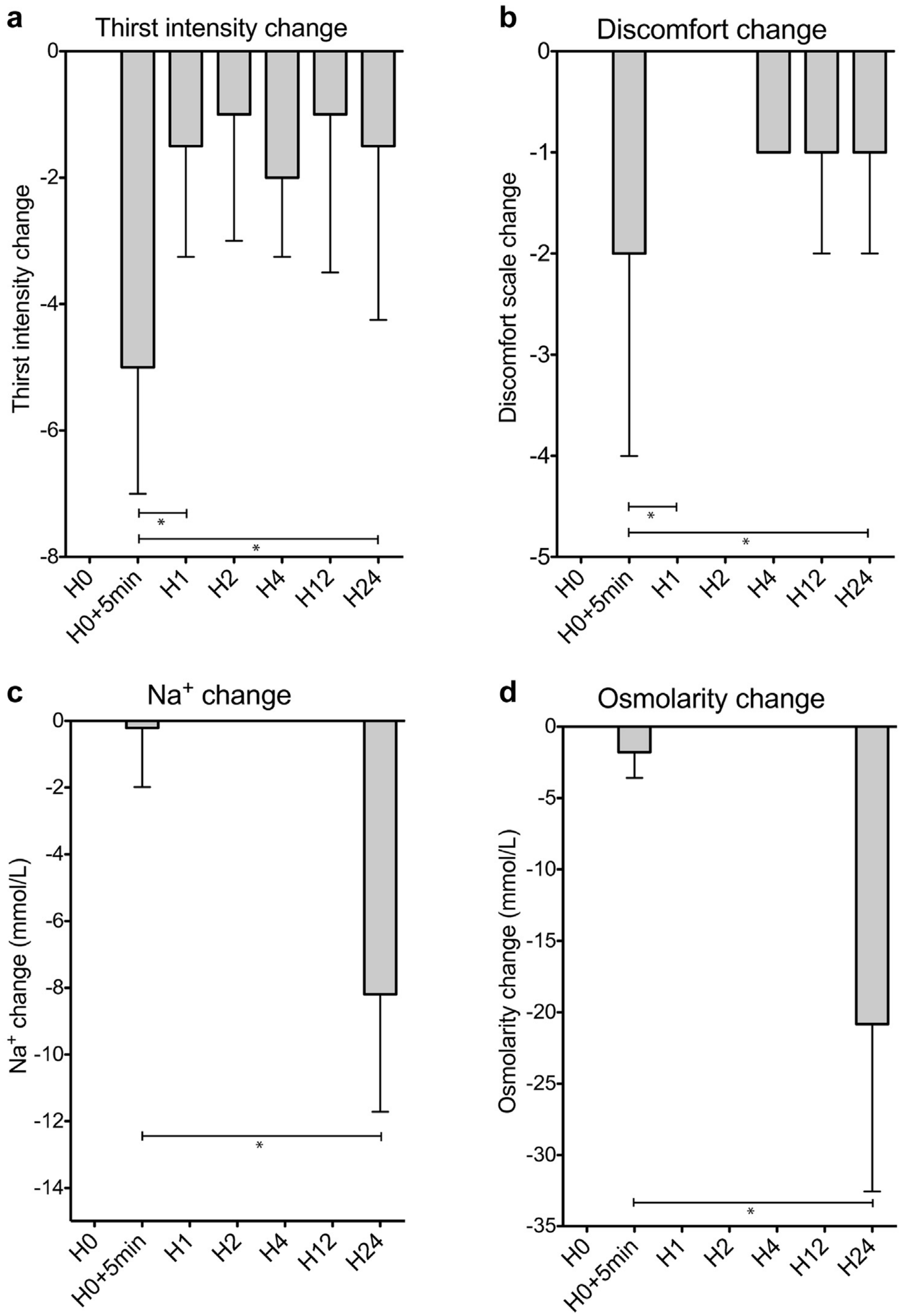

Fig. 1. a) Changes in thirst intensity, b) thirst-associated discomfort, c) blood sodium concentration, and d) plasma osmolarity, at various time points after the application of mini mint ice cubes in the patients' mouth. Na^+ = blood sodium concentration. *$P < 0.001$.

performed for blood electrolytes to compare Na^+ and osmolarity. Rehydration over the first 24 hours was intended to correct the water deficit, the route used being left at the discretion of the attending physician providing that oral intake was excluded. Details of the statistical analysis are described in the Appendix.

Results

The main characteristics of the patients are shown in Appendix Table 1. The population contains a majority of men of advanced age with a severe critical illness, as assessed by a high severity score at admission (median SAPS2 score: 47.5 [39–66]) and a high proportion of the patients (65.4%) under mechanical ventilation. At the beginning of the protocol, all the patients suffered from severe thirst (>6/10) and the median thirst intensity reached 8.5 [7–10] with 10 patients (38.5%) complaining of the worst thirst possible (10/10). Within five minutes of mini mint ice cubes application in the mouth, both thirst intensity (from 8.5 [7–10] to 4 [2–5]; $P < 0.0001$) and thirst-associated discomfort (from 5 [4–5] to 2 [1–3]; $P < 0.0001$) significantly decreased, whereas no physiologically significant changes in osmolarity or Na^+ occurred (Fig 1). Despite a significant drop in Na^+ (from 153 [150–155] to 145 [141–153] mmol/L; $P < 0.0001$) and osmolarity (from 341 [323–362] to 318 [304–358] mmol/L; $P = 0.0001$) using large intravenous and/or nasogastric hydric intake (5.2 [4–7.25] L), thirst intensity (−1.5 [−4 to 0] vs. −5 [−7 to −3]; $P = 0.0005$) and thirst-associated discomfort (−1 [−2–0] vs. −2 [−4 to −2]; $P = 0.0003$) decreased less over the first 24 hours than within the first five minutes following mini mint ice cubes application in the mouth (Fig 1).

Comment

Thirst regulation involves multiple complex physiological pathways including postabsorptive osmosensitive mechanisms and barosensitive receptors, but also psychological components and preabsorptive mechanisms. In clinical practice, several barriers—swallowing disorders, delirium, extreme weakness, vomiting, obligatory fasting imposed by an urgent or planned surgery, or simply an orotracheal tube—prevent the dehydrated patient from being rehydrated by the mouth. The present study tends to demonstrate that among all the inputs affecting the regulation of thirst, signals from the mouth seem to outbalance those resulting from postabsorptive mechanisms.[9] Along the same line, Puntillo et al. have shown that the repetitive use of refreshing oral care can significantly decrease the thirst of critically ill patients compared to the usual care group that did not benefit from a mouth-targeted intervention.[10]

Several limits have to be acknowledged. The small number of subjects ($n = 26$) may be criticized but it strictly matches the a priori power analysis that defined a number needed to be included of 21. There was no control group, but each subject was considered as its own control with a before/after intervention study design. The repetition of the mini mint ice cubes application several times a day could have boosted the relieving effect of the treatment on thirst. On one hand, a single dose of three mini mint ice cubes enabled to evaluate the duration of the observed effect on thirst. On the other hand, a repeated therapeutic action against thirst targeting the patient's mouth is known to significantly improve a patient's comfort and to reduce thirst.[10] Relatives could be involved in the iterative delivery of the mini mint ice cubes to the dehydrated subjects.[10] Of course, this physiological study may help build a large randomized controlled trial that may be needed to confirm our findings in a broad population.

Mini mint ice cubes application in the mouth immediately relieves thirst and thirst-associated discomfort despite no physiologically significant changes in Na^+ or osmolarity. On the contrary, massive hydric intake corrects osmotic disturbances but cannot totally quench thirst as long as the rehydration route shunts the individual's mouth.

Malcolm Lemyze, MD
Johann Lavoisier, MD
Department of Critical Care Medicine
Arras Hospital
Arras, France
E-mail: malcolmlemyze@yahoo.fr

Johanna Temime, MD
Department of Critical Care Medicine
Schaffner Hospital
Lens, France

Maxime Granier, MD
Department of Critical Care Medicine
Arras Hospital
Arras, France

Jihad Mallat, MD
Department of Critical Care Medicine
Schaffner Hospital
Lens, France
Department of Critical Care Medicine
Critical Care Institute
Cleveland Clinic Abu Dhabi
Abu Dhabi, UAE

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Appendix

Regarding exclusion criteria, delirium was detected using the Confusion Assessment Method (CAM-ICU) validated in intubated critically ill patients.[1] All the delirious patients were ruled out from the study.

0–10 Numeric Rating Scale of Thirst Intensity

1 Almost imperceptible
2 Very slight
3 Slight
4 Relatively slight
5 Moderate
6 Relatively severe
7 Severe
8 Very severe
9 Extremely severe
10 Worst possible thirst

Numeric Five-Point Likert Scale of Thirst-Associated Discomfort

1 Very comfortable
2 Quite comfortable
3 Acceptable
4 Quite uncomfortable
5 Very uncomfortable

Statistical Analysis

Considering that severe thirst[2]—defined as a thirst intensity score over 6/10—has a prevalence of 70% in hypernatremic patients,[3] 21 patients were needed to demonstrate a 1.5-point reduction in the thirst intensity score within five minutes following mini mint ice cubes application in the mouth, with a power of 80% and an alpha risk of 0.05 (McNemar test). Taking into account the possibility of technical problems in 10% of cases, the number of subjects to be included was therefore increased to 26. The normality of data distribution was assessed using the Kolmogorov-Smirnov test. When normally distributed, continuous data were compared using Student's t-test; otherwise, the Mann-Whitney *U* test was applied. Analysis of the discrete data was performed by using the Fisher exact test. Statistical analyses were performed using SPSS (SPSS for windows release 17.0, Chicago, IL). A *P* value of less than 0.05 was considered statistically significant for single comparisons. All reported *P* values are two sided.

Appendix Table 1
Patients' Characteristics at Admission

Parameters	Overall Population ($N = 26$)
Age (yrs)	63 [58−69]
Male, *n* (%)	21 (80.8)
Weight (kg)	84.5 [74−102]
BMI (kg/m^2)	27 [23−32]
Diagnostic, *n* (%)	
Pneumonia	8 (30.8)
Other sepsis	7 (26.9)
Diabetic acidoketosis	2 (7.7)
Other cause	9 (34.6)
Factors promoting hypernatremia, *n* (%)	
Excessive water loss	
Intra-abdominal exudative fluid	8 (30.8)
Fever	13 (50)
Diuretic	6 (23.1)
Polyuria	7 (26.9)
Gastrointestinal loss	3 (11.5)
No access to water	24 (92.3)
Voluntary water restriction	5 (19.2)
Excessive sodium intake	1 (3.9)
Severity at admission	
SAPS II	47.5 [39−66]
SOFA score	6 [4−10]
Organ failure number	
1	7 (26.9)
2	9 (34.6)
3	6 (23.1)
4	4 (15.4)
Mechanical ventilation, *n* (%)	
Intubation	12 (46.2)
Noninvasive ventilation	5 (19.2)
Thirst risk factors, *n* (%)	
Diuretics	6 (23.1)
Selective serotonin reuptake inhibitors	1 (3.9)
Opioids	2 (7.7)
Natremia (mmol/L)	153 [150−155]
Water deficiency (L)	4.6 [3.6−5.6]

BMI = body mass index; SOFA score = Sequential Organ Failure Assessment; SAPS2 = Simplified Acute Physiologic Score 2.
Data are expressed as median [interquartile range, 25-75].

Appendix References

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