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Research Article

Gargling-induced reduction in urinary Na/K ratio in dehydrated humans: Is there a dual role for oropharnygeal receptors in vasopressin regulation?

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ABSTRACT

Background: A linear relationship exists between plasma osmolality (Posm) and thirst perception (TP) and also between plasma arginine vasopressin (Pavp) and Posm. Thus, an increase in Posm leads to an increase in Pavp secretion, which are systemic indicators of thirst. Recent studies have also shown that Pavp secretion is associated with sodium retention. The role of Pavp in termination of thirst during drinking while Posm remains unchanged is however inconclusive. This informed the basis for the present study. **Methods:** Ten (10) apparently healthy male volunteers aged between 20 and 30 years, non-smokers and not on any medication prior to the experiments, were recruited for this study. They dehydrated for 18hrs and their 12-hour urine samples as well as thirst perception were measured with standard methods and compared with those of 10 euhydrate control subjects. Urine volume as well sodium and potassium concentrations were estimated. **Results:** We observed a gradual decrease in TP of the subject who gargled with D/H_2o; this decrease became significant ($P<0.05$, respectively) after 30mins and remained so till the end of the experiment. Gargling with various concentrations of saline (0.9 - 2.7%) did not show any significant change; however, in comparison with controls, the Na^+/K^+ ratio significantly decreased in all samples collected after gargling at every 30mins for 1Hr and after ad libitum distilled water drinking ($P<0.05$, respectively). Also, the Na/K ratio obtained during gargling (30mins and 60mins) were relatively stable but decreased significantly ($P<0.05$) at 90mins; which was 30mins after ad libitum drinking. **Conclusion:** We conclude that oropharygeal receptors play a dual role in stimulating immediate inhibition of vasopressin as well as aldosterone release in the regulation of thirst during dehydration and gargling, to eliminate thirst.

INTRODUCTION

Water is without question, the most important solvent in the fluid composition of living systems. The act of drinking ameliorates thirst and inhibits the secretion of vasopressin before changes in extracellular fluid volume or osmolality in both animals and man (Salata *et al.*, 1987) while thirst has been defined as a deep-seated feeling of a desire for water (Robertson, 1984) and as the conscious sensation of a need for water (Robertson, 1991). For these two definitions, studies on thirst mechanisms can only be appreciated in human subjects as animals can neither report the sensation for water nor indicate the motive for its intake. Plasma osmolality (Posm) has been linked inextricably to determine the sensation of thirst (Baylis and Robertson, 1980). Gargling is the exhaled air, forced through a liquid held in the back of the mouth, with the head tilted back, to cleanse or medicate the mouth or throat. In this context, gargling was defined as sensitization of the oropharyngeal receptors located at the upper palate at the posterior part of the mouth. This has also been documented in dogs and humans (Bruner, 1993; Haung *et al.*, 2000; Obika *et al.*, 2009). Increased plasma osmolality, thirst and increased secretion of plasma arginine vasopressin (Pavp), have been associated with

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water deprivation (Bayliss and Robertson, 1980, Stricker and Verbalis, 2002). Geelen *et al*., (1984), reported that the close relationship between Posm and Pavp is lost during the act o drinking which causes rapid suppression of vasopressin secretion before changes in Posm. We have previously reported an increased thirst perception in dehydrated humans (Obika *et al*., 2009); the role of oropharyngeal receptors in thirst perception after dehydration and rehydration was also demonstrated by Obika *et al*., 2014; however, the precise role of oropharyngeal receptors in urinary sodium potassium ratio has not been defined especially during drinking, when thirst perception would be abolished. We therefore investigated in the present study, if this process is linked with vasopressin or aldosterone mechanism.

MATERIALS AND METHODS

Subjects and experimental design: Ten (10) apparently healthy volunteers with verbal consents, between the ages of 20 and 30 years, all males, non-smokers and not on any medication as at 72hrs prior to the experiments were recruited for this study. They dehydrated for 18hrs prior to the experiment. Precisely, they stopped drinking water and abstained from fluids from 15.00hrs until 9.00hrs of the following day. Their 12hr urine samples were obtained, starting from 21.00hrs on the start day till 9.00hrs of the next day. However, subjects with discomforts during dehydration were asked to stop and drink water but exempted from the study. They were individually given 50ml of graded concentration of NaCl and distilled water to gargle and not to drink but to stimulate the oropharyngeal receptors i.e. D/H2o, 0.9%, 1.8% and 2.7% of NaCl respectively at fortnightly interval (the volume regurgitated was measured and a loss of more than 10ml indicated drinking and was disqualified from the study also). The experiment lasted for eight weeks.

Parameters measured:

Thirst ratings were assessed by Visual Analogue scale which is a 10cm long, uncalibrated line developed by Thompson in 1991. Subjects were asked the following question: 'How thirsty do you feel now? - and they were instructed to mark the line at the point they considered to represent their thirst ratings between the extremes zero thirst at the bottom and very thirsty at the 10cm mark. It was however emphasized to each subject that any mark above 0cm is a positive manifestation of some degree of thirst and that a zero rating is an absolute lack of thirst.

Other parameters measured include urine osmolality with sodium and potassium concentrations. These were obtained from the 12hr urine samples collected as well as the intermittent urine voided during the gargling procedures at 3omins interval. Standard flame photometric method was used for sodium and potassium analysis while urine specific gravity method with the chemical impregnated strip was used to determine the specific gravity of urine from which the osmolality values were extrapolated using the method of Frew *et al*., (1973), which has been validate severally by many authors. The urine volume produced after 12hrs served as adherence control for proper dehydration, any subject with urine volume greater than 700ml was exempted from the study.

Oropgaryngeal stimulation was done by gargling with 50ml of fluid at 5mins interval while the subjects mark the VAS scale every 10mins for 1hour and at the 70th minute after ad libitum water drinking.

Statistical analysis was done using the one-way anova for within groups and between groups respectively. The Mean and standard error of mean of the data were recorded. Microcal Origin 8.0 version was used for all analysis with confidence limit set at 95%.

RESULTS

Fig. 1 shows the Thirst Perception (TP) ratings observed at 10mins interval after gargling with various fluids at every 5mins. There were gradual decreases in the TP ratings of D/H_2O group which became significant ($P<0.05$, respectively) after 30mins, sustained till the end of the experiment, while gargling with various concentration of saline i.e 0.9%, 1.8% and 2.7% did not show any significant change ($P>0.05$, respectively) until the 70th minute.

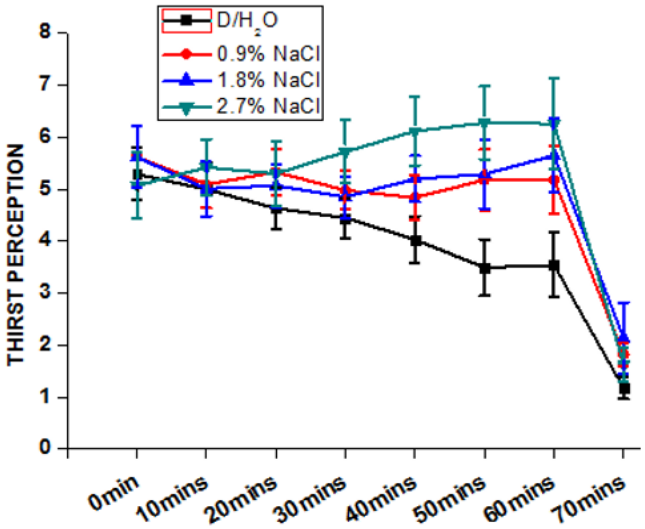

Fig 1: Thirst Perception (TP) with time before and after drinking of Distilled water. There were gradual decreases in TP of the D/H_2O group which became significant ($P<0.05$, respectively) after 30mins, sustained till the end of the experiment while gargling with various concentration of saline from 0.9% to 2.7% did not show any significant change ($P>0.05$, respectively). It is noteworthy however, that there is a significant decrease ($P<0.05$, respectively) in TP at 70mins (10mins after ad libitum drinking) in all the groups.

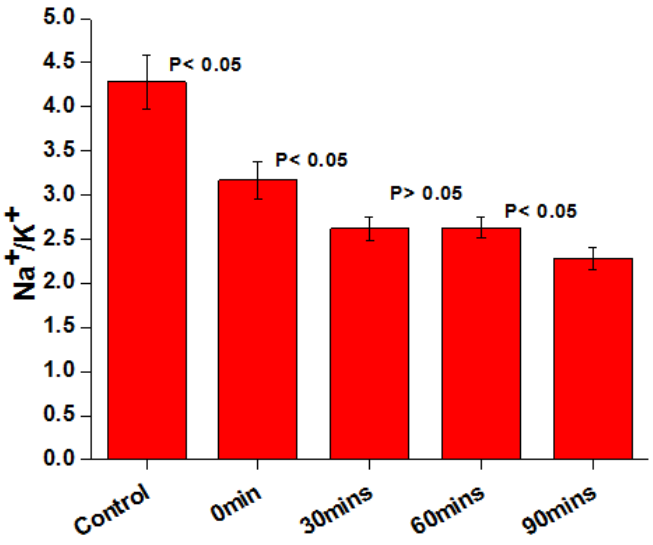

Fig 2: Urine Na+/K+ ratio in controls, 12hrs sample (0min) and after every 30mins during gargling and after 18hrs dehydration. There were statistically significant decreases between the control and all samples collected before and at after gargling at every 30mins for 1Hr and at 30mins after ad libitum distilled water drinking (P<0.05, respectively). However, the ratio obtained during gargling (30mins and 60mins) were relatively stable but decreased significantly at the 90th mins which was 30mins after ad libitum drinking (P<0.05).

The urine Na+/K+ ratio in euhydrate controls and dehydrated subjects are presented in Fig. 2. There were statistically significant decreases between the control and all urine samples collected before and after gargling at every 30mins for 1Hr and at 90mins (30mins after ad libitum distilled water drinking), (P<0.05, respectively). However, the ratio obtained during gargling (30mins and 60mins) were relatively stable but decreased significantly at the 90th mins (P<0.05).

DISCUSSION

The reliability and validity of measurements of the subjective thirst ratings have been previously reported as follows: thirst correlates positively with plasma Osmolality (Posm) (Bayliss and Thompson, 1988) and that subjective ratings using the VAS scale correlate positively with plasma osmolality (Thompson *et al*., 1986; obika *et al.*, 2014). Posm has also been inextricably linked with thirst determination and Pavp is secreted in response to increases in Posm (Bayliss and Thompson, 1980). Vasopressin acts on the distal nephron to enhance water retention thereby concentration the urine (Stout *et al.*, 1999). An unexplained neural pathway was suggested by Seekl *et al*., (1986) for the mechanism whereby Pavp secretion is inhibited during swallowing and various workers have tried to substantiate this view (Obika *et al*., 2009; 2014) but with no specific role ascribed to the aldosterone/vasopressin mechanism.

We have in this study recorded significant increase in thirst ratings at dehydrated state with concomitant decreases in thirst perception and in urinary Na^+/K^+ ratio before (12hrs urine) and after gargling with distilled water for over an hour period and a further decrease after ad libitum drinking. Also, we observed a significant decrease in the 12hrs urinary Na^+/K^+ ratio compared with that of the euhydrate controls (P<0.05) with further decreases after gargling at different times. A decrease in urinary Na^+/K^+ ratio has been defined for long by Mountcastle in 1968 as been an indication of aldosterone action. This view has been upheld in neurophysiology till date. Therefore, our results indicate a possible stimulatory role of oropharyngeal receptors on the hypothalamo- adrenocortical axis to increase the stimulation of aldosterone and vasopressin during dehydration.

The unexplained neural pathway suggested by Seekl *et al*., (1986) for the mechanism whereby Pavp secretion is inhibited during swallowing could probably be explained from this study. with a steady significant decrease in Na^+/K^+ ratio during gargling after dehydration, it is plausible to reflect on the role of oropharyngeal receptors in relaying impulses to the hypothalamus to inhibit Pavp secretion much earlier than aldosterone and a subsequent reduction in thirst perception. Pavp has been linked with sodium retention (Stockand, 2010), its activity may be faster than that of aldosterone being a peptide hormone. This will momentarily eliminate the desire to drink water when Posm has not been lowered. This mechanism seems protective against excessive drinking after a dehydration episode by metering the amount of fluid intake necessary to abolish thirst. The significant decrease recorded after ad libitum drinking at 90mins (30 mins after termination of dehydration) further buttress the resumption of aldosterone secretion and hence sodium retention with a concomitant decrease in urinary Na^+/K^+ ratio.

We conclude therefore that the oropharynx receptors play a dual role in stimulating immediate inhibition of vasopressin as well as aldosterone release in the regulation of thirst during dehydration and gargling. The Na+/K+ ratio after rehydration and gargling with 0.9% NaCl may need further investigation to highlight the influence of isotonic fluid for oral rehydration purposes.

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