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Alterations in the Hydration Status Affect Coughing in Otherwise Normal School Children

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Abstract

Purpose – Compared with adults, children have a lower thirst sensitivity often leading to insufficient water intake. A negative water balance, termed dehydration, may result in neurological, cardiovascular and metabolic disturbances. An adequate water intake is important also in maintaining homeostasis of the airway epithelium and favouring mucociliary clearance. Little is known, however, on the possible association between dehydration and respiratory symptoms, including coughing. **Aim** - To investigate the relationship between dehydration and the prevalence, frequency and duration of cough episodes in children from a free-living general population. **Methods** – A questionnaire consisting of 32 questions designed to investigate the relationships between respiratory symptom, cough episodes, and daily water intake was distributed to the families of 400 students of primary and secondary school (6-16 years). From all participants, a urine sample was collected for osmolality measurements. **Statistics**. The Pearson Chi Square and the Fisher Exact Test were used for statistical comparisons; $p < 0.05$ was taken as significant. **Results** – Valid data were obtained from 305/400 healthy students (mean \pm SD age 10.1 \pm 2.4; mean \pm SD osmolality 863.0 \pm 223.0 mOsm/kg). The prevalence of cough was related to the level of osmolality ($p < 0.001$). More specifically, in subjects with normal urine osmolality, the prevalence of cough was 54.2%; in mild dehydration it increased to 86.1%, and in severe dehydration cough prevalence rose to 93,9% ($p < 0.001$). **Conclusions** – The results suggest a correlation between dehydration and the prevalence of cough in healthy children. In consequence, an adequate daily water intake may help to reduce the number of cough episodes in children.

Keywords: cough; respiratory symptoms; children; osmolality; dehydration; water

Introduction

Water is one of the principal nutritional agents [1] as it is involved in virtually all bodily processes [2]. It seems well established that children usually drink insufficient amounts of water daily, likely due to lower sensitivity to thirst and lack of adequate dietary recommendations by the parents [3-4]. Dehydration is a condition occurring when water balance is negative, that is water loss being higher than water intake [5]. Several international studies have confirmed that children drink too little to meet their water requirements, so that they are likely to become dehydrated and have elevated urine osmolality [6-7]

Although dehydration is rarely considered a crucial factor for airway homeostasis, it has been shown that normal hydration protects the airway epithelium and favours an effective mucociliary clearance [6]. Conversely, dehydration can stimulate the production of mediators that affect the airway calibre and promote airway inflammation [8]. Whether dehydration contributes to the genesis and persistence of respiratory symptoms in otherwise healthy children has not been established.

Coughing is the most prominent and frequent clinical respiratory sign in children, and represents a high burden of recurrent doctor visits, parental stress, and worries that resolve when cough ceases (9). Therefore, we aimed to investigate the relationship between the hydration status and the frequency and duration of cough episodes in otherwise healthy school children.

The study was approved by the Ethical Board of AIST (the Italian Association for Studying

Cough) and by the Council of the School Institute. The study protocol conforms to the ethics of the World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the 64th WMA General Assembly, Fortaleza, Brazil, October 2013. For all participants, a written informed consent signed by at least one of the children's parents was obtained.

Methods

This was a monocentric, observational study. The operational tools were an anamnestic questionnaire and individual measures of urine osmolality.

A cohort of 400 students (females n=202) from the primary and secondary school attending the same institute in Bologna were enrolled on a voluntary basis. Inclusion criteria were: a) age between 6 and 16 years; b) informed consent signed by at least one parent; c) absence of an acute respiratory disorder at the time of recruitment; d) never smoking subjects. Exclusion criteria were: a) inadequate completion of the questionnaire; b) insufficient collection of the urine sample; c) children participation in regular agonistic activities; d) regular smoking habit by any family member.

The parents of children participating to the study had to fill a 22-item anonymous questionnaire (Appendix 1) aimed to investigate cough characteristics together to the prevalence, frequency and duration of cough episodes during the previous 12 months. The hydration status was assessed over a restricted period of the year (February-March, 2017) to warrant maximum availability of children and minimise as much as possible the influence of climatic factors on hydration. In all participants, urine osmolality measurements were performed on samples collected 30 minutes after breakfast to avoid the first urine emission. Urine samples were aliquoted and stored at -20°C for maximum 5 days after collection. Osmolality assessments were conducted in a centralized laboratory by means of a freezing point depressing osmometer (Osmo 3250, Advanced Instruments, Norwood, MA, USA). In keeping with previous studies [7; 10-11], subjects with osmolality values ranging 800-1000 mOsm/kg were considered mildly dehydrated and those with values higher than 1,000 mOsm/kg were considered highly dehydrated [12].

The Pearson Chi Square and Fisher Exact Test were used for statistical comparisons. In all instances, data were reported as means±SD; p<0.05 was taken as significant.

The study (# 23/CC/2016) was approved by the AIST Ethical Committee during the session of november, 2016.

Results

A total of 305 healthy students (76.2%.) returned a valid questionnaire and the results of urine osmolality assessments. Males (n= 155, 50.8%) and females (n= 150, 49.2%) were equally distributed among the population studied. In Table 1, we report anthropometrics of participants stratified by sex and age.

Mean (±SD) urine osmolality value of the overall sample was 863±223 mOsm/kg (range 148-1,293 mOsm/kg). Osmolality data stratified by age and gender are reported in Tab. 2. Whilst 39.3% of participants (n=120) had normal osmolality values, 28.2% (n=86) were mildly dehydrated, and the remaining 32.5% (n=99) were highly dehydrated. Hydration was significantly different by age (≤ or > 10 years), but not by gender.

The prevalence of cough was 54.2% when osmolality was within the normal range; however, in mild dehydration it increased to 86.1%, and in the presence of severe dehydration it rose to 93,9% (p always<0.001). The prevalence of cough episodes was similarly distributed by gender (74.2% in males and 78% in females, respectively, p=0.81) and age (79.1% and 73.3% in children aged ≤ 10 and >10 years, respectively, p=0.743). Indeed, 76.1% of subjects (n=232) suffered from at least one episode of cough during the previous year. In particular, 63.3% of subjects (n=147) claimed 1-2 episodes of cough; 27.6% (n=64) 3-5 episodes, and 9.1% (n=21) > 5 episodes over the last year. Also in these subgroups cough prevalence was independent of gender and age.

In the subjects as a group, one or more cough episodes were reported by 54.2% (65/120) of normo-hydrated subjects over the last year, compared with 86.0% (74/86) of those with mild dehydration, and to 93.9% (93/99) of those with severe dehydration.

As shown in Tab. 3, the mean number and duration of cough episodes were significantly higher in dehydrated subjects, independently of their gender and age (p=0.001). Cough episodes occurred in 53.5% (n=31); 82.2% (n=38), and 90.4% (n=47) of males with normal, mild, and high dehydration levels, respectively (p<0.001); similarly, cough episodes ensued in 54.8% (n=34); 90.2% (n=37), and 97.9% (n=46) of females with normal, mild, and high dehydration, respectively (p<0.001). In addition, cough episodes were reported by 45.8% (n=22) of subjects aged ≤10 years and with normal osmolality values, by 83.3% (n=35) of those with mild dehydration and by 93.1% (n=54) of those with severe dehydration (p<0.001). Subjects aged > 10 years developed cough episodes in 54.2% (n=39) of normo-hydrated; in 77.3% (n=34) of those with a mild dehydration, and in 95.1% (n=39) of those highly dehydrated (p<0.001).

Table 1: Anthropometrics of the sample, and statistical comparisons by gender and age

	Sample size (n=305)	Gender			Age		
		Males (n=155)	Females (n=150)	P	≤ 10 years (n=148)	>10 years (n=157)	P
Weight (kg):							
mean±SD	38.8±12.5	39.7±13.4	38.1±11.6	0.387	30.5±7.7	47.0±10.7	<0.001
median [IQR]	37.0 [30.0-46.8]	37.5 [29.3-48.9]	37.0 [30.0-45.0]		30.0 [24.0-35.0]	45.0 [40.0-53.0]	
Height (cm):							
mean±SD	145±15	146±16	145±15	0.561	134±11	156±90	<0.001

median [IQR]	146 [135-156]	145 [135-159]	147 [135-156]		135 [125-141]	156 [150-163]	
Body mass index							
mean±SD	17.9±3.0	18.1±3.2	17.8±2.8		16.8±2.6	19.1±3.0	
median [IQR]	17.5 [15.8-19.6]	17.8 [15.9-19.6]	17.4 [15.8-19.6]	0.448	16.3 [15.2-17.9]	19.0 [16.8-20.9]	<0.001

[IQR: interquartile range]

Table 2: Mean osmolality in the overall sample and by different hydration status. Statistical comparisons by gender and age

	Mean Osmolality (mOsm/kg)	Hydration status		
		Normal hydration (n=120)	Moderate dehydration (n=86)	Severe dehydration (n=99)
Gender:				
- males	876.9± 16.3		45 (29.0%)	52 (33.6%)
- females	849.8± 19.8	58 (37.4%)	41 (27.3%)	47 (31.4%)
<i>p value</i>	0.467	62 (41.3%)	0.527	
Age:				
≤ 10 years	899.9 ± 18.4	48(32.4%)	42 (28.4%)	58 (39.2%)
> 10 years	827.5± 17.4	72 (45.9%)	44 (28.0%)	41 (26.1%)
<i>p value</i>	0.003		0.004	

Table 3: Relationships between hydration status and cough by frequency and duration of cough episodes.

Frequency of cough episodes (n)	Males			Females		
	Normal hydration	Mild dehydration	Severe dehydration	Normal hydration	Mild dehydration	Severe dehydration
1-2	29 (93.6%)	23 (62.2%)	20 (42.6%)	33 (97.1%)	29 (78.4%)	13 (28.3%)
3-5	2 (6.4%)	13 (35.1%)	18 (38.3%)	1 (2.9%)	7 (18.9%)	23 (50%)
>5	0	1 (2.7%)	9 (19.1%)	0	1 (2.7%)	10 (21.7%)
<i>p</i>		0.001			0.001	
Duration of cough episodes (days)						
<7	26 (83.9%)	26 (70.3%)	18 (38.3%)	3 (9.2%)	26 (70.3%)	16 (34.8%)
7-15	5 (16.1%)	9 (24.3%)	16 (34.0%)	3 (8.8%)	8 (21.6%)	22 (47.8%)
16-30	0	2 (5.4%)	13 (27.7%)	0	3 (8.1%)	8 (17.4%)
<i>p</i>		0.001			0.001	

Discussion

To the best of our knowledge, this is the first observational study pointing to an impact by the hydration status on prevalence, duration and persistence of coughing in otherwise normal children aged 6-16.

Beyond the limitations that pertain to all observational studies [13], this study also presents with specific limitations such as being monocentric and largely based on parental reports. Nonetheless, it also relays on objective assessments that seem to match other non-objective measures. It also has strong points, such as the relatively large number of observations, the restricted observational period, and the homogeneity of the study population.

The normal water balance mainly depends on two mechanisms: the sensitivity to thirst and the extent of secretion of anti-diuretic hormone (ADH). While the former stimulates water assumption, the latter reduces water loss by favouring renal re-absorption, thus determining the urine concentration. ADH concentration relates to plasma osmolality, and this mechanism allows for homeostasis of plasma liquids by reaching a maximal urinary

concentration of 1,200 mmol/kg [14]. Dehydration increases both plasma and urinary concentrations, and such variables are widely used for *in vivo* assessment of the hydration status [15].

Normal values for urinary osmolality range 500 e 800 mOsm/kg over the 24 hours in healthy subjects [12], while values >800 mOsm/kg correspond to the presence of a mild dehydration, and those > 1,000 mOsm/kg are regarded as corresponding very closely to the maximum possible urine concentration.

In keeping with the results of previous studies, a large proportion of the children studied here displayed inadequate levels of hydration. Indeed, 60.6% of children aged 6 e 16 years had osmolality values > 800 mOsm/kg, and 33.1% of them had osmolality values greater than 1,000 mOsm/kg. A previous Italian study carried out on 515 children aged 9-11 years reported that more than 67% of them had urinary values > 800 mOsm/kg, but 35% of them had values > 1,000 mOsm/kg, being this prevalence inversely related to their water assumption [16]. Another study produced equal results in France: 62% of 529

children aged 9-11 years had urinary osmolality > 800 mOsm/kg, but 22% had values > 1,000 mOsm/kg [7]. A similar investigation carried out in the USA confirmed that urinary values > 800 mOsm/kg are obtained in 65% of children, while values > 1,000 mOsm/kg are found in 26% of them [17]. The results from an Egyptian study on children aged 9-11 years demonstrate that their urinary osmolality was >800 mOsm/kg in 57%, and > 1,000 mOsm/kg in 25 % of them [18]. Thus, the results of a wealth of studies consistently point to dehydration as a widespread problem even when comparing regions with profoundly different climatic conditions.

The effects of acute or/and chronic dehydration described in childhood are manifold [11]. For instance, dehydration can induce a lower mental and/or physic performance [3], lead to a significant decrease in attention, and impair short-term memory [19-20]. All these conditions are likely school performance. Furthermore, the loss in blood fluids can lead to a significant limitation in both aerobic and anaerobic physical children's performance, particularly during sustained exercises [21]. Even if mainly investigated in adults, these effects may be even more prominent in children, given a wider body surface resulting in stronger perspiration [22].

Dehydration has long been known to worsen respiratory symptoms and the respiratory function in patients with pre-existing respiratory diseases such as asthma, COPD, and cystic fibrosis [19]. The present study represents the first aim to focusing the relationships between dehydration and cough prevalence, frequency and duration in children. The precise mechanisms by which dehydration seems to affect the prevalence, duration and frequency of coughing in otherwise healthy children remains unclear, since this study was only designed to assess the prevalence and characteristics of this symptom in childhood.

Nonetheless, it seems worth to recall that in pathological conditions such as those mentioned above (23), dehydration can enhance histamine release by the mastocytes, thus resulting in allergic or/and asthmatic relapses [24-26]. Moreover, $2\text{-}H_1$ histamine receptors are involved also in the increase of blood vasopressin and, in turn, contribute to the regulation of the hydration status [25]. Therefore, dehydration might promote coughing simply by enhancing the histamine release, a well-known tussigenic agent [27]. In addition, an appropriate hydration level is crucial in many respiratory conditions as it favours an effective muco-ciliary clearance [23, 28-31]. Last, experimental lines of evidence demonstrated damaging of the tight junctions of airway epithelium in response to hyperosmolarity of surface fluid's composition (32). Damaging of the airway epithelium could also occur with dehydration and disruption of the epithelial tight junctions would expose airway receptors mediating cough to exogenous stimuli. Specific studies are needed to elucidate the role of these putative mechanisms.

In conclusion, this study suggests a relationship between coughing and the hydration status in healthy children. It seems therefore logical to infer that the attitude to drink water should be highly implemented in all children, with particular attention to those who are suffering from a pre-existing condition such asthma and cystic fibrosis asthmatic children and children suffering from cystic fibrosis.

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