

Hydration in severe acute asthma

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Abstract

Twenty children were studied during severe attacks of acute asthma to find out how dehydrated they were on admission to hospital. Mean body weight on admission was 97.8% of their reference stable weight seven to 10 days after the attack and in only three children was it less than 95% of the stable weight. Bedside assessment of dehydration was unreliable. The mean packed cell volume was significantly higher on admission than 7-10 days later (0.44 compared with 0.42, difference 0.02 SE 0.01). Serum sodium and potassium concentrations and osmolality on admission were within normal ranges. The degree of dehydration correlated best with a fall in blood pH. There was no association between the degree of dehydration and the recovery of the peak expiratory flow rate during the first 24 hours or thereafter. We conclude that mild dehydration is common in severe acute childhood asthma. Fluid given at a rate of 50 ml/kg/24 hours was safe and appropriate for these children.

Treatment with intravenous fluid replacement is considered to be an important part of the management of severe acute asthma,¹ but there is no consensus about the volume that should be given during the acute phase. There are two contrasting approaches; the first, based on the results of adult studies, is that patients with severe asthma become appreciably dehydrated and that the degree of dehydration is directly related to the severity and duration of the attack.²⁻⁴ Liberal correction of fluid deficits is thought to mobilise mucus plugs and to decrease narrowing of airways.^{5,6} The second approach, assumes that appreciable dehydration is not a feature of asthma and that indiscriminate correction of fluid deficits in patients having severe attacks may be harmful. This approach is largely based on the finding of raised concentrations of antidiuretic hormone in patients with acute asthma.^{7,8} Giving unnecessary additional fluids to such a patient could lead to fluid retention, pulmonary oedema, and deterioration in the patient's condition. This is particularly so if the increase in antidiuretic hormone represents an appropriate response to mild dehydration. The value of the measurement of acute weight changes as an index of dehydration in children has recently been stressed by Mackenzie *et al.*⁹

We therefore conducted a prospective study to assess the incidence and degree of dehydration in children with severe acute asthma who required admission to hospital, and to assess the

effect of their degree of hydration on their rate of recovery while on a relatively restricted fluid intake.

Patients and methods

PATIENTS

Children aged between 5 and 12 years who attended the asthma clinic regularly and who knew how to use the Mini-Wright peak flow meter were admitted to the study if they required admission to hospital for a severe attack of acute asthma. The criterion for admission was that the peak expiratory flow rate (PEFR) remained at less than half the predicted level after two doses of nebulised salbutamol 1 ml 0.5% solution with 1 ml 0.9% saline (Ventolin).¹⁰

TREATMENT PROTOCOL

During the first 24 hours after admission each child received 50 ml/kg 5% dextrose/water intravenously. Oral fluids were withheld during this period, but thereafter intravenous fluids were discontinued and free oral fluids were allowed. Hydrocortisone 2 mg/kg was given intravenously every six hours for 24 hours, with prednisone 2 mg/kg/daily thereafter, reducing to their previous dose over five days. Theophylline 5 mg/kg was given orally every six hours and inhalations of nebulised 0.5% salbutamol were given every two to four hours as required. Respiratory function was monitored by daily readings of the PEFR.

ASSESSMENT OF HYDRATION

On admission the duration of the attack was recorded, as was whether the child had been vomiting before admission, and whether the child was receiving maintenance treatment with steroids or theophylline.

A clinical estimation of the state of hydration was made at the bedside, taking account of skin turgor, mucosal moistness, and eye signs. A sphygmomanometer with appropriate cuff was used to measure the difference between the inspiratory and expiratory diastolic blood pressure.

Each child was carefully weighed on admission wearing only underclothes and weighed again 24 hours, 48 hours, and seven to 10 days later. Weights were recorded by two independent observers to the nearest 10 g and the mean weight recorded. The scales were standardised at the start of the study and the same scales were used throughout the period.

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Weight at the seven to 10 day visit was assumed to represent the child's stable reference weight, and weights on admission, and 24 hours and 48 hours later, were expressed as a percentage of this.

Serum sodium and potassium concentrations (ion elective electrode, Astra 8 Beckman), serum osmolality (Micro-osmomette Precision System), and packed cell volume (Coulter, Model 5+2) were measured at the same time that they were weighed. Urinary osmolality and ketones (Ames, Ketodiatix) were tested only on the first specimen of urine passed after admission.

PEFR was measured with a Mini-Wright peak flow meter on admission and after the initial inhalation of salbutamol and again whenever the child was weighed. The maximal value of three efforts was recorded.

DATA ANALYSIS

Statistical analysis was carried out by the Biostatistics Unit of the South African Medical Research Council, Parowvallei.

Univariate analysis of variance (Anova) was carried out using the following variables: weight, serum sodium and potassium concentrations, osmolality, packed cell volume, and percentage of predicted peak flow, to identify the variables that changed significantly over time.

Sequential values of weight and hydration indices for each patient were compared using the paired two tailed Student's *t* test, each patient acting as his own control. Spearman correlation coefficients were calculated to work out the relationship between individual variables and the degree of dehydration. Regression analysis was also carried out on all subsets to find out which variable correlated best with the degree of dehydration.

Informed parental consent was obtained for each child studied and the protocol for the study was approved by the ethics and research committee of the Faculty of Medicine, University of Cape Town.

Results

CLINICAL EVALUATION OF THE PATIENTS

Twenty children with severe acute asthma (12 girls and eight boys, mean (SD) 9.15 (2.57), range 5–12 years) were studied. The median

duration of the attack from the onset of symptoms to the time of admission was 16 hours (mean (SE) 17.7, (2.09), range 5–48). In eight the attack had lasted 12 hours or less, in 10 from 13–24 hours, and only two patients had been ill for more than 24 hours. Of the 20 children, 18 were on maintenance treatment with oral theophylline and 11 with oral steroids. Eleven children had vomited at least once.

Thirteen children were thought clinically to be about 5% dehydrated, four were thought to have borderline dehydration (2.5%), and three were considered to be normally hydrated.

DEHYDRATION AND CLINICAL AND LABORATORY MEASUREMENTS

The mean admission weight was 97.9% of stable weight ($p < 0.05$) (mean percentage dehydration = 2.11). Using a repeated measures analysis of variance to detect an overall time effect on the variables shown in the table, significant overall changes in the serial measurements were found for weight ($p = 0.002$), and percentage predicted peak flow ($p = 0.001$).

Analysis of the significant day to day differences in the variables by Student's *t* test (also shown in the table) confirmed that a marginal increase in packed cell volume was present on admission. Despite unrestricted fluids, a small but significant fall from the 24 hour weight was recorded at 48 hours. Three children were more than 5% dehydrated by weight on admission (-5.4%, -5.7% and -6.2% of stable weight). There was no correlation between the calculated percentage dehydration and the clinical assessment (Spearman rank correlation coefficient = -0.007, $p = 0.98$). The degree of dehydration on admission correlated weakly with the duration of the attack. Only one of the two children whose attack exceeded 24 hours duration was dehydrated (percentage dehydration 3.3). The children who had vomited had a mean percentage dehydration of 2.2, and those with no history of vomiting had a mean % dehydration of 2.0 ($p > 0.8$). The only baseline measurement that came anywhere near correlating with the degree of dehydration (using Spearman rank correlation coefficients) was a fall in arterial pH ($r = 0.413$, $p = 0.07$). All subsets regression analysis of the packed cell volume, oxygen and carbon dioxide tensions, bicarbonate, pH, the difference between inspiratory and expiratory

Sequential measurements of indices of hydration expressed as mean (range)

Time from admission	Weight (kg)	Percentage of stable weight	Packed cell volume	Serum potassium (mmol/l)	Percentage of predicted peak flow	Serum sodium (mmol/l)	Osmolality mmol/kg
On admission	27.9 (15.3–48.6)	97.9 (93.9–101.2)	0.44 (0.35–0.63)	3.9 (2.9–5.1)	30.9 (30–49)	137.9 (131–145)	284.9 (274–292)
At 24 hours	28.0 (15.0–48.5)	98.6 (92.0–103.0)	0.41 (0.34–0.49)	3.7 (3.0–5.0)	75.3 (41–114)	137.5 (132–143)	283.9 (275–297)
At 48 hours	27.6 (15.5–47.5)	97.3 (93.2–101.2)	0.42 (0.37–0.53)	3.9 (3.5–4.6)	93.0 (50–139)	138.5 (131–147)	286.1 (277–299)
At seven to 10 days	28.5 (16.3–49.6)	100 (Reference weight)	0.42 (0.36–0.47)	4.0 (3.4–4.8)	103.6 (80–139)	137.8 (133–143)	286.2 (279–306)
p Value Anova	0.0001	Not applicable	0.0784	0.1021	0.0001	0.5700	0.4227
SE of differences	0.16	Not applicable	1.16	0.12	5.15	0.73	1.59
Significant changes	0 v 7–10	0 v 7–10	0 v 7–10	24 v 7–10	0 v 24	None	None
p < 0.05 (Student's <i>t</i> test)	24 v 48 48 v 7–10	24 v 48 48 v 7–10	0 v 24	0 v 24	0 v 7–10 24 v 7–10		

diastolic pressure, and percentage of predicted PEFR, confirmed that the best predictor of dehydration was a fall in pH, but the level of correlation was not sufficient for practical use ($r^2=0.165$, $p=0.10$).

CLINICAL COURSE

All 20 children had uneventful hospital stays and were discharged home several days before their seven to 10 day follow up visit. Comparison of the rate of recovery in lung function (as shown by PEFR) between the children who were below the median value of percentage dehydration (-2.3%) with those who were above the median value (by analysis of variance) showed no difference between the two groups in the rate of recovery ($p=0.38$).

No complications of asthma were encountered, and all patients were clinically well with normal PEFR at the seven to 10 day follow up study.

Discussion

Few controlled studies have investigated the incidence and treatment of dehydration in severe acute asthma.¹⁰⁻¹² None of these studies have assessed the degree of dehydration normally encountered in children with severe acute asthma, or the effect of a relatively restricted fluid regimen on the rate of recovery from the attack.

In this prospective study, by serially measuring clinical and laboratory indices of hydration normally available to the clinician, we found that a mild degree of dehydration was common among children presenting with severe acute asthma. Within the range of dehydration encountered the degree of dehydration on admission bore no relation to the rate of recovery when children were treated on a relatively restricted fluid intake. Our results therefore support the argument that additional fluids above baseline requirements are unnecessary in severe acute asthmatic attacks.

Three lines of evidence support a conclusion that the children that we studied had only mild dehydration. The first, obtained by comparison of the admission weight with the seven to 10 day reference weight (baseline), showed that the mean (SD) percentage dehydration was 2.1 (2.3), range 1.6 to 6.2, median 2.3. Secondly, normal serum electrolyte concentrations and osmolality were recorded on admission and throughout the seven to 10 day observation period, and the mean packed cell volume on admission was mildly but appreciably raised. Thirdly, there was no significant weight gain once the children were allowed unrestricted fluids orally after the initial 24 hour period when fluids were restricted to 50 ml/kg/24 hours. This supports our conclusion that none of them had unrecognised significant dehydration on admission.

In our interpretation of the serial weight changes we have assumed that the weight of a child seven days after a severe acute attack who has recovered completely represents a stable baseline reference weight. We have also as-

sumed that rapid fluctuations in weight reflect fluid balance. These assumptions are reasonable, given the fact that it is practically impossible to obtain a child's reliable weight as a reference scale immediately before the onset of the acute attack of asthma. It has previously been shown that in the short term respiratory tract illnesses (for example, pneumonia and otitis media) cause no discernable retardation in the growth rate of most well nourished children.¹³

The possibility that treatment with steroids could have influenced the seven to 10 day baseline assessments must be considered. Short term weight increases associated with treatment with steroids are usually attributable to mineralocorticoid effects and some children do gain weight quite quickly on high doses of steroids. We do not consider that in our patients steroids caused any appreciable increases in weight, because in the first instance we noted a decrease in mean weight ($p<0.05$) at 48 hours (table), the point at which the patients had received their highest doses of their tailing courses of prednisone. Secondly, serial monitoring of the serum sodium and potassium concentrations and osmolality (table) provided no evidence supporting mineralocorticoid activity at any of the assessments. Thirdly, we discontinued the short course of prednisone on day 5, at least 48 hours before the seven to 10 day assessments of weight. In view of the short reported serum half life of prednisone (3.6 hours) any pharmacological effects of prednisone at the seven to 10 day assessments were likely to be minimal.¹⁴

If, however, we accept that treatment with steroids may have increased the weight in our patients, we have overassessed the degree of dehydration and the mean percentage dehydration on admission is even less than the 2.1 that we found. This would strengthen our conclusion that dehydration in severe acute asthma is usually mild. To our knowledge there are no published data on the effects of tailing off doses of prednisone on weight in the presence of mild dehydration. Our data provide reasonable evidence that any weight gain caused by the steroids in acute childhood asthma is likely to be minimal.

Factors that are likely to influence the degree of dehydration encountered during an acute asthmatic attack include the duration of the attack, ambient temperature, maintenance drug treatment (for example, steroids and theophylline), the presence of fever, oral fluid intake before and during the attack, and vomiting. Several of these factors may occur in varying degrees in a given patient and some factors may compensate for others. We found that children with a history of vomiting were not significantly more dehydrated than those who had not vomited. The clinician overestimated the degree of dehydration in 13 of 20 cases. Mouth breathing by a distressed child causes drying of the buccal mucosa and can falsely suggest dehydration to the attending clinician. In this study the degree of dehydration correlated weakly with the duration of the attack. This finding suggests that most children with acute asthma maintain hydration where possible by continuing to take oral fluids. The severity of the

attack as measured by the difference between inspiratory and expiratory diastolic pressure, and oxygen and carbon dioxide tensions, did not correlate with the degree of dehydration. A mild compensated metabolic acidosis (as shown by a fall in pH) did, however, correlate more strongly with a state of mild dehydration than changes in any of the other variables measured by multiple regression analysis.

To assess the effect of the degree of dehydration on the rate of recovery of the PEFr, the recovery of children who were more dehydrated was compared with those who were less dehydrated. A greater degree of dehydration on admission did not impair the rate of recovery, and as all the children received the same fluid regimen, it suggests that additional fluids are not required to assist airway recovery. Supporting this observation, Nadel emphasised that there have been no studies to support the assumption that fluids will reduce the viscosity of tenacious secretions or influence the mechanisms that could be expected to assist their removal from the airways.¹⁵

In animal experiments, Marchette *et al* found that in allergic sheep with antigen induced bronchial obstruction, tracheal mucus velocity, (as an index of lower airway mucociliary clearance) was impaired by 5% dextrose infusions of 25–35 ml/kg, although no impairment was observed in normal sheep.¹⁶ This raises further questions concerning the possible deleterious effects of too much fluid on children with severe acute asthma.

Baker *et al* studied the weights of asthmatic patients and warned about the dangers of over-hydration and the possibility of water intoxication.⁷ In their study of seven patients (age range 7–52 years) concentrations of antidiuretic hormone were raised in all patients and serum osmolality was decreased. Dawson *et al* measured the concentrations of antidiuretic hormone in the plasma of 10 asthmatic children and found that they were appreciably increased.

If concentrations of antidiuretic hormone are inappropriately raised, abundant oral and parenteral fluids may aggravate mucosal oedema of the airways.¹⁰ This will cause further airway narrowing, perhaps premature airway closure, and worsening of the asthmatic attack. On the other hand Bahna and Kaushik could find no evidence of the syndrome of inappropriately raised antidiuretic hormone secretion in 26 children with acute severe asthma.¹² Singleton *et al* have, none the less, shown that children with severe acute asthma have impaired water excretion after water loading and are at risk of hyponatremia if given hypotonic fluids for a prolonged period of time.¹¹ We believe that the most likely explanation for the raised concentrations of antidiuretic hormone that have been reported in severe acute asthma is the presence of mild dehydration.

Straub *et al* reported haemoconcentration in nine adult patients with asthma using erythrocytes labelled with ⁵¹Cr and a slight increase in

packed cell volume in 13 of 20 patients with severe attacks, but this did not correlate with their assessments of dehydration using serial measurements of weight. Our study also showed a slight, but significant, increase in the packed cell volumes of children presenting with severe acute asthma.

Taken collectively these studies support our conclusion that additional fluids should be given with caution to a child with severe acute asthma. As concentrations of antidiuretic hormone are increased in acute childhood asthma, we believe that the most likely explanation is that this is an appropriate response to mild dehydration rather than a syndrome of inappropriate secretion of antidiuretic hormone. Until there is evidence that the liberal giving of fluids has a beneficial effect on the course of the disease, or that withholding fluids to achieve a state of mild dehydration is beneficial, it seems prudent to aim for a state of normal fluid balance in children with severe acute asthma. When fluids cannot be taken orally, calculation of the maintenance volume of low solute intravenous fluid should be based on about twice the estimated insensible loss—that is, roughly 50 ml/kg/24 hours. This is a safe and appropriate volume, is not accompanied by significant electrolyte changes or fluid retention, and is consistent with rapid recovery in the PEFr.

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