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Severe Metabolic Acidosis and "Muti" (traditional herbal medicine) ingestion in young children.

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SUMMARY

Twenty infants and young children admitted with severe metabolic acidosis and a positive history of 'muti' ingestion were investigated. All had accompanying gastroenteritis and significant dehydration.

Biochemical data was diagnostic of high anion / gap metabolic acidosis in the majority (70 per cent).

Further biochemical data indicated that lactic acidosis and pre-renal azotaemia resulting from severe hypovolaemia were likely causes of the high anion GAP metabolic acidosis.

There was no evidence to suggest that the ingested muti *per se* was associated directly with the acidosis or acute renal failure seen in these children.

INTRODUCTION

The administration of traditional herbal infants and young children is a widespread practice in Zimbabwe. Such 'muti' is usually administered to acutely sick children with diarrhoea or unexplained fever and at times as perceived protection against illness.

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Experience from paediatric practice both at Harare and Parirenyatwa Central Hospitals has established that a positive history of prior "muti" administration can be obtained in a significant proportion of children admitted with acute gastroenteritis and biochemical evidence of severe metabolic acidosis.

Metabolic acidosis is frequently encountered in young children with acute gastroenteritis or septicaemia.

However, the degree and severity of the metabolic acidosis often seen in children with a positive history of "muti" ingestion appeared to be out of proportion to that expected from the underlying gastroenteritis suggestion that the "muti" ingestion appeared to be out of proportion to that expected from the underlying gastroenteritis suggesting that the "muti" ingestion *per se* could have contributed in some way to the degree of metabolic acidosis.

Such children also frequently presented with significant azotaemia.

We therefore studied a group of children presenting with severe metabolic acidosis and positive history of "muti" ingestion to establish:

i) If significant elevation of the anion GAP could be demonstrated to suggest endogenous or exogenous H^+ generation;
ii) If lactic acidosis was the possible major cause of a documentable elevation of the anion GAP and a possible major contributor to the metabolic acidosis;
iii) If the azotaemia commonly encountered in these children was of renal (ie: 'muti' related nephrotoxicity) or of pre-renal (hypovolaemic) origin.

PATIENTS AND METHODS

Acute ill children presenting with clinical and biochemical evidence of severe metabolic acidosis (pH < 7.2) and a definite positive history of "muti" ingestion were selected for study.

A control group of children could not be included because of unreliability of a parental denial for such "muti" administration.

On admission, arterial blood sample was obtained for blood gases, and a venous sample for the following investigations: serum electrolytes including Na, K Cl, bicarbonate, plasma urea and creatinine, blood sugar, salicylate level, and plasma

osmolality by routine methods.

Anion GAP was calculated in all patients using the following formula: anion GAP = ($Na^+ + K^+$) -($Cl^- + HCO3^-$) mmol/l.

Blood lactate was determined on venous deproteinised blood by the enzymatic UV - Test (Monotest Lactat (R) Boehringer Mannheim GmbH Diagnostica).

First voided or catheter obtained urine was sampled for the following biochemical determinations: Urinary sodium, pH, osmolality, creatine, urea, and ketone bodies (Ketostiks).

Fractional excretion of sodium (FENa) was calculated by using the following formula: /FENA = (U/S Na-) divided by (U/S Cr) x 100 (expressed as a percentage) U/S Na = (urine sodium in mmol/l divided by serum sodium in mmol/l; and U/S Cr = (urine creatinine in mmol/l divided by serum creatinine in mmol/l).

Stools were cultured for routine pathogenic bacteria.

RESULTS

Clinical Features: Twenty infants with initial blood pH below 7.2 were studied. There were 11 males and 9 females with ages ranging from two months to 18 months (mean of 6.8 months).

All, except one infant who died soon after admission, were found to be of normal nutritional status after rehydration. all patients presented with history of acute diarrhoea and vomiting, with duration ranging from 1 - 7 days.

Three also had a history of cough of short duration and 5 had definite history of fever prior to admission.

On initial examination all were found to be clinically dehydrated with deep acidotic respirations. the degree of dehydration varied from eight per cent to 20 per cent (calculated retrospectively). Eight were severely hypotonic, whilst 3 were severely shocked state and drowsy. Three of the four infants who showed signs of cerebral irritation on admission developed generalized convulsions in the ward.

Cerebrospinal fluid examination in these infants were found to be normal Hypothermia (rectal temperature < 35 degrees °C) was present in four infants and fever (>38 degrees C) in three infants. Three patients had clinical and radiological evidence of pneumonia.

TABLE 1

The standard bicarbonate, anionic gap, serua lactate serum salicylate and blood pH on admission

	pH	Bicarb m mol/l	Anion Gap m mol/l	S.Lactate m mol/l	Salicyl m mol/l
	6.654	7.3	54.5	8.0	.8
	6.790	4.3	25.3	2.4	.3
	6.809	2.5	38.5	4.4	.4
	6.865	4.1	12.9	9.5	.5
	6.929	3.1	12.6	2.7	.4
	6.932	4.1	36.0	4.2	.3
	6.935	6.1	16.9	7.6	.2
	6.974	3.7	18.2	2.8	.3
	6.981	3.9	22.0	3.2	.8
	6.981	3.0	25.7	4.7	.2
	7.005	6.1	31.9	8.2	.2
	7.034	4.6	30.5	1.2	.1
	7.043	4.8	7.5	1.7	.1
	7.063	6.1	32.1	7.0	
	7.113	3.9	12.6	1.9	.4
	7.114	4.0	19.6	1.8	.2
	7.122	4.1	9.1	3.0	.3
	7.150	5.0	11.8	2.3	
	7.172	6.5	18.9	7.5	
	7.187	9.4	18.7	9.8	.6
Mean	6.993	4.830	22.765	4.689	.2054
Range max	7.187	9.4	54.5	9.8	.8
min	6.654	2.5	7.5	1.2	.1
Std D ev	.1355	1.6131	11.4381	2.7874	.2054

In two infants *Staph. aureus* was isolated from blood cultures and in 1 *E Coli* Salmonella group B was isolated from stool culture in one patient.

Management and Outcome

All patients initially were managed with intensive rehydration therapy with intravenous fluids. Electrolyte abnormalities and metabolic acidosis were repeatedly monitored and corrected appropriately.

The average stay in hospital was five days and the infants with proven sepsis were treated with appropriate antibiotics for 10 to 12 days.

One infant aged one year with a blood pH of 6.654 died within a few hours of admission.

Biochemical Results: Table 1 shows the bicar-

TABLE 2.
Serum electroltes and fractional excretion of sodium (using creatinine) on admission

	pH	na m mol/l	K m mol/ l	Cl m mol/l	Urea m mol/l	Crt'nine m mol/l	Frac.l excre. of Na %
	6.654	136	1.3	76	14.6	1500	.73
	6.790	150	3.4	118	38.4	365	2.84
	6.809	128	2.0	89	9.1	76	1.09
	6.865	111	2.0	96	18.8	94	2.12
	6.929	134	3.7	122	20.9	136	1.37
	6.932	154	5.1	119	31.1	57	.10
	6.935	130	3.0	110	9.7	56	1.66
	6.974	159	4.9	142	29.7	142	.41
	6.981	132	5.9	112	40.6	302	1.75
	6.981	142	2.7	116	15.0	98	.64
	7.005	129	3.0	94	34.0	136	.19
	7.034	138	3.1	106	6.8	180	
	7.043	142	2.3	132	23.6	255	.21
	7.063	134	3.2	99	3.2	81	.39
	7.113	139	4.5	127	4.9	152	.22
	7.114	158	3.6	138	19.7	155	1.50
	7.122	142	5.2	134	11.8	183	.98
	7.150	129	2.8	115	28.6	94	.56
	7.172	143	2.4	120	13.3	138	.07
	7.187	133	4.1	109	10.3	81	.13
Mean	6.993	138.150	3.410	113.675	19.205	146.550	.893
Range max	7.2	159.0	5.9	142.0	40.6	365.0	2.8
min	6.7	111.0	1.3	75.5	3.2	56.0	.1
Std Dev	.1355	11.1053	1.1895	16.6765	11.0059	78.8013	.7699

bonate, anion GAP, lactate and salicylate levels in relationship to the blood pH values. Blood pH on admission ranged from 6.654 to 7.189 and the mean was 7.187.

Corresponding standard bicarbonate values were also low with a mean of 4.83 mmol/litre. 14 (70 per cent) infants had anion GAP above 16 mmol/l (normal range eight -16 mmol/l.

The highest value of 54.5 mmol/l was recorded in the infant who had a blood pH level of 6.654. No direct relationship between blood pH and the anion GAP was observed.

All serum lactate levels were above the normal level of 1 mmol/l. The maximum level was as high as 9.8 and the lowest was 1.2 and the mean was 4.7. Serum salicylate levels were unremarkably low with mean of 0.36 mmol/l. Initial blood glucose level ranged from 1.2 mmol/l to 19.8 mmol/l with a mean of 9.45 mmol/l.

Serum electrolytes, urea, creatinine and fractional excretion of sodium are listed on Table II. The mean sodium levels was 138 mmol/l, three were hypernatraemic (sodium level > 150 mmol/l) and one infant was hypernatraemic with level below 120 mmol/l.

Hypokalaemia was a common initial presentation with low mean of 3.4 mmol/l. In nine (45 per cent) infants the level was below 3mmol/l.

The average serum creatinine and urea were 147 mmol/l and 19.2 mmol/l respectively.

Fractional excretion of sodium calculation demonstrated only 2 infants with level of greater than two, indicating that the majority of the infants were in prerenal failure related to hypovolaemia due to dehydration.

Urinary pH on admission ranged from five to eight and 50 per cent an pH value of 5. Ketones (with normal blood glucose levels) were detected in only three urine samples.

The ketonuria promptly cleared on rehydration.

DISCUSSION

Comprehensive biochemical investigations undertaken in these 20 children who presented with a clinical picture of metabolic acidosis and positive history of 'muti' ingestion, confirmed the presence of severe systemic metabolic acidosis.

Arterial blood pH was <7.2 in all and the severity of the metabolic acidosis is attested to by the fact that in half of the studied children, arterial pH on admission was below 7.0.

The relevant issue that needed resolving was whether the severe metabolic acidosis encountered in these children was related to 'muti' ingestion *per se* or could be readily explained on the basis of their underlying presenting illness.

A history of preceding diarrhoea and vomiting was obtained in all the studied children and all presented with significant dehydration with three of whom were in severe hypovolaemic shock. Additionally, positive blood cultures were obtained in three children.

Anion GAP, was calculated in these children to determine the possible nature of the metabolic acidosis[1,2]. Fourteen of the 20 children studied had elevated anion GAP, All had associated decreased

serum bicarbonate, diagnostic of metabolic acidosis with high anion GAP[2], In clinical practice the main causes of high anion GAP metabolic acidosis are: uremia, ketoacidosis, lactic acidosis, salicylate toxicity methanol toxicity, ethylene glycol toxicity and paraldehyde toxicity[1,3].

In the children studied, we have the clinical setting (significant dehydration) and the biochemical basis to suggest that the documented high anion GAP metabolic acidosis resulted from lactic acidosis and acute pre-renal uremia. Elevated serum lactate was documented in all 20 children and all but three had elevated plasma urea levels.

Lactic acidosis commonly develops when tissue perfusion and oxygenation are inadequate.

The common causes of lactic acidosis in children are hypovolaemia, usually accompanying gastroenteritis and dehydration, septicaemia with shock and hypoxia from respiratory diseases.

Rarely it may be associated with certain drugs (eg salicylate, isoniazid, streptozoticin), or inborn errors of intermediate metabolism or toxins (eg phenformin) [4]. In situations associated with poor tissue perfusion lactic acidosis is attributed to over-production by hypoxic tissues[5].

However, in clinical states of hypovolaemia and shock, such as in our studied children, decreased delivery of lactate to the liver and kidney, the major sites of lactate metabolism and utilization, may be of equal importance. Overproduction and under-utilization would then contribute to maintain lactic acidosis[6].

The majority of children in this study were uremic on presentation. Uremic acidosis is a common cause of high anion GAP metabolic acidosis[1]. Estimation of fractional excretion of sodium clearly indicated the majority of the infants (90 per cent) were in prerenal failure[7].

This observation was supported by the usually prompt clinical reversal of the presented azotaemia on volume expansion and rehydration.

We found no biochemical or clinical evidence to suggest nephrotoxicity, possibly from 'muti', as the cause of the presenting acute renal failure and azotaemia in these children. Serum salicylate levels were not appreciably raised in any of these children to suggest possible salicylism as a contributor to their high anion GAP metabolic acidosis.

The clinical and biochemical observations in these very sick young children admitted with a positive history of 'muti' ingestion confirm the presence of severe high anion GAP metabolic acidosis in the majority.

Our data provides evidence that the severe metabolic acidosis in these children results principally from lactic acidosis and acute pre-renal azotaemia.

There was no evidence to support the wide spread notion that the acidosis and renal failure seen in such children results from the ingested 'muti' *per se*.

We recommend that the clinical diagnosis "muti poisoning" usually used to categorise such children be abandoned since there is so far no proven basis for such a clinical designation or association.

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