

# IMPAIRED PANCREATIC BICARBONATE SECRETION IN CHRONIC MALNUTRITION

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## ABSTRACT

*Twenty three children with recurrent episodes of diarrhea and chronic malnutrition were studied for -pancreatic duct function. These children were subjected to pancreatic stimulation with pancreozymin and secretin. Grade I malnourished children, as per Gomez classification, formed the control group. The water output from pancreas increased in malnourished children ( $p < 0.05$ ). It correlated significantly to cationic transport ( $p < 0.01$ ). Sodium and potassium together accounted for significant proportion of water output in pancreatic fluid. Potassium transport increased with increasing severity of malnutrition and may be responsible for the hypokalemia observed in malnourished children. Pancreatic secretion of bicarbonate decreased in severe malnutrition inspite of increased flow rate of pancreatic secretion. This is probably due to defective bicarbonate secretion likely to be located at pancreatic duct epithelial cell membrane.*

**Keywords:** Malnutrition, Secretory bicarbonate, Pancreatic secretion, Cations.

The exocrine pancreas has dual function. It secretes water, bicarbonate and digestive enzymes. The digestive enzymes are secreted from the pancreatic acinii, water and bicarbonate is secreted from the pancreatic ductal cells. The bicarbonate is actively secreted by epithelial cell membrane of the pancreatic duct and is considered to be the important force in ionic drive for fluid secretion(1). There are conflicting reports about bicarbonate and water secretion in protein energy malnutrition (PEM)(2-4). These differences, probably, are due to the application of varying criteria used for comparison and expression of results. This study was, therefore, undertaken to evaluate pancreatic ductal cell function in cases of recurrent diarrhea associated with chronic malnutrition.

## Material and Methods

Twenty three malnourished children, with recurrent diarrhea, in the age group of 9 months to 9 years were studied. Their nutritional status was assessed as percentage of height at the 50th centile of NCHS (National Centre for Health Statistics) reference height(5) with respect to the weight age of the child, as height remained static during the state of nutritional deprivation. Hence, it was a more reliable index of

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*Received for publication: August 3, 1992;*

*Accepted: October 4, 1994*

chronicity of nutritional deprivation than the weight of the child.

These cases were subdivided into grades of malnutrition as per Gomez classification modified by Jelliffe(6). There were 5 cases of Grade I malnutrition. This group formed the control group as their height for age corresponded to their chronological age. There were 6, 5 and 7 cases each of Grades II, III and IV malnutrition, respectively. Children of grades III and IV were combined to form severe grade of malnutrition.

Investigations included a complete hemogram and blood levels of protein, electrolytes, urea, creatinine, sugar, SGOT, SGPT and alkaline phosphatase. Mantoux test using 1 TU of purified protein derivative was administered to all patients. A chest radiograph was obtained. Stools were collected for culture, pH and estimation of reducing substances and was also examined for ova and cysts. Cystic fibrosis was excluded by measuring levels of sweat chloride.

Pancreatic stimulation test was undertaken after treatment for dehydration, if any.

Written consent of one of the parents was obtained after explaining the procedure of pancreatic stimulation test. The study was approved by the hospital ethics committee.

#### *Pancreatic Stimulation Test*

Following an overnight fast for 6-8 hours, duodenal juice was aspirated by gamma-ray sterilized radio-opaque tube which along with capillary tube was positioned by fluoroscopy in the duodenum so that the capillary tube was at the

ampulla of vater and the radio-opaque tube opened near the ligament of Treitz. Pancreatic secretory output was assessed using marker perfusion pancreatic function test. A non-absorbable marker solution of 0.01% sulfo-bromophthalein (Bromosulphthalein-BSP) in 5% mannitol was infused at a constant rate through capillary tube. Duodenal juice containing marker and pancreatic secretion was aspirated throughout the collection period. Stomach contents were aspirated separately during the entire procedure.

Perfusion and aspiration of duodenal juice was carried out for 30 minutes in order to achieve basal status. The secretagogues, secretin and pancreozymin (Boots Pure Drug Co., UK) were continuously infused at a rate of 0.125 units/kg per minute for one hour. Samples were collected in a sterile glass tube kept in an ice-cooled flask. They were processed immediately and if required were stored at  $-20^{\circ}\text{C}$ .

Trypsin was assayed by Hummel's method(6). Bicarbonate was estimated by titrimetric method(9). Duodenal pH was checked by pH meter. Sodium, potassium and chloride levels were determined by Ion Selective Electrolyte Analyzer (ISE 2020 Boehringer Knoll).

BSP in aspirate was measured by the method of Seligson(10). Water output was calculated by multiplying the volume collected by the ratio of BSP aspirated. The infused volume of marker solution was then subtracted to obtain the net fluid secretion. This was expressed as ml/kg per hour. Trypsin and electrolyte secretion were determined by correcting for measured losses using

percentage recovery of marker and were expressed in units/kg per hour and mEq/kg per hour, respectively.

A two tailed Student's 't' test was used to compare the mean values of groups. The coefficient of correlation was used to determine the pairwise relationship.

## Results

There was no significant difference in the mean water and electrolyte output from the pancreas in marasmus (n=11) and marasmic kwashiorkor (n=12) (Table I). All cases were, therefore, graded according to their height in relation to their weight-age. The mean fluid secretion in Grade I malnutrition was 7.0 ml/kg/h. There was a significant increase in water output of pancreas in all malnourished children (p <0.05). The transport of cations in pancreatic secretion was increased in Grades III and IV malnutrition. The bicarbonate secretion in pancreatic juice was low and chloride secretion increased significantly (p <0.01) in severe malnutrition (Table II). Mean plasma osmolality of all malnourished children was  $250.67 \pm 7.40$  mosmol/kg.

Transport of cations in pancreatic juice was significantly related to water output in malnourished children ( $r = 0.806$ ,  $p < 0.01$ ) (Figs. 1 & 2). The regression line indicated that fluid output in all grades of malnutrition increased along with subsequent increase in sodium transport in pancreatic secretion. Potassium transport also increased significantly in severely malnourished patients.

There was no significant change in trypsin output in various grades of malnutrition. There was however a positive correlation between low trypsin and chloride secretion ( $r = 0.6$ ,  $p < 0.01$ ). It was also observed that chloride secretion was increased whenever fluid secretion was increased which was  $r = 0.9$ ,  $p < 0.001$ , when trypsin secretion was more than 500 u/kg/h. Fig. 3 shows the bicarbonate and chloride secretion of pancreatic fluid. The bicarbonate secretion was very vague and was seen in malnourished children of all grades as compared to chloride levels which was concentrated at the mean values.

## Discussion

Pancreatic duct epithelial cell function was assessed in children with

TABLE I—Pancreatic Trypsin and Electrolyte Secretion (Mean  $\pm$  SD) in Nutritional Disorders\*

Disorder	Trypsin U/kg/h	HCO <sub>3</sub> <sup>-</sup> mEq/kg/h	Cl <sup>-</sup> mEq/kg/h	Na <sup>+</sup> mEq/kg/h	K <sup>+</sup> mEq/kg/h	Fluid ml/kg/h
Marasmus (n=11)	505.45 $\pm 231.93$	0.129 $\pm 0.066$	0.071 $\pm 0.757$	0.815 $\pm 0.443$	0.044 $\pm 0.026$	23.97 $\pm 21.70$
Marasmic- kwashiorkor (n=12)	842.33 $\pm 475.13$	0.250 $\pm 0.119$	0.762 $\pm 0.630$	0.826 $\pm 0.386$	0.034 $\pm 0.013$	17.35 $\pm 15.47$

\* None of the differences are statistically significant.

TABLE II—Pancreatic Trypsin and Electrolyte Secretion (Mean  $\pm$  SD) in Different Grades of Malnutrition

Grade No.	Trypsin U/kg/h	HCO <sub>3</sub> <sup>-</sup> mEq/kg/h	Cl <sup>-</sup>	Na <sup>+</sup>	K <sup>+</sup>	Fluid
I 5	588.40 $\pm$ 226.22	0.255 $\pm$ 0.132	0.383 $\pm$ 0.263	0.577 $\pm$ 0.291	0.013 $\pm$ 0.006	6.954 $\pm$ 3.636
II 6	501.83 $\pm$ 417.24	0.170 $\pm$ 0.103	0.463 $\pm$ 0.042	0.722 $\pm$ 0.275	0.020 $\pm$ 0.004	17.59* $\pm$ 10.00
III 5	1141.14* $\pm$ 476.39	0.279 $\pm$ 0.144	1.580** $\pm$ 0.581	0.991 $\pm$ 0.286	0.025 $\pm$ 0.008	37.95* $\pm$ 23.76
IV 7	664.20 $\pm$ 203.57	0.125* $\pm$ 0.045	1.041** $\pm$ 0.889	0.959* $\pm$ 0.290	0.058** $\pm$ 0.019	18.530* $\pm$ 11.001
Severe 12 (Gr III+IV)	833.45 $\pm$ 481.51	0.215 $\pm$ 0.119	1.180** $\pm$ 0.756	0.959* $\pm$ 0.299	0.044* $\pm$ 0.025	26.57* $\pm$ 19.04

\*  $p < 0.05$  as compared to Grade I malnutrition.

\*\*  $p < 0.01$  as compared to Grade I malnutrition.

chronic recurrent diarrhea associated with protein energy malnutrition (PEM) after stimulating the pancreas with pancreozymin and secretin. The water output in pancreatic juice was increased and correlated significantly with cation

in all grades of malnutrition. Various workers have performed pancreatic duct epithelial cell function in PEM and results obtained show a reduction in bicarbonate concentration with relatively low volume of water secretion by

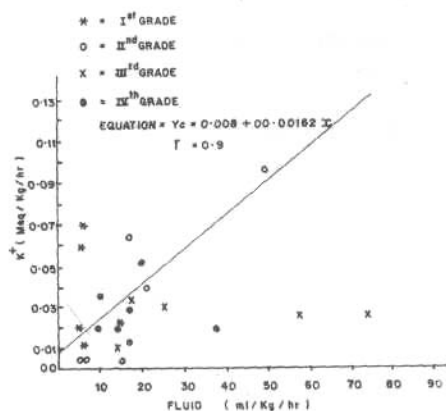


Fig. 1. Correlation of fluid output and K<sup>+</sup> transport in pancreatic secretion.

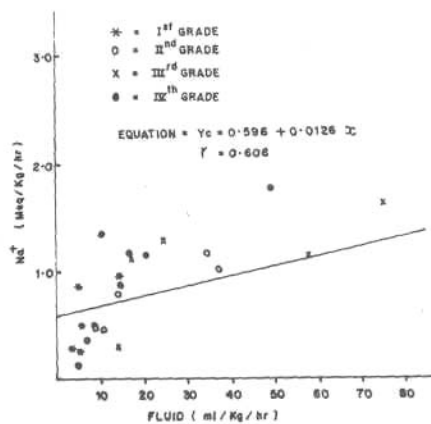


Fig. 2. Correlation of fluid output and Na<sup>+</sup> transport in pancreatic secretion.

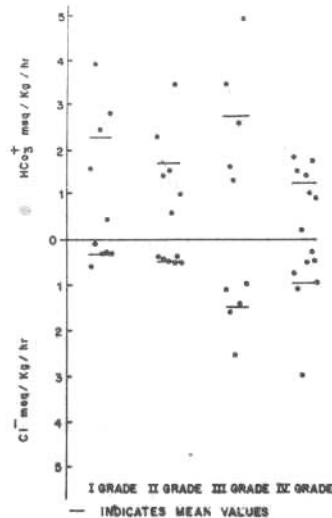


Fig. 3. Ratio of bicarbonate and chloride in pancreatic secretion.

pancreas(2-4). Tandon *et al.*(3) reported a decrease in the output of bicarbonate and water in PEM. However, Barbezat *et al.* (4) found that children with PEM secreted normal volume of duodenal juice in relation to their body weight.

In the present study, we found that in spite of a significant increase in water output there was a decrease in bicarbonate level in the severe grade of malnutrition. The discrepancy between our results and those reported so far are probably due to the differences in methodology employed and standards used in expressing these results. As most of these studies did not use perfusion technique, the loss of fluids and electrolytes in the gut during pancreatic stimulation test were not considered. The marker perfusion technique enabled to correct these losses in the great during the procedure by determining the recovery of marker.

Sodium concentration in pancreatic fluid is reported to correlate plasma osmolality(11,12). The regression line predicting fluid output from sodium transport in all grades of malnutrition indicated that malnourished children secreted more water and transported more sodium than the control group. Potassium transport was also significantly increased in malnourished patients. The sodium and potassium together accounted for significant proportion of water output in malnutrition as was also observed by Case *et al.* (13) in animal experiments.

The rate of pancreatic fluid secretion is directly proportional to the concentration of anions in aspirate. Thus, with increasing flow rate, bicarbonate secretion is also increased, but only to a certain limit, after which bicarbonate becomes constant. Secretion of bicarbonate ion by duct epithelium is also considered driving force for pancreatic fluid secretion. The secretion of bicarbonate, however, decreased in spite of increased flow rate of pancreatic secretion in malnourished children. In chronic malnutrition, even though sodium transport was normal and correlated well with increased fluid output. Pancreatic bicarbonate secretion decreased with reciprocal increase in chloride output. This was also reported by Veghely, *et al.*(17). However, Thompson(18) showed a reduction in bicarbonate secretion in PEM with low water output.

Various workers have reported a low enzyme output in PEM(3,4,17,18). Trypsin as an indicator of pancreatic acinar function was also low in malnourished children, its level did not change with grades of malnutrition. At

higher trypsin levels, fluid output correlated well to the increased chloride secretion as a result of chloride rich fluid secreted by pancreatic acinii. Pancreas thus manipulated the secretion of electrolytes in order to maintain osmolality between duodenal juice and plasma in PEM. Case(13,14) and Ribet(15) in their animal experiments observed that mammalian pancreas maintained isosmolality between pancreatic secretion and perfusate. It was thus clear that pancreas had retained this ability even in severe nutritional disorder.

In malnutrition, water output in pancreatic juice increased; bicarbonate secretion from duct epithelial cell membrane decreased, the former could be obligatory because of increased cation transport to duct lumen from blood with the help of cyclic AMP acting through  $\text{Na}^+ - \text{H}^+$  exchange(10,20). Potassium level in pancreatic fluid increased with increasing severity of malnutrition. Loss of potassium from pancreatic fluid might be responsible for hypokalaemia often observed in malnourished children.

The decreased level of bicarbonate in pancreatic secretion could probably be due to the defective anionic transport likely to be located at epithelial cell membrane restricting primary  $\text{H}^+$  transport and primary  $\text{HCO}_3^-$  transport but freely allowing transport of cations. These observations were unlike in cystic fibrosis, where reduced level of bicarbonate and chloride dependant secretion was postulated by Kopelman *et al.* (23,24). to be due to defective anionic transport. The defect in anionic transport might be reversible in malnourished children.

### Acknowledgements

The authors wish to thank Dr. (Mrs.) P.M. Pai, Dean, Seth G.S. Medical College and K.E.M. Hospital, Bombay for allowing us to publish the data. The project was funded by Research Society of K.E.M. Hospital, Bombay.

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