الخلاصة

# Electrolytes & [H<sup>+</sup>] Disturbances in Peptic Ulcer Patients

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### Abstract

n the body even a very small pH changes are important and result in change in body physiology. We describe in our study the presence of alteration in electrolytes and acid-base status in patients with peptic ulcer disease.

The study was carried out over a period of three years. 273 patients with peptic ulcer disease diagnosed on endoscopy, of these 228 duodenal ulcer and 45 gastric ulcer, in addition 84 subjects were considered as a healthy control.

20 ml of gastric juice obtained for analysis and 5 ml blood sample were taken and pH determination and [H+] estimated by electric sensitive method including the use of electronic sensitive pH – meter. The pH – electrode was initially calibrated in buffer solution of pH 7 (Ian 1969). Also the total acidity of gastric effluents were estimated by titration to pH 7 with 0.1 NaOH. The K+ and Na+ concentrations determined by using flame photometric method (Sood 1987) The results of the study show that DU patients had significantly lower gastric secretion pH and higher H+ concentration in the blood than normal control subjects and total acidity of gastric secretion also was higher than control.

ان نسبة تركيز ألاملاح وتركيز أيون ألهايدروجين ألحامضي تبقى دائماً بصورة طبيعية وتعكس ألحالة ألصحية للفرد ويلعب ألجهاز ألهضمي دورا فعالاً في عملية بقاء هذه ألتراكيز في ألحالة ألطبيعية وفي هذه الدراسة لوحظ اضطراب في هذه ألتراكيز لدى مرضى ألفرحة ألهضمية . حيث تم دراسة ٢٧٣ مريض مصاب بألقرحة ألهضمية ( ٢٢٨ مريض لديهم قرحة ألاثني عشري و ٤٥ مريض مصاب بقرحة ألمعدة ) و ٨٤ عينة ألسيطرة لايعانون من ألقرحة الهضمية ( أشخاص أصحاء ) ومدة ألدراسة استغرقت تُثلاث سنوات . وقمنا في ألدراسة قياس نسبة أملاح ألصوديوم وألبوتاسيوم في ألدم وسائل او عصارة ألمعدة وكذلك تركيز أيونات ألهيدروجين ألحامضي في ألدر اسة قياس نسبة أملاح ألصوديوم وألبوتاسيوم في ألدم وسائل او عصارة ألمعدة وكانت ألنتائج وألاستنتاجات تشير الى وجود تغيرات ذات قيمة معنوية في نسبة تراكيز ألصوديوم وألبوتاسيوم في ألدم وسائل او عصارة ألمعدة بينما لاتوجين ألحامضي في ألدر اسة قياس نسبة أملاح فلصوديوم وألبوتاسيوم في ألدم وسائل او عصارة ألمعدة وكانت ألنتائج وألاستنتاجات تشير الى وجود تغيرات ذات قيمة معنوية في نسبة تراكيز ألصوديوم وألبوتاسيوم في ألدم وسائل او عصارة ألمعدة بينما لاتوجد تغيرات ذات قيمة معنوية لهذه ألاملاح في ألدم . كذلك لوحظ زيادة ذات قيمة معنوية في سائل عصارة ألمعدة بينما لاتوجد تغيرات ذات قيمة معنوية لهذه ألملاح في ألدم . كذلك لوحظ زيادة ذات قيمة معنوية في دم المرضى ألمصابين بألقرحة ألهضمية في نسبة تركيز أيونات ألهيدروجين ( ألحموضة )

pH) ونزول معنوي في قيمة ( أس ها ) في عصارة المعدة عند مرضى الفرحة الهضمية ونستنتج من الدراسة بأن مرضى القرحة الهضمية لديهم حماض أيضية في الدم

## Introduction

During discovery of gastric acid, four phases of discovery led to general acceptance that the stomach secretes HCL and these include firstly the appreciation that gastric contents might be acid, secondly long arguments established whether, this acid was secreted by the stomach or whether it is produced by fermentation of food , and then qualitative determination of acid and followed by quantitative measurement of basal and maximal acid output .(1) There are at present two contenders : a chemical enzyme inhibitors associated with the NSAIDs induced ulcers & the role produced by H. pylori infection as a second contender. During the 6<sup>th</sup>. Century BC The Babylonian Talmud notes the effect of saliva& churning action of the stomach in digestion. This mean that the GIT problems are always present throughout human history .The problem of gastric acid secretion was demonstrated by William Prout in 1824, he demonstrated the presence of hydrochloric acid in gastric juice , and in 1915 B. W. Sippy advocates an acidneutralization regimen for treatment of peptic ulcer . In 1972 A. Allen and associates begin their studies on the biochemistry of gastric mucus and in 1977 G. Flemstrom and associates elucidate the kinetics & mechanism of gastric bicarbonates production . The concept of cytoprotection against development of ulcer suggested earlier by T. K. Chaudhur & E. D. Jacobson ( 1978) and at the same period J. I. Rotter et al. proposed that elevated serum pepsinogenI serves as a marker for predisposition to D U. In 1983 J. R. Warren & B.J. Marshall rediscover H. pylori and its association with antral gastritis and peptic ulcer. (2)

It is known fact that peptic ulcer disease refers to the underlying tendency to develop mucosal ulcer at sites that exposed to acid & pepsin and compared with agematched controls patients with DU secretes more acid during the day & night and exogenous and endogenous factors alter the lines of mucosal defense , allowing back diffusion of H+ ions and subsequent injury of epithelial cells . (3)

Acid – Base balance (ABB) modulates the gut electrolytes transport both in vivo & in vitro. Changes C/W metabolic acidosis are potent stimulators of electroneural sodium chloride absorption. whereas metabolic alkalosis inhibits this transport process. (4, 5) involving measurements Studies of intracellular pH suggest that intracellular bicarbonate concentration may modulate basal chloride secretion and intracellular pH and P CO2 may alter Na+ : H+ exchange and this might contribute to alteration in H+ ions secretion in conditions of (ABB) disturbances

. The blood H+ concentration is maintained within a tight limits in health. Normal level between 35 - 45 nmol/L, and now it is better to describe H+ concentration than to say the pH and this is maintained about 40 nmol/L by the normal pattern of both renal & respiratory systems function(.6,7.)

In the body even a very small pH changes are important and result in change in body physiology. We describe in our study the presence of alteration in electrolytes and acid-base status in patients with peptic ulcer disease.

# **Patients and Methods**

The study was carried out over a period of three years . 273 patients with peptic ulcer disease diagnosed on endoscopy , of these 228 duodenal ulcer and 45 gastric ulcer , in addition 84 subjects were considered as a healthy control .

20 ml of gastric juice obtained for analysis and 5 ml blood sample were taken and pH determination and [H+] estimated by electric sensitive method including the use of electronic sensitive pH - meter . The pH electrode was initially calibrated in buffer solution of pH 7 (Ian 1969) (8). Also the total acidity of gastric effluents were estimated by titration to pH 7 with 0.1 NaOH. The K+ and Na+ concentrations determined by using flame photometric method (Sood 1987) (9). The serum Calcium was estimated by colorimetric microdetermination technique and the Ca - Ocp - Kit was used . ( Harold, et al .1980),(10)

Statistical methods were expressed as mean  $\pm$  SE. The data were analysed using t-test and taking ( P value < 0.05 ) as lowest limit of significance and to determine significant correlation qui square test was used.

### The results

The results of the study show that DU patients had significantly lower gastric secretion pH and higher H+ concentration in the blood than normal control subjects and total acidity of gastric secretion also was higher than control. (See table I ) We measure the total acidity of gastric secretion in patients with GU and it was lower than control groups. During the course of the study we had noticed that patients with peptic ulcer infected with H. pylori show higher total acidity than patients having no H. pylori infection.

In DU patients , there is significant (P < 0.01) increase in the concentration of gastric secretion of K+ compared with the control and in contrast , there is significant (P < 0.01) decrease in the concentration of gastric secretion of K+ in GU patients compared with control subjects . (see table II) There is non- significant differences (P > 0.05) in the concentrations of serum K+ between peptic ulcer patients & control.

DU patients have significantly (P < 0.01) lower concentration of Na+ in gastric secretion than control , whereas GU patients show higher concentration of gastric secretion Na+ than control .Also during the course of study we noticed H. pylori positive patients show decrease in the concentration of gastric secretion Na+ than normal control subjects and H. pylori negative patients . There was no significant differences in the concentration of serum Na+ in P U patients and control groups .

There was a significantly higher concentration of serum calcium in PU patients than control. (see table III ) And see also figures No. 1 to figure No. 5 which demonstrate gastric secretions pH , Na+ , K+ and also serum Na+ and serum Calcium ions.

Subjects	H+ nmol/L
DU +ve Hp	78.67±8
DU –ve Hp	$67 \pm 12$
GU +ve Hp( H. Pylori )	$30.5 \pm 1.2$
GU –ve Hp	$28.5 \pm 3$
Control	$40 \pm 5.5$
P value	P < 0.01

Table 2. Shows concentrations of K+, Na+ in gastric secretions of DU patients, GU patients , and

	control	
Subjects	Mean and SD in mmol/L of K+ conc.	Mean & SD in mmol/L of Na+ conc.
DU	22± 2	64± 6
DU with Hp infection	$25 \pm 3$	$60 \pm 7$
GU	$11 \pm 3$	$100.5 \pm 7$
GU with Hp infection	$13 \pm 1$	$95 \pm 6$
Control	$16 \pm 3$	$90.5 \pm 8$
P value	( P < 0.05 )	( P < 0.05 )

Table (3) shows the serum Calcium concentration in peptic ulcer patients & control groups :

Subjects	Serum Calcium mg/dl
DU	$11.21 \pm 1$
GU	$10.91 \pm 1.2$
Control	$9.52 \pm 0.7$
P value	(P<0.01)

#### **Discussion & Conclusion**

Patients with DU disease show disturbances in electrolytes in the gastric secretion, which also associated with with excess HCL secretion. In general Na+ concentration in gastric juice is inversely proportional to the H+ concentration in gastric secretion and this might reflect the fact that electrolytes are involved in exchanges of H+, but not in the integrity of gastric barrier, although Daven port showed that measurement of electrolytes exchange across the mucosa gives a reliable estimation of integrity of gastric mucosal barrier .(11)

DU patients show significantly lower concentration of Na+ in gasric secretion than control, whereas GU patients show higher values (12)

The elevated serum calcium level is consistent with other several studies (13). and it had been suggested that calcium has a role in the pathogenesis of PU through the obligatory effect in stimulation of gastric acid secretion through , gastrin, histamine and & these might be an important cvclic AMP steps in pathogenesis of peptic ulcer and mucosal injury . (14,15,16,17)Also the effect of elevated calcium in PU disease might be attributed to hormonal effect (18,19,20)

In one study which enrolled 74 patients with DU, 28 patients with chronic gastritis and 16 healthy control, the secretion was studied initially, then in administration of ranitidine and in stimulation of hydrochloric acid . The result of this study showed that DU patients demonstrated a significant reduction of gastric secretion of HCO3<sup>-</sup> in basal & stimulated phases and three fold increase in the proportion of alkaline / acid secretion and there was also trend toward acidosis, this consistent with our study which suggest there is high concentration of H+ in the blood in patient with PU .In addition to acidosis, HCO3<sup>-</sup> deficiency is an important element in pathogenesis of DU. (21) Gastric mucosal acid – base balance play a significant role in

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protection against development of mucosal injuries and if there is loss of the protective alkaline efflux & exposure to further intraluminal acid and any barrier-breaking agents result in intracellular acidosis . (22)

In another study which concludes that acidosis contributes to exacerbation of peptic ulcer & givining Ranitidine to these patients restored acid- base balances. (23) Our study goes with the conclusion of Malov who said that acid – base balance & gastric secretion of HCO3<sup>-</sup> are related and acidosis in peptic ulcer patients lead to reduction of HCO3<sup>-</sup> production and intensification of of hydrochloric acid secretion .(24)

In Conclusion : PU disease is associated with disturbances in Electrolytes and Hydrogen ions concentration in the blood & gastric secretion . Also in DU patients , there is metabolic acidosis which leads to disturbance of cytoprotective mechanism of gastroduodenal mucosa and mucosal production of HCO3<sup>-</sup>.

## References

- Baron, J. H. (1979). The discovery of 1 gastric acid . Gastroenterolgy ; 76 : 1056-64 .
- Chen , Thomas S. , Chen , Peter S. , History 2. of Gatroenterology ; Essays on its developments and accomplishments . 1995 Parthenon Publishing Group Ltd : 261-282.
- M. Sleisenger, 3 Feldman, M. H. Scharschmidt B. F. ( editors ) in Sleisenger & Fordtran's . GI and Liver diseases Pathophysiology, Diagnosis, Managemant, 6<sup>th</sup> ed. Philadelphia, WB Saunders Company .1998
- 4. Charney, A.N. and Feldman, G.M. Systemic Acid-Base disorders and intestinal electrolytes transport . Am. J. Physiol. 247 :61,1984.
- 5. DeSoignie, R. and Sellin, J.H. Acid Base regulation & ions transport in rabbit ileum in Vitro . Gastroenterology . 99 :132, 1990.
- 6. Allan Gaw, Robert A. C., Denis St. O'Reilly , Michael , J. , Stewart James Shepherd . Acid - Base balance in Clinical Biochemistry, 2<sup>nd</sup> ed., Churchill Livingstone, 1999.
- Zilva, J. F., Pannall, P.R. (1984) Disorders 7. involving changes in hydrogen ion . In

clinical Chemistry in Diagnosis and Treatment : 89 – 119 .Lloyyd – Luke ( Medical Books ) Ltd. 4<sup>th</sup> ed.

- Ian , A. D. B. (1969) Clinical Investigation of GIT function . 1<sup>st</sup> ed. BlackWell Scientific Publications Oxford : 60 – 80.
- 9. Sood, R. (1987) Medical Labarotary Technology, in peptic ulcer disease. Clinical Science; 89:405.
- Harold, V. A., Maurice, B. (1980). Pract. Clin. Biochemistry . 5<sup>th</sup> ed. William Heinemann (Medical Books) Ltd, London: 301-310.
- Davenport , H. W. (1972). Physiology of Digestive tract . 3<sup>rd</sup> ed. Year book , medical publishers incorporation . Chicago .
- charney , A. N. ,Egnor, R. W. , NaCl absorption in rabbit gut& effect of acid – base variables . Gastroenterology . 100: 403, 1991.
- Hellstrom , J. (195) Hyperparathyroidism & Gastroduodenal ulcer. Acta Chir. Scand. 116: 207-221.
- 14. Charinym, B. I., et. al. (1987) Calcium Channel Blockers protect against indomethacin – induced gastric lesion in rats. Gastroenterology; 92.
- 15. Barras R. F. (1973) Calcium and gastric secretion .Gastroenterology 64 : 1168 1184.

- 16. Robbins, S. L. ( 2000 ) The GIT in Pathology . 4<sup>th</sup> ed.; ( 2 ) : 244- 246 .
- 17. Anthony , J. , Dimarino , J. R. , Stanley , B. ( 1997 ) PU disease . Gastroenterology ; (1) : 285 .
- 18. Jay , H. S. ( 1994 ) Internal medicine . Year Book  $4^{th}$  ed. , USA
- Makhlouf , G. M. Neural & Hormonal regulation of function in the Gut . Hosp. Pract.; 25 : 59 (1990)
- Sobocki , J . ,et. al. The effects of pentagastrin on calcium ion concentration in gastric juice . Folia Med. Cracov .1999 ;40(3-4):83-92 .
- 21. Malov, IuS., Kulikov, A. N. Bicarbonates deficiency and duodenal peptic ulcer disease. Ter Arkh; 1998; 70 (2): 28-32.
- 22. Kivilaakso, E., Kiviluoto, T., Mustonen, H., Paimela, H., Gastric Mucosal Acid- Base Balance. J. Intern. Med. Suppl.(1990); 732: 63-8.
- 23. Malov, IuS and et. al. (2000) Acid Base Balance in ulcer patients. Klin. Med. (Mosk) ; 78 (5):31-4.
- 24. Malov IuS, Ivashkina T. G., relationof acidbas balance& gastric secretion of Hydrogen ion, Carbonates ions in patients with PU. Ter Arkh, 2001; 73 (2):6-10.Figures No. 1 to 5: