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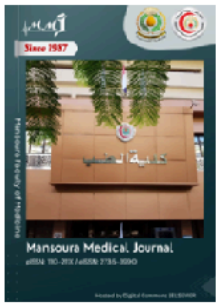


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# ASCORBIC ACID CONCENTRATION IN GASTRIC JUICE AND PLASMA BEFORE AND AFTER ERADICATION OF HELICOBACTER PYLORI

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# ASCORBIC ACID CONCENTRATION IN GASTRIC JUICE AND PLASMA BEFORE AND AFTER ERADICATION OF HELICOBACTER PYLORI

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## ABSTRACT

Ascorbic acid, the reduced form of vitamin - C, is secreted by the normal stomach and may protect against gastric carcinoma and peptic ulceration . This study examined the effect of helicobacter Pylori (H.P) on the secretion of ascorbic acid into gastric juice and examined if H.P. eradication improves gastric juice ascorbate values. Eighty six patients with dyspeptic symptoms were included into the study. Fasting plasma and gastric juice ascorbic acid measurement, anti H.P. IgG, rapid urease slide test and bacteriological examination for antral & corpus biopsy specimens during endoscopy were done for all patients at entery into the study. Gastric juice ascorbic acid concentrations in 76 H.P. positive patients were significantly lower (374.9±66.6 micromol/dl) than those in 10 H.P. negative controls, (507.8±9.04 micromol/dl) (P<0.0001). Likewise, plasma ascorbic acid concentrations in H.P. positive patients were significantly lower (322.7 ± 92.2 micromol / dl) than those of H.P. negative control (513.1 ± 17.5 micromol /dl) (P<0.0001). Of the 76 H.P positive patients who received one - week triple therapy (Omeprazol, Amoxicillin & Metronidazole), H.P. was successfully eradicated in 66 (86.8%), and after one month, their mean gastric juice ascorbic acid concentrations rose to 453. ± 76.01 micromol/dl (P< 0.0001) and their mean plasma ascorbic acid concentration rose to (419.3± 104.4 mi-

cromol/dl) (P<0.0001). We concluded that H.P. positive patients has plasma and gastric juice ascorbic acid concentrations significantly lower than those of H.P.negative subjects. Secondly, successful eradication of H.P. improves secretion of ascorbic acid into gastric juice. It is speculated that this may increase protection against gastric carcinoma and peptic ulceration.

## INTRODUCTION

Ascorbic acid, the reduced form of vitamin - C, is secreted in high concentration into the normal stomach (Sobala et al., 1989). The importance of this secretory mechanism may lie in the ability of ascorbic acid to protect against the development of gastric cancer (Chen et al., 1988) and possibly also against developing peptic ulceration .

In subjects with chronic gastritis, gastric juice ascorbic acid concentrations are considerably lower than those in healthy controls (Sobala et al., 1989 & Rathbone et al., 1989). The major cause of chronic gastritis is Helicobacter Pylori (H.P.) infection and the change in gastric juice ascorbic acid concentrations may play a part in the association of H.P. infection with both peptic ulceration (Rauws et al., 1989) and gastric carcinoma (Forman et al., 1991).

Some previous studies have done to establish wether the low gastric juice ascorbic acid concentrations associated with H.P. related gastritis are a consequence of the infection, or a predisposing cause to the infection (sobala et, al., 1993, & Banergee et al., 1994 and Rokkas et al., 1995) . those studies concluded that H.P. infection causes a reversible lowering of gastric juice ascorbic acid concentrations. However, those studies comprised small number of patients. We have studied subjects with and without H.P infection and also subjects before and after its eradication. This study examined the effect of H.P. infection on gastric juice and plasma ascorbic acid concentrations and can these concentrations be changed by eradication of H.P.

## PATIENTS AND METHODES

This study was conducted on 86 subjects (all are male) admitted to Gastroenterology Unit, Medical Department, Mansoura University Hospital. All subjects were complaining of dyspeptic symptoms (epigastric pain, heart burn, post - prandial fullness

and, or vomiting).

The excluding criteria from the study includes: patients with previous gastrointestinal surgery, patients suffering from other medical conditions, patients taking antisecretory or analgesic drugs and lastly patients in whom initial endoscopy revealed upper gastrointestinal lesions other than gastritis, duodenitis or duodenal ulcer.

All subjects in the study were submitted to thorough history taking and clinical examination, and to the following investigations (After 12 hours overnight fasting):

**A- A 5 ml of venous blood was withdrawn for:**

1- serological diagnosis of H.P. using ELISA test for identification of anti H.P. IgG.
2- Measurement of plasma ascorbic acid using method discribed by Lee et al. ( l997) which was carried out at the Clinical Chemistry Unit, Clinical Pathology Department .

**B- Upper gastrointestinal endoscopy: through which the following were done:**

1- Aspiration of 5 ml of fasting gastric juice through sterile plastic canula for determination of gastric juice ascorbic acid concentration using method discribed by Lee et al. (1997) .
2- Then after evaluation of the upper gastrointestinal tract, endoscopic biopsies were taken:

I- Antral biopsy for rapid urease slide test for detection of H.P.
II- 2 antral and 2 corpus biopsy specimens for bacteriological examination for H.P. in Unit of Microbiology diagnosis and Infection control in Mansoura Faculty of Medicine .

* **Classification:** According to results of investigations, subjects were devided into 2 groups:

1- H.P. negative group (control group): comprised 10 subjects, they were urease, culture and serology negative for H.P., their ages ranged from 28- 60 years.
2- H.P. positive (patient group): comprised 76 patients with H.P. in fection as proved by urease & culture tests (with/or without positive serology), their ages ranged from 25-61 years.

**Treatment :** Eradication of H.P. was attempted in 76 H.P. positive patients using triple therapy for one week: Omeprazole 20 mg twice daily,

amoxycillin Igm twice daily and metronidazole 500 mg twice daily (OAM) .

**Follow up :** H.P. positive patients had a repeat venesection and endoscopy 4 weeks after completing their treatment to check their H.P. state and ascorbic acid concentration in plasma and gastric juice.

**Statistical analysis :** Was carried out using SPSS program for window, standard version, release-6, (Gieseke, 1994). The analysis was performed using paired and unparied student t - test, fisher exact test, one way ANOVA (t- test) (for comparing the means of more than 2 groups).

## RESULTS

Endoscopy at entry showed diffuse gastritis in 16 patients, antral gastritis in 27 patients and chronic active duodenal ulcer in 43 patients .

All 10 patients of the control group were urease, culture and serology negatives for H.P. In the patients group, 76 were urease and culture positive, while 69 (90.7%) were serology positive for anti H.P. IgG (i.e. 7 patients were serology negative). So, in relation to culture, the sensitivity of serology was 90.8%, specificity was 100%, positive predictive value was 100%, negative predictive vaue was 58.8% and overall predictability was 91.9%.

Of the 76 patients who received one week triple therapy (OAM), H.P. was successfully eradicated in 66 (86.8%) as determined by a negative urease slide test and absence of the bacterium on microscopy & culture of antral biopsy specimens at 4 weeks after treatment has finished. However, healing of the lesions was complete in all these 76 patients irrespective of H.P. eradication.

At entery into the study, gastric juice PH of H.P negative patients (2.01±0.09) was statistically significantly higer (less acidity) than those in H.P. positive patients (1.67±0.12) ($P<0.0001$). Plasma ascorbic acid concentrations in H.P. positive patients (322.7±92.2micromol/dl) were significantly lower than those in H.P. negative subjects (513.1±17.5 micromol/dl) ($P< 0.0001$). Likewise, gastric juice ascorbic acid concentrations in H.P. positive patients (374.9±66.6 micromol/ dl) were lower than those in H.P negative patients (507.8 ± 9.04 micromol/dl) ($P<0.0001$) (table 1). At 4 weeks after eradication course has

finished, mean gastric juice ascorbic acid concentrations in the 76 H.P. positive patients rose from 374.9± 66.6 micromol / dl to 453.2± 6.01 micromol/dl (P<0.0001), and their gastric juice PH rose (Less acidity) from 1.67± 0.12 to 1.97 ± 0.21 (P< 0.0001). There was also a significant rise in their mean plasma ascorbic acid concentration from 322. 7± 92.2 micromol/ dl to 419 ±104.4 micromol/ dl (P<0.001)(table 2).

When comparing 66 H.P. positive patients who were sucessfully eradicated to 10 patients H.P, positive without eradication before the treatment, it was found that there was no statistically significant difference between both groups as regard gastric juice PH, plasma ascorbic acid and gastric juice ascorbic acid concentrations, while comparison after treatment showed significant rise in gastric juice PH, mean gastric juice and plasma ascorbic acid concentrations in successful eradicated patients (table 3&4) .

Also when comparing 66 patients with successful eradication of H.P. before and 4 weeks after treatment, there was significant rise in gastric PH (1.67±0.13 to 1.99± 0.21, P<0.0001), plasma ascorbic acid concentration (322.8 ±96.8 to 439.1 ± 95.5 micromol/dl, P<0.0001) and gastric juice ascorbic acid concentration (376.0± 68.4 to 467.5 ± 67.8 micromol/dl, P<0.0001) after treatment (table 5).

**Table (1) :** Comparison of values between H.P. positive patients and H.P. negative subjects at entery into the study .

| | Gastric juice PH | Plasma ascorbic acid (micromol/dl) | Gastric juice ascorbic acid (micromol/dl) |
|---|---|---|---|
| H.P + ve (n=76) | 1.67±0.12 | 322.7±92.2 | 374.9±66.6 |
| H.P - ve (n=10) | 2.01±0.09 | 513.1±17.5 | 507.8±9.04 |
| statistics | P<0.0001 | P<0.0001 | P<0.0001 |

Results expressed as mean ± S.D.

**Table (2) :** Comparison of values in 76 H.P. positive patients before and at 4 weeks after eradication of H.P.

| | Gastric juice PH | Plasma ascorbic acid (micromol/dl) | Gastric juice ascorbic acid (micromol/dl) |
|---|---|---|---|
| Before eradication (n=76) | 1.67±0.12 | 322.7±92.2 | 374.9±66.6 |
| After eradication (n=76) | 1.97±0.21 | 419.3±104.4 | 453.2±76.01 |
| statistics | P<0.0001 | P<0.0001 | P<0.0001 |

**Table (3) :** Comparison of values between eradicated and noneradicated group at entery into the study .

| | Gastric juice PH | Plasma ascorbic acid (micromol/dl) | Gastric juice ascorbic acid (micromol/dl) |
|---|---|---|---|
| Eradicated group (n=66) | 1.68±0.13 | 323±96.8 | 376±68.4 |
| Non eradicated group (n=10) | 1.6±0.04 | 323±56.1 | 367±55.9 |
| statistics | P=0.081 | P=0.965 | P=0.703 |

**Table (4) :** Comparison of values between eradicated and non-eradicated group at 4 weeks after eradication .

| | Gastric juice PH | Plasma ascorbic acid (micromol/dl) | Gastric juice ascorbic acid (micromol/dl) |
|---|---|---|---|
| Eradicated group (n=66) | 1.99±0.12 | 439.1±95.51 | 467.5±76.82 |
| Non eradicated group (n=10) | 1.81±0.12 | 288.7±56.61 | 358.6±59.03 |
| Statistics | P<0.008 | P<0.0001 | P<0.0001 |

Table (5) : Comparison of values in 66 H.P. positive patients before and after eradication of H.P.

| | Gastric juice PH | Plasma ascorbic acid (micromol/dl) | Gastric juice ascorbic acid (micromol/dl) |
|---|---|---|---|
| Before eradication (n=66) | 1.67±0.13 | 322.8±96.84 | 376.0±68.42 |
| After eradication (n=66) | 1.99±0.21 | 439.1±95.51 | 467.5±67.82 |
| Statistics | P<0.0001 | P<0.0001 | P<0.0001 |

## DISCUSSION

Ascorbic acid, a powerful antioxidant, is potentially important in the prevention of gastric cancer through inhibition of the formation of carcinogenic N-nitroso compounds by scavenging the nitric precursor and other free radicle spices (Chen et al., 1988 and Niki, 1991). H.P. infection is now recognised as a major independent risk factor in the cause of gastric cancer. Reduction in gastric ascorbate secretion may be one mechanism by which increases the risk (Forman et al., 1991).

Our results confirm previous findings that H.P. gastritis is associated with low gastric juice ascorbic acid concentrations (Ranthbone et al., 1989; Sobala et al., 1989; Sobala et al., 1993, Banerjee et al., 1994 and Rokkas et al., 1995). They suggested that this fall is not due to difference in plasma ascorbic acid concentrations or vitamin-C intake. Sobala et al. (1989) postulated that the lower gastric juice ascorbic acid level in the presence of H.P. gastritis may be accounted for by reduced secretion, disruption of active uptake, increased back diffusion through unhealtyy mucosa and increased utilization by H.P. Banerjee et al. (1994) explained the mechanism whereby H.P. infection lowers gastric juice ascorbic acid secretory mechanism as a result of cytopathic toxins released by the bacterium . They also postulated that a product of the polymorphonuclear cells could impair the ascorbic acid secretory mechanism itself, or increase the consumption & degredation of ascorbic acid in antral mucosa, resulting in lower amounts being available for secretion into the gastric juice . H.P. has been shown to potentiate the polymorphonuclear leucocytes oxidative burst (Mooney et al., 1991) which is accompanied by a considerable production of reactive oxygen metabolites. Plasma ascorbic

acid within the microcirculation of the gastric mucosa may be consumed in the course of scavenging these reactive oxygen metabolites.

Eradication rate (86.8%) of one week triple regimen (OAM) in our study was nearly similar to that of previous studies using the same regimen: 80% (Pieamico et al., 1996), 81.25% (Pilotto et al., 1998) and 87% (Ell et al., 1998).

In this study, gastric juice concentrations of ascorbic acid were improved by eradication of H.P. As eradication of H.P. is known to restore chronic gastritis to normal ( Rauws et al., 1988), this is in agreement with findings of low juice ascorbate concentrations in H.P. chronic gastritis and high concentrations in patients with normal gastric mucosa (Chen et al., 1988, Rothbone et al., 1989 and sobala et al.,1989). Our finding is in agreement with that of sobala et al. (1993), Banerjee et al. (1994) and Rokkas et al. (1995) who concluded that H.P. causes considerable but reversible lowering of gastric juice ascorbic acid concentrations.

Plasma ascorbic acid concentrations showed significant increase after H.P eradication. This is in agreement with that of Banerjee et al. (1994) who explained this finding by decreased tissue degradation of vitamin - C after resolution of gastric inflammation and may also to improved nutrition of the patients after resolution of dyspepsia after H.P. eradication. On the other hand, sobala et al. (1993) found that plasma ascorbic acid concentrations did not change significantly with treatment. They explained this by that plasma ascorbic acid is mainly determined by the dietary vitamin-C intake while the gastric juice ascorbic acid is mainly determined by the active secretory mechanisms of the gastric mucosa which is impaired by H.P. induced inflammation .

The ability of ascorbic acid to scavenge reactive oxygen metabolites (Niki, 1991) may protect against the development of gastric carcinoma (Chen et al., 1988) and may also protect against gastric mucosal ulcerations. Reactive oxygen metabolites cause lipid peroxidation and adversely affect the basement membrane, epithelial function and mucous layer. Allopurinol, the free radical scavenger, has been reported to be more effective than cimetidine in preventing duodenal ulcer relapse (Salim, 1990),

and given concurrently with H2 receptor blockers may accelerate the healing of intractable duodenal ulcer (Salim, 1991).

Our study concluded that H.P. infection results in impairment of gastric antioxidant defences in the form of lowering gastric juice ascorbic acid concentrations and that eradication of H.P. enhances gastric juice ascorbate secretion . This may be an important factor in the link between H.P. infection and both gastric carcinoma and peptic ulceration .

## REFERENCES

**Banerjee, S.; Hawksby, C.; Miller, S.; Dahill, A.; Beattie, A.D. and McColl, K.E.L. (1994) :** Effect of H.P. and its eradication on gastric juice ascorbic acid. Gut, 35:317-22.

**Chen, I . H.; Boissoneault, A.G. and Glauert, H.P. (1988) :** Vitamin C, vitamin - E and cancer. Anticancer Res., 8:739-48. .

**Ell, C.; Rollinghoff, M.; Stolte, M . and Moser, W. (1998) :** Amoxicillin and metronidazole in eradication of H.P. infection. Gut, septamber, A91.

**Forman, D.; Newell, D.G.; Fullerton, F.; Yarnell, J.W.G.; stacey, A.R.; Wald , N. et al. (1991) :** Association between infection with H.P. and the risk gastric cancer: evidence from a prospective investigation, B.M.J., 302: 1302-5.

**Gieseck, J. (1994) :** Clinical epidemiology, sensitivity, specificity misclassification. Modern Inf. Dis & Epidemiology, 4:66-77.

**Lee, W.; Roberts, S.M. and Labbe, R. F. (1997) :** Ascorbic acid determination with an automated enzymatic procedure. Clinical Chemistry, 43 (1): 154-7 .

**Mooney, C.; Keenan, J. Munster, D.; Wilson, I.; Allardyce, R.; Bagshaw, P. et al., (1991) :** neutrophil activation by H.P. Gut, 32 : 853-7.

**Niki, E. (1991) :** Action of ascorbic

acid as scavenger of active and stable oxygen radicles. Am. J. Clin. Nutr., 54: 1119-24 S.

**Pieamico, O.; Zanetti, M.V. and Innerhofer, M. (1996) :** Omeprazole based triple therapy for eradication of H.P. infection. Gastroenterol., 110(4):273-6.

**Pilotto, A.; Dalbo, N.; Franceschi, M. and Bazzola, L (1998) :** Comparison of three proton pump inhibitor in combination with amoxycillin and metronidazole for one week to cure H.P. infection in the elderly. Gut, Sept. A 127.

**Ranthbone, B.J.; Johnson, A. W.; Wyatt J.L.; Keileher, J.; Heatley, R.V. and Losowsky, M.S. (1989) :** Ascorbic acid: a factor concentrated in human gastric juice . Clin. Sci., 76: 237-41.

**Rauws, E.A.J.; Langenberg, W.; Houthoff, H.J.; Zanen, H.C. and Tytgat, G.N.J. (1988) :** Compylobacter pyloridis associated chronic antral gastritis. A prospective study of its prevalence and the effects of antibacterial and antiulcer treatment. Gastroenterol., 94:33- 40 .

**Rokkas, T.; Papatheodorou, G.; Karameris, A; Maverogeorgis, A. et al. (1995) :** Helicobacter Pylori infection and gastric juice vitamin -C levels- Impact of eradications. Dig. Dis. Sci., 40 (3) : 615-21.

**Salim, A. (1990) :** Oxygen derived free radical and the prevention of duodenal ulcer relapse: a new approach. Am. J. Med. Sci., 300: 1-6

**Salim, A. (1991) :** A possible new approach to the problem. of refractory peptic ulceration. A role for free radical scavengers. Scott. Med. J., 36:19-20 .

**Sobala, G. M.; Schorah, C.J.; sanderson, M.; Dixon, M.F.; Tampkins, D.S.; Godwin, P. et al. (1989) :** Ascorbic

acid in human stomach. Gastroenterol., 97 (2): 357-63.

**Sobala, G.M.; Schorah, C.J.; shires, S.; Lynch, D.A.F.; Gallacher, B., Dixon, M.F. and Axon, A.T.R. (1993) :** Effect of eradication of H.P. on gastric ascorbic acid concentrations. Gut, 34: 1038-1041.

# مستوى حمض الأسكوربيك فى العصاره المعديه والبلازما قبل وبعد إبادة بكتريا الهليكوباكتر بايلورى

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**مقدمه :-**

تفرز المعده كميات كبيره من حمض الاسكوربيك مع عصارتها ويعتبر حمض الاسكوربيك من العوامل الراقيه من الاصابه بسرطان المعده والقرح المعديه كما ثبت أن أفراز هذا الحمض يقل عند الاصابه ببكتريا الهليكوباكتر بايلورى .

**الهدف من البحث :-**

البحث فى تأثير الاصابه ببكتريا الهليكوباكتر بايلورى على إفراز المعده لحمض الاسكوربيك ومستواه بالبلازما وكذلك البحث فى معرفه تأثير القضاء على بكتريا الهليكوباكتر بايلورى على مستوى حمض الاسكوربيك بالعصاره المعديه والبلازما .

**خطة البحث :-**

شمل البحث ٨٦ شخص يعانون من إضطرابات بالجزء العلوى من القناه الهضميه والذين ثبت بالمنظار وجود التهابات بالمعده أو التهابات وقرح بالأثنى عشر. خضع جميع المرضى إلى أخذ التاريخ المرضى وفحص أكينيكى كامل - منظار للمعده والأثنى عشر مع أخذ عينات من جدار المعده لفحصها لأكتشاف باكتريا الهليكوباكتر عن طريق المزرعه وكذلك بواسطة إختبار اليورياز الفورى، كما تم عمل إختبار سيرولوچى للكشف عن مضاد بكتريا الهليكوباكتر بايلورى بالدم مع تحديد مستوى حمض الاسكوربيك بالعصاره المعديه والبلازما .

**ثم بعد ذلك تم تقسيم المرضى إلي مجموعتين :-**

أ- مجموعه موجبه للبكتريا وتشمل ٧٦ وهؤلاء تم علاجهم لمدة أسبوع بواسطة عقار الامبرازول والأموكسيسللين والمترونيدازول وبعد شهر من العلاج تم عمل جميع الفحوص السابقه.

ب- مجموعه سالبه للبكتريا وتشمل ١٠ أشخاص حيث لم يتم عمل علاج أو تحاليل لهم بعد ذلك .

**نتائج البحث :-**

١- ثبت أن العلاج ثلاثى العقار لمدة أسبوع أباد بكتريا الهليكوباكتر فى ٦٦ شخص (بنسبة ٨٦ر٦٪) .

٢- ثبت أن مستوى حمض الاسكوربيك فى العصاره المعديه والبلازما منخفض إنخفاضاً ذو دلاله إحصائيه فى المرضى المصابين ببكتريا الهليكوباكتر بايلورى عنه فى الأشخاص الغير مصابين بهذه البكتريا .

٣- عند مقارنة مستوى حمض الاسكوربيك بالعصاره المعديه والبلازما قبل وبعد شهر من العلاج الثلاثى للمرضى المصابين بالبكتريا وجد أن هناك زياده ذات دلاله إحصائيه بعد العلاج.

**ونستخلص من ذلك :-**

١- الأصابه ببكتريا الهليكوباكتر بايلورى يسبب هبوط مستوى حمض الاسكوربيك بالعصاره المعديه والبلازما .

٢- القضاء على بكتريا الهليكوباكتر بايلورى ترفع من مستوى حمض الاسكوربيك بالعصاره المعديه والبلازما .