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The effect of ranitidine on gastric acid secretion after vagotomy*

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After vagotomy for complicated duodenal ulcer disease, the role of H_2 - receptor antagonist in the early postoperative period is controversial, mainly due to the lack of data on the effect of this group of drugs on acid secretion after vagotomy. Forty - three patients who had had an emergency truncal vagotomy + pyloroplasty for perforated duodenal ulcer were randomized into 2 groups. Group 1 patients were given intravenous ranitidine 50 mg every 8 hours immediately after operation for 2 days, after which the drug was stopped. In group 2, patients were not given ranitidine until the 3^{rd} postoperative day. Pentagastrin tests were performed twice for each patient, on the 2^{nd} and 4^{th} postoperative day. Statistical significance was evaluated with the paired t - test.

Some gastric aspirates were contaminated with saliva, mucus, blood and food particles which interfered with acid measurement. Thus only 13 patients in each group had a complete gastric analysis. In both groups, the basal and maximal out put were found to be significantly reduced while the patients were on ranitidine ($P<0.001$) and <0.01 respectively) However, the clinical relevance of these findings remains to be determined.

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ทวีสิน ตันประยูร, ชาญวิทย์ ตันติ์พิพัฒน์, ชูชัย ศรชำนิ, เจษฎา แสงสุพรรณ. ผลของรานิทิดีนต่อการหลั่งกรดในผู้ป่วยหลังการผ่าตัดเส้นประสาทเวกัส. จุฬาลงกรณ์เวชสาร 2533 ธันวาคม; 34(12): 925-930

ผลของรานิทิดีนต่อการหลั่งกรดในผู้ป่วยหลังการผ่าตัด vagotomy ใหม่ ๆ ยังไม่ทราบแน่ชัด เนื่องจากยังขาดข้อมูลจากการศึกษาทางด้านนี้ การศึกษานี้ได้รวบรวมข้อมูลแบบไปข้างหน้าในผู้ป่วย 43 ราย ที่ได้รับการผ่าตัด truncal vagotomy และ pyloroplasty เพื่อรักษาโรคแผลทะลุที่ดูโอดินั่ม ได้แบ่งผู้ป่วยออกเป็นสองกลุ่ม กลุ่มแรกให้รานิทิดีน 50 มิลลิกรัม ฉีดเข้าเส้นเลือดดำทุก 8 ชั่วโมงเป็นเวลา 2 วันแรก หลังจากนั้นจึงหยุดยา ผู้ป่วยกลุ่มที่สองไม่ได้รับรานิทิดีนใน 2 วันแรก แต่จะได้ยาดังกล่าวในวันที่ 3 และวันที่ 4 หลังการผ่าตัด การทดสอบการหลั่งกรดด้วยเพนตาแกสตรินจะทำ 2 ครั้งในผู้ป่วยแต่ละราย ในวันที่ 2 และวันที่ 4 หลังการผ่าตัดหานัยสำคัญทางสถิติโดยใช้ paired t-test

มีผู้ป่วย 17 ราย ที่ผลการตรวจการหลั่งของกรดไม่สมบูรณ์ เพราะมีมูกหรือเลือด หรือเศษอาหารปนมากจากน้ำที่ดูดจากกระเพาะ ดังนั้นจึงมีผู้ป่วย 13 ราย ในแต่ละกลุ่ม รวมเป็น 26 ราย ที่สามารถนำมาศึกษาเปรียบเทียบได้ พบว่าเมื่อกระตุ้นด้วยเพนตาแกสตรินแล้ว ค่า BAO และ MAO ในกลุ่มที่ได้รับรานิทิดีนลดลง เมื่อเทียบกับกลุ่มที่ไม่ได้รับยารานิทิดีนอย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตามการนำผลการทดลองนี้ไปใช้เพื่อประโยชน์ในการรักษาผู้ป่วยยังต้องศึกษาต่อไป

Vagotomy suppresses the cephalic phase of gastric secretion and reduces the sensitivity of the parietal cells to circulating gastrin. After vagotomy the basal acid output is reduecd by approximately 90 percent and the maximal acid output in response to pentagastrin or histamine, by 50-70 percent.[1-3] Histamine H_2 antagonists (H_2A) are potent inhibitors of all phases of gastric secretion from the vagally intact stomach. They act by inhibiting the action of histamine at the histamine H_2 receptors of the parietal cells, as well as by inhibiting the secretion caused by muscarinic stimuli and gastrin. However, the effect of H_2A on gastric acid secretion after vagotomy has not been fully documented, particularly in the first few days after vagotomy. This study attempts to determine whether there is any further reduction of acid secretion in the early post vagotomy period by giving ranitidine.

Patients and methods

Patients with perforated duodenal ulcer seen by the autohrs at Chulalongkorn Hospital were studied. Excluded were patients who were found to have marked peritoneal soiling during operation, and those suffering from serious medical illnesses. The treatment of enrolled patients was standardized, including the operative procedure, perioperative care and antibiotics. A truncal vagotomy and pyloroplasty was perfomed in all patients either by third year surgical residents or by the staff. A nasogatric tube was retained for at least 4 days for the purpose of gastric analysis which was performed on the second and fourth postoperative days.

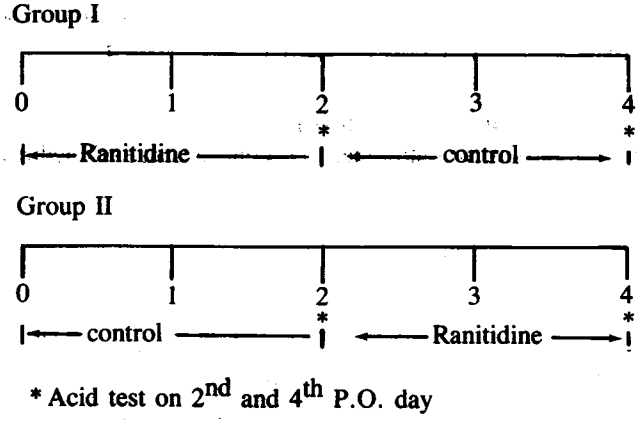

Figure 1. The administration of ranitidine and acid tests.

Immediately after operation the patients were randomised into 2 groups. Group I patients were given ranitidine (50 mg every 8 hours) intravenously during the first 2 postoperative days only, where as group II patients received the first dose of ranitidine on the third postoperative day after the first pentagastrin test had been completed. Figure I summarises the timing of ranitidine administration and pentagastrin tests in the 2 groups. The rationale for randomisation was to balance the possible effects of pain, analgesics and metabolic changes on acid secretion during the first 4 postoperative days. (Fig. 1)

Pentagastrin tests were performed by an experienced technician. Gastric aspiration was carried out manually and the aspirate was collected in 15 minute-samples. The basal secretion was collected for 1 hour after a 12 hour-fast. Pentagastrin was then given in a dosage of 6 μg/kg intramuscularly, followed by another hour of gastric aspiration. Each sample of gastric aspirate was titrated with 0.1 N NaOH to pH 7. Values are presented as basal acid output (BAO) and maximal acid output (MAO) in mmol/hr.

The unpaired t-test was used to compare the mean acid secretion between groups I and II. The paired t-test was used for the pooled results before and after the administration of ranitidine.

Results

Forty-three patients with perforated duodenal ulcer who were treated surgically with a truncal vagotomy and pyloroplasty were enrolled into the study between May 1987 and January 1989. The patients were comparable for age and sex (table 1). There were no deaths and no major postoperative complications in any of the patients. Nine patients in group I and 8 patients in group II were considered technical failures and were excluded from further analysis since each of them had at least one unsatisfactory pentagastrin test, usually because of the presence of excessive mucus or blood in the gastric aspirate. Thus 13 patients in each group completed both their pentagastrin tests satisfactorily.

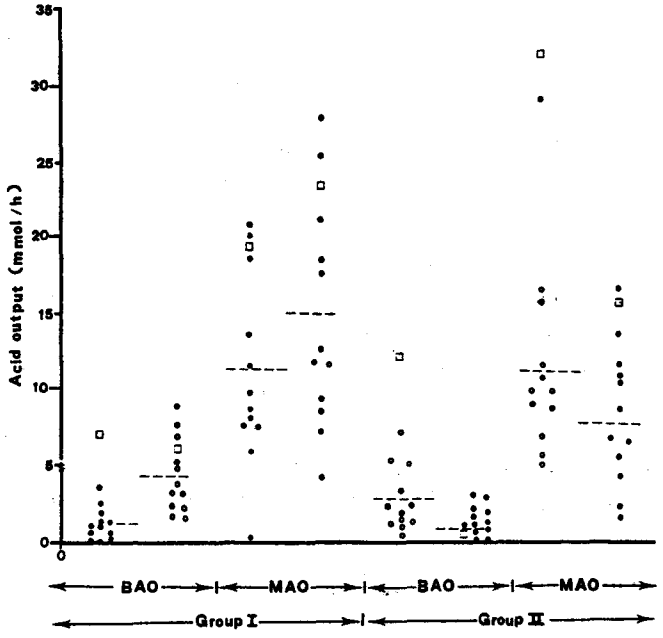

Figure 2. Gastric acid secretions in Group I and Group II patients. (n = 26)
(● = with ranitidine, ○ = without ranitidine, □ = one patient excluded from each of Group I and II)

Table 1. Data of the patients.

Characteristics	Group I (n=22)	Group II (n=21)
Age (years)		
X±SD	40.6±12.8	37.9±11.6
Sex ratio :		
Male : Female	22 : 0	20 : 1
Number of completed study	13	13
Number acid test failure	9	8

The acid secretions before and after ranitidine in group I and group II patients are shown in figure 2.

The BAO and MAO before and after ranitidine between groups I and II patients were not statistically significantly different (table 2). Therefore their data were pooled into BAO and MAO before and after ranitidine.

Ranitidine significantly reduced BAO from 3.25±2.30 mmol/hr to 1.03±0.88 mmol/hr ($P<0.001$), a mean reduction of 68.3 percent. MAO was also significantly reduced by ranitidine from 13.05±7.03 mmol/hr to 9.52±5.56 mmol/hr ($P<0.01$), a mean reduction of 26.28 percent (table 3).

Table 2. Comparison between Group I and Group II.

Gastric Acid Secretion (m.mol/hr)	Group I* (n=12)	Group II* (N=12)	Statistical Significant difference
Basal Acid Output			
before ranitidine	3.98±2.46	2.51±1.95	NS
after ranitidine	0.98±0.89	1.09±0.91	NS
Maximal Acid Output			
before ranitidine	14.59±7.43	11.50±6.54	NS
after ranitidine	10.91±6.28	8.13±4.59	NS

* One patient was excluded with an abnormally high value.

Table 3. Effect of Ranitidine on 24 vagotomized patients.

Gastric Acid Secretion (m.mol/h)	Before Ranitidine (n=24)	After Ranitidine (n=24)	Acid Reduction (%)	Statistical Signigicant difference
BAO (X±SD)	3.25±2.30	1.03±0.88	68.30	<0.001
MAO (X±SD)	13.05±7.03	9.52±5.56	26.28	<0.01

Discussion

There are 3 main endogenous substances that result in stimulation of gastric acid secretion.[4,5] They are acetylcholine, gastrin and hitamine. Each of these substances has its own specific receptor in the parietal cells.[6] Vagal nerve stimulation is responsible for the release of the neurotransmitter acetylcholine. A complete vagotomy has been shown to reduce BAO by approximately 90 percent and MAO by 50-70 percent.[1-3] The effect of H_2A after vagotomy has not been well documented. By infusing pentagastrin and cimetidine on 9 duodenal ulcer patients before and 2-3 months after a proximal gastric vagotomy, Aadland et al demonstrated that cimetidine reduced the mean gastric acid output by the same magnitude (79 percent) before and after vagotomy.[7] Our study on patients during the first 4 days after a truncal vagotomy also showed a significant acid reduction by ranitidine, 68.3 percent for BAO and 26.3 percent for MAO. Our results could not be compared with those of Aadland et al since the patients, the operation, and the method and timing of the studies were different. From the clinical point of view there may be some patients who could benefit from further reduction of acid secretion after an emergency vagotomy for complications of duodenal ulcer, such as patients who may have had an incomplete vagotomy or those operated on for a bleeding ulcer. However, further clinical studies are necessary to evaluate the potential benefit of H_2A in the early post-vagotomy period.

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