THE USE OF BANTHINE IN THE TREATMENT OF DUODENAL ULCER

A Preliminary Report

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THE treatment of duodenal ulcer and its complications was reviewed recently by one of us (Collins[1]). Eighty-five per cent of our patients obtain relief on the treatment outlined and do not require surgery. The remaining 15 per cent recently have been subjected to vagotomy and gastroenterostomy. Because of this small group demonstrating intractable ulcers, and because of the inconvenience of hourly feedings and medication (which interferes, frequently, with the patient's livelihood), we are interested in any new preparation that serves to relieve pain, heal the ulcer, and eliminate the necessity for surgery.

Longino, Grimson et al[2] reported that Banthine*, an anticholinergic drug, caused prolonged depression of gastrointestinal motility and usually reduction in volume and acidity of secretions from the stomach. Banthine may serve the purpose of a "medical vagotomy." Such treatment for peptic ulcer is not new. Belladonna and atropine derivatives have been used for a long time as adjuncts in the treatment of peptic ulcer. Belladonna and atropine frequently cause severe side effects, however, such as dryness of the mouth and blurring of vision, which make them impractical in the reduction of gastric acidity. Grimson et al[3] have reported the beneficial use of Banthine in 100 patients having duodenal ulcer. Because the drug appears to be effective in reducing gastric acidity without inducing distressing complications, we became interested in its application for duodenal ulcers which had not responded to conventional therapy.

Inasmuch as the results have been unusually satisfactory, we present this preliminary report on our experience with Banthine.

Results

Since January 1950 we have administered Banthine (methantheline bromide) for at least 2 months to 30 of our patients with duodenal ulcer. This is a sufficient period of time in which to determine the patient's response to the medication. The drug, generally, was given only to ulcer patients who had experienced recurrence of the ulcer or some other complication. We preferred to prescribe Banthine in instances where ulcer craters existed, so that some objective evidence concerning the effect might be elicited. Progress roentgen

*We are indebted to Dr. Irwin C. Winter of G. D. Searle and Company for generously supplying Banthine for clinical purposes.

examinations were obtained within 4 to 8 weeks; patients having come from some distance were unable to obtain these roentgenograms.

Symptomatic Effect of Banthine in Duodenal Ulcer Patients

The majority of the 30 patients given this medication had been troubled with ulcer symptoms for many years (table 1). Three had experienced perforations and 6 hemorrhages; surgery had been considered in most of the patients because of night distress, symptoms of penetration, and lack of response to the prescribed therapy. The symptoms had subsided on the usual ulcer program, but the crater was still evident in 5 patients on roentgenologic examination.

Of the remaining 25 who demonstrated symptoms of active ulcer, only 1 patient exhibited intolerance to the drug. Two patients obtained no relief in 10 and 15 days respectively; surgery was required in 1 patient. Only partial relief was obtained in 3 who required intermediate feedings or antacids in addition to Banthine. Nineteen patients obtained definite and immediate relief with Banthine medication. These 19 did not require intermediate meals or antacids after having been on this therapy for a short time.

Typical comments were: "Most comfortable 6 weeks of my life"; "Now eating things I have avoided for 30 years—even take an occasional drink"; "Much better than I have been for years." These statements are similar to those made by patients who have undergone bilateral vagotomy and gastroenterostomy.

In 19 of the 25 patients with relatively intractable ulcers not improved by previous therapy, the symptoms disappeared usually in 1 to 4 days following introduction of Banthine. This drug has, apparently, an extremely useful function in the treatment of duodenal ulcers, and is capable of performing "medical vagotomies" when prescribed in appropriate dosages. Many patients, because of personal reactions and job requirements, are unable to adhere to the modified Sippy program of ulcer therapy. The most dynamic, active and tense patient may take Banthine 4 times a day without difficulty.

Roentgenologic Observations

In the group of 30 cases of duodenal ulcer observed, 3 patients did not continue the medication; therefore progress roentgenograms were not obtained. Since many of our patients live in communities at a great distance from the Clinic, progress x-rays were not available in an additional 9. In 18 patients, stomach roentgenograms were obtained 4 to 8 weeks after Banthine therapy was initiated. Because we attempted to restrict the use of this drug to patients with active ulcer craters for the purpose of obtaining objective evidence, each of the 18 demonstrated this defect on initial examination. Progress examinations of 17 of these patients revealed disappearance of the ulcer craters; in the remaining case a questionable crater was reported. We have not observed such remarkable results with any other type of ulcer therapy.

Table 1

EFFECT OF BANTHINE ON PATIENTS WITH DUODENAL ULCER

No.	Age	Sex	Duration	Complications	Effect of Banthine	X-Ray Findings	
						Before Banthine	After Banthine
1.	42	M	12 years	Perforation, 1946; recurrences	Immediate relief	Ulcer crater	Not available
2.	50	M	26 years	Repeated recurrences	No relief (15 days)	Ulcer crater	
3.	54	M	2 months	Symptoms responded to usual ulcer program but crater persisted	None	Ulcer crater	No crater
4.	45	M	20 years	Repeated recurrences; surgery advised	Complete relief	Marked deformity; crater	No crater
5.	65	M	25 years	Responded to usual ulcer program but crater remained	None	Crater	No crater
6.	39	M	20 years	Repeated recurrence	Prompt relief	Crater	No crater
7.	41	M	24 years	Responded to usual ulcer program but crater persisted	None	Crater	No crater
8.	32	M	15 years	Repeated recurrence	Prompt relief	Crater and deformity	No crater; less deformity
9.	39	M	13 years	Repeated recurrence	Prompt relief	Crater and deformity	No crater, less deformity
10.	35	M	17 years	Repeated recurrence when not on ulcer program	Prompt relief	Crater and deformity	No crater
11.	54	M	15 years	Responded to usual ulcer program but crater persisted	None	Crater	No crater, some deformity
12.	48	M	5 years	Usual ulcer symptoms; hemorrhage, 1949	Immediate relief	Crater and deformity	Not available
13.	41	M	12 years	Hemorrhage, 1939, 1950; symptoms disappeared on usual ulcer program but crater remained	None	Crater	No crater, minimal deformity
14.	28	M	6 months	Usual ulcer symptoms	Immediate relief	Ulcer crater	No crater, minimal deformity
15.	36	M	13 years	Repeated recurrence: hemorrhage, 1950	Prompt relief	Questionable crater and deformity	Not available

Table 1 (continued)

No.	Age	Sex	Duration	Complications	Effect of Banthine	X-Ray Findings	
						Before Banthine	After Banthine
16.	35	M	12 years	Repeated recurrence	Prompt relief	Deformity and crater	No crater, less deformity
17.	58	M	20 years	Night distress, back pain; had not responded to usual ulcer program	Immediate relief	Deformity and crater	Normal bulb
18.	42	F	5 years	Symptoms disappeared but crater remained	Did not tolerate drug		
19.	35	M	7 years	Repeated recurrence of ulcer	Immediate relief	Deformity and crater	Not available
20.	46	M	6 months	Usual ulcer symptoms	Prompt relief	Deformity and crater	Not available
21.	39	M	9 months	Considerable night distress	Prompt relief	Deformity and crater	No crater, little deformity
22.	38	M	9 months	Pain in back, vomiting	Prompt relief	Marked deformity, large crater	Deformity, questionable crater
23.	45	M	25 years	Considerable night distress	No relief in 10 days; Banthine discontinued	Deformity; no crater	
24.	23	M	2 years	Usual ulcer symptoms; hemorrhage	Immediate relief	Ulcer deformity	Not available
25.	34	M	12 years	Usual ulcer symptoms, 1 hemorrhage and 1 perforation; symptoms persisted despite usual treatment	Prompt relief	Deformity and crater	Not available
26.	50	F	8 years	Repeated recurrence	Partial relief	Deformity and crater	Not available
27.	52	M	20 years	Repeated recurrence, 3 hemorrhages	Prompt relief	Deformity and crater	Not available
28.	34	M	2 years	Repeated recurrence	Immediate relief	Deformity and crater	Not available
29.	37	M	10 years	Repeated recurrence, 1 perforation	Partial relief	Marked deformity	Not available
30.	44	F	20 years	Repeated recurrence; surgery advised	Immediate relief	Ulcer crater	No crater

Use of Banthine in Other Conditions

The effect of this drug in several other gastrointestinal conditions is presented in Table 2.

Levin, Kirsner and Palmer,[4] and Levin et al[5] have shown that gastric ulcers do not have the continued noctural acid secretion or the high acidity typical of duodenal ulcers; consequently vagal stimulation probably has little to do with the pathogenesis of gastric ulcers in contrast to duodenal ulcers. The two conditions appear to be two separate diseases. On an experimental basis, Banthine was prescribed to 2 patients with gastric ulcers. One of these was unable to tolerate the drug. The other patient was given Banthine for a period of almost 3 months. At the conclusion of this therapy the ulcer of the latter patient was as large as at the onset of treatment, and gastric resection was necessary. Banthine had no effect upon this benign gastric ulcer.

Inasmuch as marginal ulcers have responded favorably to surgical vagotomy, this is recognized as the treatment of choice. One patient who had a long ulcer history, accompanied by recurrences and 12 hemorrhages for which a gastroenterostomy was performed in 1941, followed by a vagotomy 8 years later, was placed on Banthine therapy for a marginal ulcer. The ulcer pain disappeared completely, and on progress roentgen examination 6 weeks later the crater could no longer be visualized. The patient, however, objected to the excessive dryness produced by even one 50 mg. tablet taken daily, and discontinued the use of the drug.

Factors of nervous tension and the psychosomatic aspects of ulcerative colitis have been given recent extensive study. Although bilateral vagotomies have been performed for the treatment of ulcerative colitis, we do not believe the procedure to be physiologic for the reason that the vagus nerve, at the most, innervates only the right colon, whereas the disease begins in the rectum and extends proximally. Because Banthine produces some effect on each division of the parasympathetic system, 1 patient with ulcerative colitis was placed on this therapy. The patient underwent a relapse while on Banthine medication.

Two patients who demonstrated syndromes of severe hyperacidity simulating peptic ulcer, but whose roentgenologic examinations were negative, were treated with Banthine. In both instances night pain ceased, and each patient believed this medication to have been of more positive value than the usual ulcer program. Another who manifested the irritable colon syndrome, with belching and epigastric fullness following meals, obtained no relief from Banthine. A patient having a severely irritable bladder condition, associated with an acute Hunner's ulcer, showed a pronounced decrease in urinary symptoms after Banthine therapy.

Many other conditions exist, such as irritable colon, functional bladder disturbances, dysmenorrhea and ulcerative colitis, in which definite nervous factors are present, which might conceivably respond to Banthine medication. However, the results in these other conditions have not been outstanding, although too few patients have been given Banthine to warrant definite conclusions.

Table 2
USE OF BANTHINE IN THE THERAPY OF OTHER CONDITIONS

1. **Gastric ulcer**						
	43	M	6 years	Recurrent symptoms	Gastric ulcer	Continued to have pain; ulcer crater, remained same size despite 3 months of Banthine therapy
	58	M	10 years	Repeated recurrences	Gastric ulcer	Did not tolerate Banthine
2. **Marginal ulcer**						
	42	M	20 years	Repeated recurrences; 12 hemorrhages; gastroenterostomy 1941; vagotomy 1949	Marginal ulcer	Pain disappeared and crater disappeared; stopped drug after 1 month because of dryness
3. **Ulcerative colitis**						
	44	M		Developed relapse of acute toxic ulcerative colitis while on Banthine		
4. **Hyperacidity syndrome**						
	39	M	15 years	Severe ulcer-like symptoms, night distress; partially relieved by ulcer program	Repeated x-rays negative	No night pain while on Banthine; continued on intermediate feedings; more relief than with other medication
	35	M	11 years	Ulcer-like symptoms with night distress	Repeated x-rays negative	Excellent result; more relief than on ulcer program or any other therapy
5. **Irritable colon**						
	53	M	7 years	Belching and fullness after meals	Negative	No relief with Banthine

Toxic Effects of Banthine

Pharmacologically, the action of Banthine is anticholinergic and provides autonomic ganglion blockade, principally effecting the parasympathetic division. Side reactions of the drug are usually mild. In only 3 of the 37 were complications severe enough to warrant cessation of the therapy. One of these patients had a duodenal ulcer, another a gastric ulcer, and a third a marginal ulcer. Excessive dryness of the mouth and disturbances of vision necessitated discontinuance of Banthine medication.

The full dose of 8 tablets was given daily to 28 patients. In 15 no appreciable side reactions developed. Thirteen manifested accompanying complications with symptoms of severe dryness evident in 11, slow urinary stream in 6, impaired visual focus in 5, and constipation, hoarseness and impotence in 1. Because of these reactions the dosage was reduced in 6 of the 28 patients; 9 were placed on a smaller dose consisting of either 4 or 6 tablets a day. Of

these latter, 2 had visual disturbances and 2 dryness of the mouth. These reactions were more severe during the first week of treatment, and usually subsided thereafter. No apparently extreme toxic symptoms occurred in any of our patients.

Because of occasional difficulty in urination, this medication is contraindicated in a patient with prostatic hypertrophy. A 67-year-old man recently admitted to the hospital on the service of Dr. C. C. Higgins illustrates this point clearly. This patient gave a history of nocturia, slow urinary stream and a decrease in the size of the stream, "rolling" abdominal discomfort and diarrhea of 3 years' duration. He was given Banthine by a local druggist without the advice of a physician. The following day he developed acute urinary retention. Cystoscopic examination was negative except for a large prostate. He was treated by the use of an indwelling catheter and subsequent prostatectomy. This medication should not be given to patients with prostatic enlargement and should not be dispensed except on the advice of a physician.

Whether long-continued use of this drug will result in intolerance to the medication or severe toxic reactions has not, as yet, been determined, inasmuch as none of our patients have undergone the therapy for a significant interval.

Summary

A new anticholinergic drug, Banthine, was prescribed for 30 patients with duodenal ulcers. Out of the group of 25 having active symptoms, 19 obtained definite and immediate symptomatic relief. Seventeen of 18 patients originally demonstrating ulcer craters showed healing of the crater on progress examination.

The majority of patients under observation tolerated the full dose of 100 mg. every 6 hours without undue complications. Out of a total of 37, 3 discontinued the drug because of distressing reactions which included dryness of the mouth, visual difficulties, slowness of urination and, rarely, constipation and hoarseness. The drug should not be given to patients with enlarged prostates or bladder neck obstructions. One patient with an enlarged prostate developed acute urinary retention after one day's medication with Banthine.

Seven patients presenting other gastrointestinal problems were given the medication. This group is not sufficiently large to warrant any conclusions; preliminary results were disappointing in this small group, however. Empirically, the drug may be of value in such conditions as irritable colon, the syndrome of hyperacidity, ulcerative colitis, functional bladder difficulties, and dysmenorrhea.

This report is entirely preliminary. Further studies on gastric acidity and nocturnal secretion, as well as the employment of a similar-appearing placebo tablet (for control), are indicated. It will be interesting to determine whether a small dose of the drug, such as 50 mg. 4 times a day, may be effective in preventing recurrences of duodenal ulcer.

References

1. Collins, E. N.: Treatment of peptic ulcer. Cleveland Clin. Quart. **17**:129 (July) 1950.
2. Longino, F. H., Grimson, K. S., Chittum, J. R. and Metcalf, B. H.: Orally effective quaternary amine, Banthine, capable of reducing gastric motility and secretions. Gastroenterology **14**:301 (Feb.) 1950.
3. Grimson, K. S., Lyons, C. K. and Reeves, R. J.: Clinical trial of Banthine in 100 patients with peptic ulcer. J.A.M.A. **143**:873 (July 8) 1950.
4. Levin, E., Kirsner, J. B. and Palmer, W. C.: Nocturnal gastric secretion in patients with gastric carcinoma; comparison with normal individuals and patients with duodenal ulcer and with gastric ulcer. Gastroenterology **12**:561 (April) 1949.
5. Levin, E., Kirsner, J. B., Palmer, W. C. and Butter, C.: Comparison of fasting and nocturnal gastric secretion in patients with duodenal ulcer and in normal individuals. Gastroenterology **10**:952 (June) 1948.
6. Dennis, C. et al.: Response to vagotomy in idiopathic ulcerative colitis and regional enteritis. Ann. Surg. **128**:479 (Sept.) 1948.