Belladonna Alkaloid-Sedative Mixture

Effects on gastric acidity and motility

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Controversy still exists as to the causative factor of pain in peptic ulceration. Some believe that acid is the *sine qua non* in the production of pain. This belief started with the demonstration by Bonniger¹ that the introduction of 0.1N hydrochloric acid into the stomach of a patient with active peptic ulcer would produce typical pain. It was supported later by Palmer and his coworkers² and by Bonney and Pickering.³ Others felt that pain was the result of increased motility and spasm,⁴ and still others that pain was produced by the acid-causing spasm in or near the ulcer site. Studies by Ruffin and associates, however, showed that the relief of pain after vagotomy⁵ and following methantheline bromide⁶ was apparently due mainly to effects on motility rather than on acidity. They also felt that elevation of the pain threshold will relieve ulcer pain, a mechanism through which sedatives and narcotics seem to work.

While there exists controversy as to the cause of pain in peptic ulcer, it is generally assumed that spasm of smooth muscle is the cause of pain experienced by patients with functional digestive disorders. Hence, the use of antispasmodic substances as an adjuvant therapeutic agent has become an established practice in the treatment of diseases of the digestive tract, whether they are on an organic or functional basis.

For many years the belladonna alkaloids were the only anticholinergic drugs available. These were of limited value when employed singly, partly because the clinically effective dose, as determined by objective tests, was frequently associated with certain undesirable side effects such as xerostomia and mydriasis. While the effects upon accommodation of the eye and upon intraocular pressure are produced by local instillation, actual disturbances in vision are rarely if ever

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encountered from oral administration of the alkaloids. Diminished salivary secretion is probably the earliest and most conspicuous side effect; in reality it is a safeguard against overdosage. The principal alkaloid of belladonna, \( l \)-hyoscyamine, is seldom employed in clinical practice, probably because of its tendency to undergo spontaneous racemization under varying conditions of storage and in certain types of pharmaceutical preparations. Stabilization may be accomplished by conversion with racemic atropine or by the presence of the other natural alkaloids in the proper amounts to create a stable equilibrium state. The presence of hyoscine, or scopolamine, contributes certain desirable actions which are not observed in the use of hyoscyamine alone.

In recent years many different antispasmodic mixtures and many cholinergic blocking agents have been introduced and studied experimentally and clinically. These studies demonstrated that besides their clinical symptomatic effect some of them had a definite inhibitory effect on gastric motility and acidity.\(^7\)

In this paper the results of our studies—experimental and clinical—with a mixture of natural belladonna alkaloids with phenobarbital\(^*\) are being reported. The antisecretory and antimotility effect was studied in ulcer patients and the relationship between acidity and motility noted. The clinical effects were observed on patients with abdominal symptoms who fell into the following diagnostic categories: (a) duodenal or (b) gastric ulcer, (c) irritable bowel which included hypertrophic gastritis, pylorospasm, postcholecystectomy syndrome, duodenitis, diverticulosis and diverticulitis, (d) ulcerative colitis, (e) amebiasis, (f) gallbladder disease, and (g) postoperative cases of carcinoma of the colon.

**MATERIAL AND METHODS**

The data which form the basis of this report were acquired from observations upon 176 patients (Table 1), 29 of whom were hospitalized and 147 were patients seen in the gastrointestinal clinic or private office. Of the 29 hospitalized patients 11 had peptic ulcer (9 duodenal and 2 gastric), 1 had gallbladder disease, and 17 had functional disorders of the gastrointestinal tract.

Of the 176 patients, 86 were males and 90 females. The ages ranged among the males from 14 to 75, with an average of 43 years, and

\(^*\) Donnatal. Supplied to us through the courtesy of William R. Bond, M.D., Director of Clinical Research, A. H. Robins Company, Inc., Richmond, Va.