Gastrointestinal Radiography with Glucagon

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Abstract. This report summarizes the results of nine diagnostic radiographic studies done double blind crossover comparing glucagon to placebo and to anticholinergic drugs in volunteers. In seven studies the subjects were administered drug intramuscularly and in two studies intravenously. There were five diagnostic studies of the upper gastrointestinal tract, one for esophageal varices and three of the colon. The results indicate that glucagon can be given intramuscularly and intravenously. When given intravenously it has a rapid onset and predictable length of action depending on the dose given. Reports of side effects were few consisting primarily of nausea and or vomiting. These results indicate that glucagon is the drug of choice for hypotonic diagnostic examinations.

Key words: Gastrointestinal tract, effect of drugs — Hypotonic radiography, methods and results — Intestine, motility.

Hypotonic duodenography was first introduced by Porcher in 1944 [1]. He used morphine to relax the duodenum, but since then parenteral anticholinergics have been used for this purpose. Recently the anticholinergic drugs are being replaced by glucagon [2]. The temporary duodenal atony and distension induced by drugs is the procedure of choice for detecting lesions of the duodenum and pancreas [3–8]. The barium air-contrast study has been done with and without duodenal intubation [9, 10].

Recently Obata [11], Nishizawa et al. [12], and Shirakabe et al. [13] reported on the use of double-contrast techniques to find very small cancers of the stomach. With relaxation and distension of the stomach during a double-contrast examination, both profile and en face views of the interior stomach can be made and minute areas of relative fixation and mucosal infiltration are more easily seen. Using these techniques Nishizawa et al. [12] visualized 8 of 13 cancers 5 to 10 mm in diameter. Shirakabe et al. [13], in a larger series collected from several institutions, reported 62% of 196 early cancers less than 1 cm in size detected on roentgenographic examination. These clinicians generally used an anticholinergic known as Buscopan®. Although not available in the United States, it is similar to anticholinergics generally available in this country.

For barium enema examinations when the colon does not fill properly because of muscle spasm or for other reasons, anticholinergic drugs are also administered. In 1958 and 1967 Welin [14, 15] recommended that, with few exceptions, atropine be given routinely to patients prior to air-contrast studies of the colon. Use of the anticholinergic reduced smooth muscle spasm and prevented the vasovagal reflex, allowing the radiologist to accomplish a more detailed and complete examination with less discomfort to the patient. Recently Ferrucci and Benedict [16] advocated the use of antispasmodic drugs for regular and air-contrast colon examinations.

These procedures appear to be relatively safe, and most reports of side effects are related to use of the anticholinergic drugs [16–21]. From reports in the literature some radiologists are not aware that symptoms following the parenteral use of propantheline bromide or atropine sulfate may arise and persist long after the diagnostic examination has been completed. Undesirable symptoms reported include transient tachycardia, blurring of vision, urinary hesitancy and retention, dryness of the mouth, headache, general malaise [5, 9, 16, 20–22], and, rarely, massive gastric dilatation [18]. A single dose of the anticho-
linergic given parenterally, sufficient to induce hypotonia of the gut, is usually much larger than that ordinarily given orally. Thus all subjects reported mild to severe side effects of significant duration [9, 16, 20–22]. Ferrucci and Benedict [16] recommend that patients be instructed not to drive for several hours after the administration of an anticholinergic agent because of the effect of the drug on accommodation. Furthermore, in patients who require hypotonic studies, anticholinergic drugs are often contraindicated since they may aggravate preexisting medical conditions. Therefore, there is a need for a drug with a short predictable duration of action and with few side effects. Our studies and those of others indicate that glucagon fulfills these requirements.

While studying the effect of glucagon on the gallbladder [23], we observed that the contrast material retained in the duodenum indicated the organ was relaxed. Relaxation of the bowel by glucagon had been previously reported by others [24–27] and was confirmed by us [19–21, 28]. Following this lead we began a series of investigations. This article then summarizes several double-blind crossover barium studies in normal volunteers. In these studies the effect of glucagon on gastrointestinal tonicity and motility was compared to those of atropine sulfate, propantheline bromide, or placebo.

Upper Gastrointestinal Roentgenography

In the initial study [28] we gave 12 asymptomatic volunteers 2 mg of glucagon and placebo i.v. double blind and crossover. Using fluoroscopic and radiographic observations the radiologist reported a significant (p < 0.001) decrease in duodenal motility and tonicity when glucagon was compared to placebo. A favorable response to glucagon was noted at 10 and 30 min. At 60 min the glucagon effect was no longer distinguishable from that of placebo. In effect, the gastrointestinal tract had returned to normal 1 h after drug was given.

In subsequent studies [19, 20] we gave 12 asymptomatic volunteers 2 mg of glucagon, 1 mg of atropine sulfate, or placebo. An additional 12 volunteers received 2 mg of glucagon, 30 mg of propantheline bromide, and placebo. Medication in both studies was given intramuscularly, double blind and crossover.

Although both atropine sulfate and propantheline bromide were found to be effective (p < 0.05), glucagon was significantly (p < 0.05) better than either anticholinergic in the examination of the stomach, duodenal bulb, and duodenal loop and equal to these drugs in the examination of the small bowel. When compared to placebo, glucagon was no longer active at 1 h whereas the anticholinergic drugs still had a significant effect at 1 h. The effectiveness of glucagon to relax the upper gastrointestinal tract has since been confirmed in patients by Bertrand et al. [29] and Carlsen and Finby [30].

One of the authors (REM) has previously used atropine sulfate for retrograde small bowel examination. He has since reported that glucagon greatly facilitated retrograde small bowel examinations by making the patient more comfortable and the small bowel more relaxed [31]. This clinical impression has been confirmed by a double-blind barium enema study [21]. It was observed during the barium enema study that when a specified quantity of barium was given to each subject, the barium filled a greater length of small bowel when placebo, atropine sulfate, or the combination of atropine sulfate with glucagon was given than when glucagon alone was injected. This suggested that if the colon is relaxed, more of the barium sulfate remains in the colon and less is available for reflux into the small bowel. This occurred with glucagon and placebo at the end of 1 h. With the return of small bowel peristalsis to normal, barium moved readily from the small bowel into the colon. We believe that this is related to the short action of glucagon.

Dose-Response Studies

In dose-response studies [32] we gave 15 male and female cooperative volunteers placebo or 0.25, 0.5, 1.0, or 2 mg of glucagon intravenously. The stomach, duodenum, and small bowel were carefully observed for onset and duration of drug effect on the motility and tonicity of these organs. Onset of drug effect was observed in approximately 45 sec regardless of the dose of glucagon given. There was a definite decrease (p < 0.01) in gastrointestinal motility and tonicity with all doses.

The duration of drug effect was proportionate to the size of the dose. When 0.25 mg of glucagon was given i.v., there was atonicity of the duodenum and jejunum for an average of 8 min and hypotonicity lasting an average of 12 min. The stomach was atonic for an average of 5 min and showed moderate hypotonicity for an average of 8.5 min. This interval is ordinarily adequate for a complete hypotonic study by an experienced examiner.

When 2 mg of glucagon was administered, there was atonicity of the duodenum and jejunum for an average time of 18 min and moderate hypotonicity lasting for an average of 24 min. Moderate hypotonia is considered adequate for the experienced gastrointestinal radiologist to obtain a good hypotonic