Clinical Comparison of Iocetamic Acid (Cholebrine) and Ipodate Sodium (Oragrafin)

RUTH REID NEAL,[1] KEVIN G. HARVEY,[2] KATHLEEN G. CANTWELL,[2] AND HARRY C. PRESS, JR.[2]

Iocetamic acid (Cholebrine) and ipodate sodium (Oragrafin) were compared in a double blind study of 503 patients. The radiographs were evaluated for contrast density, visualization of common duct, gallstones, residual in the intestinal tract, and side effects. Cholebrine demonstrated better opacification, fewer repeat examinations, slightly greater common duct opacification, and more frequent visualization of gallstones. Oragrafin had less residue. Side effects were minimal with both contrast agents.

Cholecystography has been shown to be valuable for evaluating the gallbladder for evidence of disease [1–4]. Iocetamic acid (Cholebrine) is a cholecystographic agent now being used in the United States. Ipodate sodium (Oragrafin) was compared to iocetamic acid (Cholebrine) in weight dependent dosages and evaluated for efficacy and adverse side reactions.

Subjects and Methods

All hospital inpatients recommended for cholecystography were randomly included in a double blind study to receive either contrast agent. Of the 573 patients selected, 70 were excluded due to discharge from hospital, lack of sufficient laboratory data, pediatric age, or change to intravenous cholangiography.

With iocetamic acid, either a 3 g (four tablets) or 4.5 g (six tablets) dosage was recommended by the manufacturer, with no weight dependent breakdown. The four-tablet dose was assigned to patients weighing 67.5 kg or less, and the six-tablet dose to patients weighing more than 67.5 kg. With ipodate sodium, the manufacturer's specified weight-dependent dosage of 3–6 g (six to twelve 500 mg tablets) was administered (45–56 kg, six tablets; 56–67.5 kg, eight tablets; 67.5–90 kg, 10 tablets; and 90–101 kg, 12 tablets).

Iopdate sodium (500 mg/tablet) contains 61.7% organically bound iodine; iocetamic acid (700 mg/tablet) contains 62%. As administered in our study, iodine content was 1,850–3,700 mg for ipodate sodium and 1,730–2,600 mg for iocetamic acid.

The patients were given a fat-free meal the evening before administration of the contrast agent. After administration, nothing was permitted by mouth. The radiographic examination was performed by the technologist between 7:00 and 9:00 the next morning in the standard prone and oblique views with erect spot films. Patients were questioned by the technologist, who was unaware of the contrast material given to the patient, concerning the occurrence of nausea, vomiting, itching, diarrhea, or fainting.

The films were evaluated independently by two radiologists regarding contrast density and visualization of the common duct, gallstones, and residual contrast in the intestinal tract (table 1). The radiologists were unaware of the contrast material used. Contrast agents were administered randomly, without regard to age, sex, history of allergy, or clinical condition.

In cases of nonvisualization of the gallbladder (grade 0, table 1) the patient was given the same dosage of the same contrast agent in repeat examination the next morning. No dietary restrictions were imposed for the morning or midday meal, but a fat-free meal was again given the evening before examination.

Results

The findings of comparative evaluation of 503 patients are summarized in tables 1 and 2. Chi square analysis [5] provided a quantitative method of determining the significance of the results. Probability values less than 0.05 are significant. Probability values between 0.05 and 0.10 are probably significant.

The number of patients with excellent contrast (grade 3, table 1) in gallbladder visualization was significantly higher with iocetamic acid than with ipodate sodium ($P < 0.05$) (table 1). The number of patients in whom gallstones were demonstrated was significantly higher with iocetamic acid than with ipodate sodium (table 2). Common duct opacification was also significantly higher with iocetamic acid than with ipodate sodium.

Side effects, consisting of nausea and vomiting, were reported by two patients receiving iocetamic acid and by five patients receiving ipodate sodium. There were no reports of skin reactions, diarrhea, or fainting.

The number of patients who required repeat examinations due to nonvisualization of the gallbaldder (grade 0) on the first examination was 22 (8.9%) with iocetamic acid and 66 (25.8%) with ipodate sodium. Residual contrast material was found in the gastrointestinal tract in 22 (8.9%) patients with iocetamic acid and in four (1.6%) patients with ipodate sodium.

Discussion

Several investigators have considered the effectiveness of various cholecystographic agents, but no prior direct comparison has been made using iocetamic acid (Cholebrine) and ipodate sodium (Oragrafin). Juhl et al. [6] concluded that ipodate sodium was equal to iopanoic acid (Telepaque) in gallbladder opacification, but with fewer side effects. Stanley et al. [7] found iocetamic acid to give the densest shadows and highest diagnostic yield when compared with iopanoic acid or tyropanoate sodium (Bilopaque). Russell and Frederick [8] found iopanoic acid produced denser gallbladder shadows and higher frequency of stone demonstration compared with

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[1]Department of Radiology, Medical College of Georgia, Augusta, Georgia 30902.
[2]Department of Radiology, Howard University Hospital, Washington, D.C. 20060. Address reprint requests to H. C. Press, Jr.

TABLE 1

Density of Gallbladder Shadows, Single Dose

Grade	Criteria	Contrast Material			
		Iocetamic Acid (*N* = 247)		Ipodate Sodium (*N* = 256)	
		No.	%	No.	%
3, Excellent	Very bright, equal to density of vertebral body	55	22.3	41	16.0
2, Good	Bright, equal to ribs 11 or 12	136	55.0	128	50.0
1, Fair	Density adequate for stone visualization, but less than ribs 11 or 12	34	13.8	21	8.2
0, None	Nonvisualization	22	8.9	66	25.8

TABLE 2

Comparison of Results

Contrast Medium	Common Duct Opacification (SD = 1.31)	Demonstration of Stones (SD = 0.84)	Side Effects
Iocetamic acid (*N* = 247)	49 (19.8%)	31 (12.6%)	2 (0.8%)
Ipodate sodium (*N* = 256)	28 (10.9%)	18 (7.0%)	5 (2.0%)

Note.—With an observed difference of greater than twice the standard error, we conclude that its occurrence by chance is very unlikely [5].

ipodate sodium or tyropanoate sodium, but had a higher incidence of side effects. Parks [9] favored iocetamic acid in either of two dosage forms compared with tyropanoate sodium or iopanoic acid because of its better opacification of the gallbladder and lower incidence of repeat examinations.

Our study directly compared iocetamic acid and ipodate sodium for relative opacification of the gallbladder, repeat examinations, demonstration of gallstones, and side effects. Opacity of the common bile duct and residual contrast in the gastrointestinal tract were also considered.

According to our study, iocetamic acid gives better gallbladder opacity than ipodate sodium, as evidenced by a higher proportion of good and excellent grades of opacification. The proportion of patients demonstrating excellent contrast (grade 3) was significantly higher with iocetamic acid than with ipodate sodium at the 5% level of confidence. Demonstration of gallstones was better with iocetamic acid than with ipodate sodium. The number of repeat examinations required due to nonvisualization of the gallbladder was also statistically significant, with iocetamic acid requiring fewer repeats.

Reported side effects (nausea and vomiting) were minimal with both agents; the skin reactions reported with iocetamic acid by Janower and Hannon [10] and Zeit [11] were not seen.

Contrast residue was found more frequently in the gastrointestinal tract with iocetamic acid, but did not obscure visualization of the gallbladder [9]. The common bile duct was visualized in the studies with the greatest opacification of the gallbladder, consistent with the findings of Russell and Frederick [8].

Our study indicates that in routine cholecystographic examinations, iocetamic acid (Cholebrine) is as effective as, or better than, ipodate sodium (Oragrafin), gives a higher proportion of excellent grades of opacification of the gallbladder, requires fewer repeat examinations due to nonvisualization, and better demonstrates the common bile duct and gallstones. When side effects were evaluated, nausea and vomiting were minimal with both agents.

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