PRELIMINARY STUDY OF A NEW CHOLECYSTOGRAPHIC MEDIUM

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EXPERIMENTAL studies[1] recently have resulted in the preparation of a new organic iodine compound, 3-(3-amino-2, 4, 6-triiodophenyl)-2-ethylpropanoic acid (Telepaque*) for cholecystography. On the basis of animal experimentation[2,3,4] this compound compared favorably with iodoalphionic acid (Priodax) from the viewpoint of both toxicity and gallbladder concentration. In view of the high percentage of side effects encountered with Priodax, particularly nausea and diarrhea, clinical trial of this new medium appeared justified. The following preliminary report embodies the results obtained regarding both gallbladder visualization and side effects in a series of 232 unselected cases, half of whom received Priodax and half Telepaque.

Telepaque is a cream-colored solid, containing 66.68 per cent iodine by weight, in organic combination (compared with 51.38 per cent in Priodax). It is insoluble in water, and soluble in dilute alkali and various organic solvents. Hoppe,[2] in experiments on dogs and cats, showed that the gallbladder visualization obtained with Telepaque compared favorably with that produced by Priodax. His studies on dogs revealed that 500 mg./Kg. of Telepaque effected as dense a gallbladder shadow as 1,000 mg./Kg. of Priodax. Acute intravenous toxicity studies in mice[2] showed Telepaque to be slightly more toxic than Priodax. However, on oral administration, the former proved to be less than one-third as toxic. Tolerance studies in dogs following repeated massive oral doses of Telepaque have been reported by Hoppe,[2] McAuliff and McChesney[3] and Goble.[4] Renal and hepatic function tests, as well as gross and microscopic tissue studies, showed no evidence of pathologic change attributable either to Telepaque or Priodax.

In the early part of the present study it was decided to examine 5 recipients of each drug daily. Later, this number was increased to 20. No attempt was made to select patients on the basis of weight, history, sex, or other criterion. Each was instructed to eat a low fat meal on the evening before examination. Patients receiving Priodax were prescribed 6 tablets (3 Gm.) immediately following this meal, and 3 tablets (1.5 Gm.) 3 hours later. (Previous experience indicated that 4.5 Gm. was the most satisfactory routine dose.) Those who received Telepaque were instructed to take 6 tablets (3 Gm.) at 9 p.m. on the evening prior to examination, regardless of the time at which the meal was eaten. The appropriate time for administration had been determined by preliminary studies** on humans who showed an optimum gallbladder shadow

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Table 1

SIDE EFFECTS

	CASES	NAUSEA		VOMITING	DIARRHEA			DYSURIA
		Mild	Severe	Total	Mild	Severe	Total	
PRIODAX (4.5 Gm.)	116	8.6%	3.4%	12.0%	0.8%	30.1%	12%	42.1%	5.1%
Total side effects	60%								
TELEPAQUE (3 Gm.)	116	6%	2.6%	8.6%	0%	10.3%	1.7%	12.0%	0.8%
Total side effects	21.4%								

VISUALIZATION

	CASES	Excellent	Good	Fair	Poor	No Visualization
PRIODAX (4.5 Gm.)	116	20.5%	64.6%	6.9%	5.1%	2.6%
TELEPAQUE (3 Gm.)	116	40%	43%	9.6%	2.8%	4.4%

10 to 12 hours after the ingestion of Telepaque. All patients were requested to drink nothing after midnight except for one cup of black coffee or tea before 7 a.m. Films were made between 7:45 and 8:15 on the following morning. Each patient had a routine posteroanterior and right lateral decubitus film. Where necessary, pitressin was used to dispel confusing gas shadows.

Each patient was interviewed before any films were made and the following questions asked: 1. Did your gallbladder pills cause you discomfort? 2. Did you experience nausea, vomiting, or diarrhea since taking them? 3. Did they cause you any other discomfort? Whenever an affirmative answer was given details were elicited.

In the interests of accuracy the following definitions were arbitrarily adopted: 1. Mild nausea—duration 15 minutes to 1 hour. (A small number of patients complained of nausea of shorter duration immediately after taking tablets of either medium. It was decided to disregard this complaint, as these patients appeared unable to distinguish between actual nausea and mere distaste for the tablets.) 2. Severe nausea—duration longer than 1 hour. 3. Mild diarrhea—2 to 3 loose bowel movements. 4. Severe diarrhea—more than 3 bowel movements.

Later, the films were reviewed and evaluated without reference to the recorded side effects. In the evaluation of the films the following definitions, modified from Hoppe[2] were adopted: (a) Excellent: sharp outline and brilliant contrast. (b) Good: a distinct shadow with satisfactory intensity and definition. (c) Fair: a faint shadow, easily recognizable, but of insufficient intensity to demonstrate any existing small radiolucent calculi. (d) Poor: faint gallbladder shadow, recognizable only on close inspection. (e) Nonvisualization: no definite gallbladder shadow. The influence of technical error was avoided, as far as

Table 2

SIDE EFFECTS WITH 3 GM. IODOALPHIONIC ACID

Authors	Cases	Nausea	Vomiting	Diarrhea	Dysuria
Ochsner[5]	300	26%	2.6%	15%	5%
Bryan[6]	845	20%	2.0%	33%	12%
Paul, Pohle and Benson[7]*	114	28.1%	1%	22.8%	15%
Ochsner[8]	600	24.6%	5%	14%	5%
Kemp[9]**	77	41.6%	5%	24%	11.7%

Using various dosage routines.

***4.2 Gm.*

possible, by repeating the film procedure until exposures of satisfactory quality were obtained.

Our results are summarized in table 1. Approximately one-third as many patients experienced side effects with Telepaque as with Priodax and only one-fourth as many had severe side effects. The striking feature with Telepaque was the pronounced decrease in the incidence of diarrhea.

The incidence of nausea which we encountered with Priodax is lower than that generally recorded in the literature (table 2). This may be associated with the fact that our patients were all ambulatory. Conversely, the incidence of diarrhea in our patients given Priodax is considerably higher than that usually observed (table 2). This is possibly due to a variation in definition of terms as well as to our use of 9 tablets of the compound.

From the viewpoint of gallbladder concentration only one significant difference between the two media is apparent, namely the higher incidence of dense gallbladder shadows observed with Telepaque. This suggests that a lower dose of Telepaque may prove satisfactory for gallbladder visualization and at the same time further decrease the incidence of side effects. Accordingly a study is being undertaken of a second series of patients using 2 Gm. dosages of Telepaque; to date the results have been encouraging. In this second series an attempt will be made to determine whether or not a less dense concentration of the dye is preferable and less likely to obscure small, nonopaque calculi.

Summary

This preliminary report indicates: (1) that there is a significant reduction in the number of side effects with Telepaque in comparison with Priodax, and (2) that adequate visualization is obtained with Telepaque.

References

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