THYROID UPTAKE OF ^{131}I: FURTHER COMPARISONS OF CAPSULES AND LIQUID PREPARATIONS

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Comparisons were made of thyroid uptake of three commercially available preparations of ^{131}I, using a double-blind design, in 125 patients with normal thyroid function. Uptakes with Squibb Iodotope Diagnostic capsules were significantly lower than those with Squibb Iodotope Oral liquid at 4 hr ($p < 0.01$) and 24 hr ($p < 0.05$) after ingestion in both the general population and in all patients less than 45 years of age. Uptakes of Radiocaps I-131 (Abbott Laboratories) and Iodotope Oral liquid were indistinguishable under identical conditions. Our findings indicate that interference with either absorption or metabolism of a pharmaceutical can result from the vehicle used to administer it.

The use of encapsulated radioiodine for thyroid uptake studies has gained in popularity primarily because it provides a more convenient vehicle for administration than liquid preparations. Recently Halpern et al (*1*) showed that healthy individuals gave lower uptake figures after a capsule dose of ^{131}I than they did after a liquid dose. In fact, three out of 11 subjects in that study had abnormally low uptakes with capsules and normal uptakes with liquid. Robertson et al (*2*) have since suggested that the Gelfoam filler used in commercially available ^{131}I capsules in some way interferes with ^{131}I absorption. To further evaluate this problem a prospective study was undertaken to compare thyroid uptake values using encapsulated radioiodine from two different manufacturers and radioiodine administered in liquid form.

MATERIALS AND METHODS

From September 1973 to January 1974, 225 patients were referred to us for thyroid evaluation that included a radioiodine uptake study. The uptake studies were performed with 10–100 mCi of ^{131}I administered either in capsule or liquid form. Each patient was randomly assigned one of three forms of radioiodine: Group A, Radiocaps I-131 (Abbott Laboratories, North Chicago, Ill.); Group B, Iodotope Diagnostic capsules (Squibb and Sons, Princeton, N.J.); and Group C, Iodotope Oral liquid (Squibb). All patients had in vitro tests including T_3 resin uptake, T_4, and free thyroxine equivalent (*3*). Detailed histories were obtained to determine if a patient's radioiodine uptake might be altered by recent medical procedures, medications, or dietary habits. Using both clinical judgment and the three chemical determinations, 125 patients were considered to be entirely within normal limits as regards thyroid function. They ranged from 17 to 80 years in age and included 31 men and 94 women. This group of normal patients was the subject of this study.

All capsules were checked upon receipt from the manufacturer for uniformity of activity within the same lot number. Uptakes were measured at 4 and 24 hr after ingestion of the radioiodine. All patients fasted for at least 8 hr before the dose and 1 hr after. Uptakes were measured by counting at a distance of 25 cm with a 2-in. scintillation detector and a scaler. A Plexiglas water-filled phantom was used to ensure that the dose was counted with as close to identical geometry as possible. Appropriate corrections were made for room and patient background.

The three groups were compared using the Student t-test. While the parent populations might not have a normal distribution, the central limit theorem asserts that their arithmetic means will be normally distributed if the sample size is large ($n \geq 30$) and that such statistics as the Student t-test may be used with satisfactory results (*4*).

Received June 5, 1975; revision accepted Nov. 11, 1975.

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TABLE 1. COMPARISON OF RADIOIODINE UPTAKES: ALL AGES

Time	Mean level ± 1 standard deviation*			Statistical evaluation of intergroup differences	
	Group A† (capsule)	Group B† (capsule)	Group C† (liquid)	Groups A and C	Groups B and C
4 hr	11.57 ± 3.58	9.34 ± 3.40	12.77 ± 4.35	$t = 1.38$ 80 df Not sig.	$t = 3.93$ 77 df $p < 0.01$
24 hr	22.12 ± 7.24	19.57 ± 6.78	23.06 ± 7.71	$t = 0.57$ 80 df Not sig.	$t = 2.14$ 77 df $p < 0.05$

* The normal 4- and 24-hr uptake ranges for the authors' laboratory are 5–20% and 10–40%, respectively.
† Group A comprised 46 patients (35 female, 11 male), Group B comprised 43 patients (32 female, 11 male), and Group C comprised 36 patients (27 female, 9 male).

TABLE 2. COMPARISON OF RADIOIODINE UPTAKES: LESS THAN 45 YEARS OF AGE

Time	Mean level ± 1 standard deviation*			Statistical evaluation of intergroup differences	
	Group A† (capsule)	Group B† (capsule)	Group C† (liquid)	Groups A and C	Groups B and C
4 hr	11.35 ± 3.60	9.04 ± 3.27	13.12 ± 4.56	$t = 1.60$ 53 df Not sig.	$t = 3.78$ 51 df $p < 0.01$
24 hr	22.91 ± 7.17	18.74 ± 6.62	23.52 ± 8.00	$t = 0.30$ 53 df Not sig.	$t = 2.38$ 51 df $p < 0.05$

* The normal 4- and 24-hr uptake ranges for the authors' laboratory are 5–20% and 10–40%, respectively.
† These groups were obtained from the groups in Table 1 by excluding all patients 45 years of age or older. Group A: 30 patients (24 female, 6 male); Group B: 28 patients (22 female, 6 male); Group C: 25 patients (17 female, 8 male).

RESULTS

The uptake studies performed with Iodotope Diagnostic capsules gave significantly lower values than those performed with the Iodotope Oral liquid preparation at 4 hr ($p < 0.01$) and at 24 hr ($p < 0.05$). The statistical significance of this discrepancy was found to vary with the age of the patients. Subgroups consisting of patients under 45 years of age gave the same results at the same levels of significance, whereas there was no significant difference for patients above 45 years of age. Also, uptake studies performed with Radiocaps I-131 showed no significant difference from those performed with Iodotope Oral liquid at all levels of comparison. These results are summarized in Tables 1 and 2.

The in vitro studies showed no significant difference among the three groups and were well within the expected normal ranges for the authors' laboratory.

DISCUSSION

The reliability of ^{131}I capsules in performing thyroid uptake studies was seriously questioned recently by Halpern et al (*1*), who found about 6% lower uptakes after a capsular dose of ^{131}I as compared to a liquid dose. Our study substantiated this report. However, we found significantly lower uptakes with only one of two commercially available ^{131}I capsules. We also found that patients over 45 years of age showed no significant difference in uptakes with the oral solution and the two different brands of encapsulated ^{131}I. There is no obvious explanation for this finding. Although iodine-containing dyes are sometimes used for color in capsule preparation, the capsules used in this study did not contain significant amounts of iodine.

The two most obvious reasons for the discrepancy between the uptake values are (A) incomplete dissolution of the capsule or filler, and (B) the formation of ^{131}I-gelatin complexes (*5*) that make iodine unavailable for trapping by the thyroid gland. Credence is given to the filler postulate in this study, since only the Iodotope Diagnostic capsules contain filler. Other pharmaceuticals may suffer similarly.

ACKNOWLEDGMENT

The authors wish to express thanks to Robert Mollett for expert technical assistance.

The opinions or assertions expressed in the above article are those of the authors and are not to be construed as official or representing the views of the Navy Department or the naval service at large.

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