^{131}I THYROID UPTAKES: CAPSULE VERSUS LIQUID

S. Halpern, N. Alazraki, R. Littenberg, S. Hurwitz, J. Green, J. Kunsa, and W. Ashburn

University of California, San Diego, School of Medicine, La Jolla, California and Veterans Administration Hospital, La Jolla, California

Studies were performed that indicate that normal, healthy individuals have a lower thyroidal uptake of ^{131}I following a capsule dose of ^{131}I than they do following a liquid dose. Two possible mechanisms for this are offered, the first being the variable amount of time it takes for the ingested capsule to dissolve completely and the second being the formation of iodine gelatin complexes in the GI tract. In the latter case, the labeled iodine would not appear to be in a form that would allow it to be trapped by the thyroid gland. It is recommended that if early uptake values are important in assessing the clinical state of the patient, liquid ^{131}I be used in preference to capsulized ^{131}I. Furthermore, the possibility exists that the fall in ^{131}I uptake values noted in the past several years may in part be due to the widespread use of ^{131}I capsules.

Recent studies have shown that within the past few years there has been a decrease in the thyroidal iodine ^{131}I-NaI uptake throughout the United States (*1–3*). Studies performed in our own laboratory indicated that while there was indeed a change in the mean and mode of our ^{131}I uptakes, the ranges surprisingly remained the same (*4*). Shortly after this, we studied a patient who had a ^{131}I uptake of less than 2% at 4 hr and 21% at 24 hr. Because there was a possibility of ovarian dysfunction (the patient had amenorrhea), a rectilinear scan of her pelvis was performed 4 hr post ^{131}I-capsule ingestion in an effort to detect struma ovarii if it existed. The scan showed a very intense accumulation of radioactivity in the region of the right ovary. The abdomen was again scanned at 24 hr postingestion. No evidence for uptake in the right ovary existed at the time of the second scan, nor were there any other areas in the abdomen, with the exception of the urinary bladder, that contained radioactivity. The possibility therefore existed that the etiology of the increased area of uptake in the right lower quadrant was secondary to some undissolved capsule that contained residual ^{131}I. A prospective study was then undertaken to evaluate the effects of ^{131}I capsules on thyroidal uptake values.

MATERIALS AND METHODS

Eleven healthy volunteers ranging in age from 25 to 51 years were the subjects of this study. Each subject had at least two ^{131}I uptakes (one with capsule, one with liquid ^{131}I) using 3–10 μCi. Some received the capsule first while others received liquid ^{131}I first. Uptakes were performed at 0 (background), 15, 30, 45, 60, 90, 120, 180, and 240 min and finally 24 hr postingestion of the radiopharmaceutical. All uptakes were performed by first counting the dose at 25 cm distance in an IAEA phantom using a Picker Spectroscaler III A counter. The same geometry was used for the thyroid uptakes. All uptakes were performed by the same examiner in an identical manner. Each recorded value (see Table 1) is an average of 3-min counts beginning 1 min before and ending 1 min after the indicated recording time. Four hours postingestion the subject urinated, and counts were obtained with the single-probe detector placed first over an area the center of which was 3 cm inferior to the tip of the xyphoid in the midline of the abdomen, corresponding roughly to the stomach, and then at a point the center of which was on a line halfway between the anterior superior iliac spine and the umbilicus corresponding roughly to

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For reprints contact: Samuel E. Halpern, Div. of Nuclear Medicine, University Hospital of San Diego County, 225 West Dickinson St., San Diego, Calif. 92103.

the area noted on the patient described. Repeat studies were performed approximately 2 weeks after the first study with the background from the previous thyroid uptake subtracted. Every effort was made to maintain a constant geometry, and each person remained on his normal diet. None of the subjects received medication containing iodine nor did they ingest other than their usual quantity of sea food. No sea food was eaten 24 hr before each study.

RESULTS

Table 1 shows the results of the study. In every subject, trapping by the thyroid gland had already begun by 15 min following the oral administration of the liquid ^{131}I. Conversely, 0 uptake was noted at 15 min in eight of the patients administered capsules. Three of the five studies (Subjects 1, 4, 9) showed uptake values greater than background at 15 min with the capsule dose, but the uptake fell at 30 min, suggesting that the 15-min uptake in those individuals was secondary to background fluctuation. Subject 7 did not show evidence of uptake until 120 min after ingestion of the capsule. In the majority of the cases in which the capsule was administered, significant uptakes did not begin until 45 min following ingestion. In only one case, however, did significant uptake of the liquid ^{131}I not occur at 15 min (Subject 3). To check the reproducibility of the capsular uptake, the study was repeated in Subjects 1 and 4 with virtually identical results.

No consistent difference was noted in the counting rate over the stomach and caecal regions at 4 hr although, on an average, the values were higher with the capsule than with the liquid as regards the right lower quadrant. The difficulty in accurately determining the quantity of radionuclide remaining in the abdomen using the technique described is obvious.

TABLE 1. COUNTS CORRECTED FOR

Subject no.	Dose (cpm)‡	15 min	30 min	45 min	60 min	90 min
*1	9,579	0(0)	0(0)	45(.47)	117(1.2)	255(2.7)
†1	7,265	109[1.5]	254[3.5]	317[4.4]	553[7.6]	513[7.1]
*1	9,593	41(.43)	14(.15)	30(.31)	130(1.4)	185(1.9)
*2	10,344	26(.25)	255(2.5)	333(3.2)	376(3.6)	520(5.0)
†2	8,257	95[1.2]	200[2.4]	272[3.3]	314[3.8]	388[4.7]
*3	7,824	0(0)	28(1.1)	47(.60)	84(1.1)	186(2.4)
†3	3,949	11[.36]	87[2.2]	123[3.1]	161[4.1]	193[4.9]
*4	4,837	15(.31)	6(.12)	17(.35)	69(1.4)	105(2.2)
†4	12,336	157[1.3]	273[2.2]	387[3.1]	439[3.6]	456[3.7]
*4	2,650	0(0)	0(0)	25(.94)	50(1.9)	54(2.0)
*5	8,814	0(0)	0(0)	79(.90)	73(.83)	157(1.8)
†5	7,900	25[.32]	154[1.9]	233[3.0]	256[3.2]	286[3.6]
*6	9,089	25(.28)	61(.67)	145(1.6)	219(2.4)	267(2.9)
†6	7,908	143[1.8]	253[3.2]	311[3.9]	402[5.1]	447[5.7]
*7	5,139	0(0)	0(0)	0(0)	0(0)	0(0)
†7	6,986	56[.80]	125[1.8]	168[2.4]	231[3.3]	283[4.1]
*8	8,752	0(0)	11(.12)	69(.79)	110(1.3)	184(2.1)
†8	5,400	81[1.5]	177[3.3]	212[3.9]	312[5.8]	329[6.1]
*9	9,068	20(.22)	15(.17)	95(1.1)	113(1.2)	179(2.0)
†9	3,092	54[1.7]	86[2.8]	107[3.5]	123[4.0]	128[4.1]
*10	10,842	0(0)	59(.54)	102(.94)	147(1.4)	222(2.0)
†10	2,842	37[1.3]	84[3.0]	127[4.5]	109[3.8]	132[4.6]
*11	5,325	0(0)	18(.34)	67(1.3)	120(2.3)	176(3.3)
†11	6,182	40[.65]	88[1.4]	161[2.6]	210[3.4]	266[4.3]

* Iodine-131 uptake values from 11 subjects. All patients were fasting 12 hr before and during the first 4 hr of the study.
( )—percent uptake capsule
*—capsule (Squibb)
†—^{131}I-NaI liquid
‡—counts per min
[ ]—percent uptake liquid
ave—average

DISCUSSION

The data presented in this study throw at least some doubt on the use of gelatin capsules for the oral administration of ^{131}I. We have witnessed, in the last 10 years, a major shift in the ^{131}I uptake values around the country. Simultaneously, a shift towards using gelatin capsules for the standard thyroid uptake has probably occurred. The explanation for the lowered uptake values has been attributed to an increase in the elemental iodine (*1*) in our diet, chiefly in bread. There does not seem to be any doubt that the quantity of ingested iodine has increased in American diets by the latter mechanism; however, the authors submit the possibility that at least one cause might be the increasing popularity of gelatin capsules. The mechanism whereby the uptake values are diminished is not clear cut. However, at least two major possibilities must be considered. The first and most obvious explanation for the very early, (15, 30, 45 min) uptake values is that it takes a finite amount of time for the gelatin capsule to dissolve. If this were the only reason for diminished uptake, one might then expect to see equivalent uptakes (liquid versus capsule) per unit time from this point onward. Such is not the case, because in the subjects studied, with only a single exception (Subject 8), the thyroid continues to take up iodine at a faster rate in the final 20 hr of the study when liquid ^{131}I is administered than when the ^{131}I is given by capsule. Reasonable explanations for this phenomena might be that either some of the capsular ^{131}I is not in an absorbable form, remains in the gut, and is then excreted in the stool, or that some of the capsular ^{131}I that is absorbed is in a form that cannot be trapped by the thyroid. Peyrin, et al (*5*) have shown convincingly that there are products of the digestion of capsule in the plasma that are labeled with ^{131}I following its ingestion. From a chemical

BACKGROUND AND DECAY

120 min	180 min	240 min	24 hr	RL Q (4 hr)	Stomach (4 hr)
294(3.1)	435(4.5)	627(6.6)	1,675(17.5)	974(10.1)	120(1.3)
635[8.7]	782[10.8]	1,013[14]	2,160[29.7]	512[7.0]	172[2.3]
303(3.2)	510(5.3)	605(6.3)	1,921(20.0)	623(6.5)	285(3.0)
533(5.2)	632(6.1)	640(6.2)	1,255(12.1)	163(1.6)	240(2.3)
472[5.7]	570[6.9]	661[8.7]	1,430[17.3]	71[.86]	171[2.1]
220(2.8)	343(4.4)	446(5.6)	1,070(13.7)	426(5.4)	147(1.9)
214[5.4]	300[7.6]	334[8.5]	653[16.5]	107[2.7]	170[4.3]
96(2.0)	150(3.1)	197(4.1)	464(9.6)	220(4.5)	142(2.9)
549[4.5]	667[5.4]	747[6.1]	1,655[13.4]	198[1.6]	600[4.9]
58(2.2)	142(5.4)	127(4.8)	289(10.9)	132(5.0)	114(4.3)
—	114(1.3)	195(2.2)	715(8.1)	459(5.2)	107(1.2)
345[4.4]	469[5.9]	488[6.2]	1,120[14.2]	91[1.1]	114[1.4]
375(4.1)	450(5.0)	566(6.2)	— —	181(2.0)	249(2.7)
521[6.6]	736[9.3]	943[11.9]	1,950[24.7]	82[1.0]	238[3.0]
87(1.7)	162(3.2)	269(5.2)	880(17.1)	355(6.9)	88(1.7)
384[5.5]	482[6.9]	643[9.2]	1,940[27.8]	145[2.1]	148[2.1]
283(3.2)	419(4.8)	540(6.2)	1,560(17.8)	580(6.6)	213(2.4)
395[7.3]	478[8.9]	570[10.6]	1,180[21.9]	114[2.1]	139[2.6]
188(2.1)	255(2.8)	310(3.4)	715(7.9)	49(.54)	213(2.3)
140[4.5]	195[6.3]	196[6.3]	400[12.9]	39[1.2]	138[4.4]
235(2.2)	311(2.9)	379(3.5)	985(9.7)	72(.66)	97(.89)
145[5.1]	164[5.8]	164[5.8]	450[15·8]	44[1.5]	55[1.9]
270(5.1)	349(6.6)	377(7.1)	845(15.9) (53 hr)	232(4.4)	167(3.1)
344[5.6]	449[7.3]	518[8.4]	1,103[17.8]	67[1.1]	154[2.5]

* 4 hr ave = 5.2
† 4 hr ave = 8.7
* 24 hr ave = 12.3
† 24 hr ave = 19.3

point of view, this seems entirely plausible because conditions prevail in the stomach and small intestine that would allow labeling of the iodide ion to proteins. Furthermore, the degree of labeling would probably vary with the chain length of the end product of digestion, and this might vary to some extent in different individuals, especially since gelatin has markedly varying molecular weight entities within any one batch (*6*). Peyrin, et al (*5*) show that even in vitro dissolution of the capsule results in approximately 30% labeling of the capsule.

Indeed, it is possible that the reasons for the marked delay in the early uptakes is that a great deal of the first products of digestion and absorption of the capsule are ^{131}I-labeled to gelatin.

It should also be remembered that these tests were carried out on healthy, predominantly young individuals with apparently normal thyroid function. One obvious question raised is: What happens to elderly persons with multiple organ disease, e.g., the patient with gastrointestinal disease, or the patient with hyper- or hypothyroidism who often has achlorhydria. Further work is being undertaken to assess this problem. Finally, it should be remembered that the gelatin capsules currently on the market are not all made in the same way; thus, what may be characteristic for one capsule may not be for another. It is the opinion of the authors that until further work is performed in assessing the accuracy, reproducibility, and interchangeability of capsulized ^{131}I, liquid (oral) ^{131}I should probably be used. The possibility exists that intravenous ^{131}I might be more accurate in assessing ^{131}I uptakes since it bypasses all problems of gastrointestinal absorption. Data from Hays and Solomon (*7*) indicate that 180-min intravenous uptake values were considerably higher than those determined by our group using capsules or oral liquid.

To emphasize the point of this presentation more dramatically, had the eleven subjects of this study been referred to our laboratory for thyroid evaluation, we might have recommended TSH stimulation tests in three of the subjects (Nos. 5, 9, and 10) whose values fell into the gray zone of our normal 24-hr thyroid uptake range (6–49% in our laboratory).

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