Esophageal Passage of Iodine-131 Capsules

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The purpose of this study was to determine the orogastric transit time of standard 131I capsules and the incidence of transit delay.

Methods: We studied 58 consecutive subjects receiving outpatient diagnostic and therapeutic 131I dosages. A standard ion chamber survey meter, placed over the left upper quadrant of the abdomen, monitored orogastric transit. Each subject had ample water to subjectively swallow their capsule. Orogastic transit times, volume of water ingested, capsule size, and demographic and historical data were recorded for each subject.

Results: Seventeen subjects (29%) had delayed transit, with an orogastric transit time >90 sec (median 140 sec, range 100–930 sec). Forty-one subjects had normal transit (median 14 sec, range 4–51 sec). We identified delayed transit in 7 of 37 women (19%) and 10 of 21 men (48%) (p = 0.035). Age, capsule size and initial water volume ingested did not differ significantly between subject groups.

Conclusion: Men were more likely than women to have prolonged orogastric transit of standard 131I capsules. Other than sex, we found no identifiable clinical feature or medical history to predict delayed orogastric transit. A standard survey meter can identify adherent capsules to minimize esophageal radiation exposure.

Key Words: radioiodine; orogastric transit; beta radiation


Radioiodine (such as 131I) is used extensively for both therapy and diagnostic testing of thyroid disorders. Both liquid and capsule formulations are available. Under favorable conditions the liquid 131I− iodide anion readily oxidizes to produce volatile elemental 131I2 iodine and hydrogen 131I− iodide. Both forms present a potential health hazard to personnel handling 131I solutions (1). Alternatively, encapsulated 131I within a standard gelatin shell minimizes volatility, spillage and aerosolization, thus, reducing contamination and exposure risks.

Although seemingly well-tolerated, capsule retention poses a theoretical long-term medical concern. Our experience, however, does not suggest dysphagia as a significant complaint among 131I patients. In fact, dysphagia is an uncommon symptom within the general population. However, studies have shown that both tablets and capsules may adhere to the esophagus despite asymptomatic swallowing (2,3). Since first described in 1970, various authors have described the incidence of injury and complications of incomplete esophageal passage of several different capsule and pill formulations, such as ferrous sulfate tablets, doxycycline capsules and potassium chloride tablets (4–8).

The goal of our study was to determine the incidence of delayed esophageal passage, and to confirm the capsule’s complete orogastric transit before releasing each subject from direct observation.

MATERIALS AND METHODS

We enrolled 58 consecutive patients in the study approved by the Walter Reed Army Medical Center’s Clinical Investigation Committee and Human Use Committee/Institutional Review Board. Each subject enrolled in the study voluntarily agreed to participate and gave written informed consent.

A common nuclear medicine instrument, a Victoreen 450 ion chamber survey meter (Victoreen Inc., Cleveland, OH), was used in this study. Prior to the start of the study, we created a phantom model to validate the survey meter’s accuracy in locating an outpatient 131I capsule within the chest or upper abdomen shortly after ingestion. The survey meter’s accuracy was measured by various physicians, technologists and pharmacists in the clinic. Our standard therapeutic and diagnostic capsule sizes were 0 (21.8-mm length; 7.63 mm o.d.; density >1) and 1 (19.5-mm length; 6.90 mm o.d.; density >1), respectively (Mallinckrodt Medical Inc., St. Louis, MO).

Before collecting our data, we selected 90 sec as the upper limit for normal orogastric transit. The choice of 90 sec was based on our review of the literature (9,10). Each subject was seated upright and the survey meter was placed over the left upper quadrant of the abdomen for continuous monitoring during the first 90 sec after capsule ingestion. The subject first drank 30 ml of water as a lubricant. We administered the
capsule with two to three 200-ml cups of water. The subject was instructed to drink as much water as necessary to completely swallow the capsule. No further instructions were given unless incomplete passage was determined at 90 sec. The capsule location was then determined within the esophagus, and the subject was instructed to drink additional aliquots of water until the capsule reached the stomach.

We recorded each subject’s transit time, location of any retained capsule(s), volume of water ingested, demographics, medical history and capsule size. The relationship of orogastric transit time with demographic and clinical characteristics was analyzed using Fisher’s Exact test and the Mann-Whitney U-test. All tests were two-tailed, with \( p < 0.05 \) considered statistically significant.

### RESULTS

The demographic and clinical characteristics of the two subject groups, based on the orogastric transit times, are given in Table 1. Overall, 29.3% (95% CI: 18.4%–42.9%) of the subjects had an orogastric transit time exceeding 90 sec; 36% of the subjects had a transit time between 11 and 30 sec. The frequencies are shown graphically in Figure 1. Of particular note, one male subject showed asymptomatic incomplete esophageal passage at 15 min, despite repeated swallowing of water and with position changes (i.e., from sitting to standing). The capsule promptly completed its orogastric transit only after the subject swallowed a small piece of bagel given to him by the investigator.

As shown in Table 1, there was a statistically significant difference between the two groups with regard to sex; men were more likely to experience an orogastric transit time of >90 sec \( (p = 0.035) \). This finding is underscored when comparing the median orogastric transit time between male and female subjects in our study. This difference was found to be statistically significant, even when we removed from statistical analysis the male subject noted above \( (p = 0.049) \). However, no statistically significant difference was seen between groups based on age \( (p = 0.36) \), capsule size \( (p = 0.56) \) or initial volume of water ingested \( (p = 0.46) \). Among the other demographic and historical characteristics, none was useful in predicting delayed transit. Prolonged orogastric transit was observed in 3 of the 6 subjects with a dysphagia history \( (p = 0.35) \), 4 of the 11 with related esophageal disorders \( (p = 0.71) \), 10 of the 25 status post-thyroidectomy \( (p = 0.15) \), and 5 of the 17 with other medical conditions besides their underlying thyroid disorder \( (p = 0.99) \).

Twenty-six of 41 subjects with a normal transit time and 13 of 17 with delayed transit initially swallowed their capsule with at least one cupful (200 ml) of water. Among the 17 subjects with delayed orogastric transit, 12, two and three capsules were found in the middle, upper and lower esophagus, respectively.

### DISCUSSION

Kikendall and Johnson (11) reviewed 756 published cases of pill-induced esophageal injury with more than 75 different medications. They found esophageal retention occurs not infrequently among the population as a whole. Predisposing factors appear to be increasing age, depressed esophageal peristalsis and left atrial enlargement. Additional controllable factors are patient positioning, time of day and amount of water taken with the pill or capsule.

A majority of the reported cases have involved women, a finding which Kikendall and Johnson (11) have attributed to the high prevalence of reports involving antibiotics and emepronium bromide used to treat urinary tract infections and associated bladder irritability. Their review suggests that the demographics of patients with pill-induced esophageal injury closely follows that of the underlying disease being studied (11).

Alternatively, our results supported neither trend. The proportion of men in the delayed orogastric transit group, 10/21 = 48%, was over two times greater than the proportion of women in this group, 7/37 = 19%. This difference in relative proportions was found to be statistically significant. This discrepancy suggests that the relationship between sex and orogastric transit time needs further analysis.

Other than sex, we could find no historical feature, physical characteristic or symptomatology that could accurately predict

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**TABLE 1**  
Orogastric Transit Time

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>&lt;90 sec (n = 41)</th>
<th>&gt;90 sec (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (yr) (range)</td>
<td>42 (18-82)</td>
<td>48 (25-73)</td>
</tr>
<tr>
<td>Median transit time (sec) (range)</td>
<td>14 (4-51)</td>
<td>140 (100-930)</td>
</tr>
<tr>
<td>Number of men (%)</td>
<td>11 (27)</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Number of women (%)</td>
<td>30 (73)</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Number of size #0 capsules (%)</td>
<td>19 (46)</td>
<td>6 (35)</td>
</tr>
<tr>
<td>Number of size #1 capsules (%)</td>
<td>22 (54)</td>
<td>11 (65)</td>
</tr>
<tr>
<td>Median initial volume ingested (ml)</td>
<td>200 (42-400)</td>
<td>200 (50-200)</td>
</tr>
</tbody>
</table>

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**FIGURE 1.** Histogram of orogastric transit times.
delayed orogastric transit. This generally fits with Kikendall and Johnson’s findings, although typical features have been described (11).

Based on previous studies and subsequent recommendations (2,3,11), our subjects were given optimal conditions to effectively and quickly swallow their capsule(s). Each dosage was administered in the morning. The subjects were seated upright and given 30 ml of water as a lubricant, followed with liberal amounts of water, both with the capsule and as a chaser. They were encouraged initially to drink as much water as needed to completely swallow each capsule. The majority of subjects drank 200 ml of water (i.e., one cupful). We did not find a relationship between the volume of water ingested and delayed orogastric transit.

Prior studies have shown esophageal retention rate variations based on formulation (i.e., pill versus capsule) and size (10,12). This is due in large part to the hygroscopic nature of the hard gelatin capsules which are typically 12%–16% water (13). In spite of this drawback, capsules are used in nuclear medicine, as they provide the only nonliquid option for individualized 131I dosages.

Hard gelatin capsules are supplied in a variety of sizes, ranging from 000, the largest size that can be swallowed, to 5, which is the smallest. The specific capsule sizes used in nuclear medicine clinics are selected based on the amount of material each can safely hold (13).

Diagnostic and outpatient therapeutic capsules generally contain 131I sodium mixed with a granulated powder mixture (I). Since granular powders are not readily packed within a capsule (13), and because minor dosage adjustments may be necessary, relatively large size 0 capsules are used. Slightly smaller inpatient therapeutic capsules can be used because the higher activity 131I is typically mixed with semisolid polyethylene glycol, and left as a small blob or adsorbed on anhydrous sodium phosphate within the capsule (I). Dosage changes are made by adjusting the number, rather than the contents, of the capsules.

As with previous studies reviewed by Kikendall and Johnson (11), we found an increased incidence of midesophageal localization compared to both the upper and lower esophagus. This region is characterized by external compression by the aortic arch, transition from skeletal to smooth muscle, and by a physiologic reduction in peristaltic wave amplitude (11,14).

Because we did not acquire sequential scintigraphic images of the esophagus during swallowing, we cannot conclusively say whether the capsules: adhered to the esophagus due to the hygroscopic nature of the capsule; retained within the esophagus due to variations in intraluminal diameter from external compression; or moved slowly due to abnormal esophageal peristalsis. Regardless of the specific underlying process, the esophagus in these cases received a radiation dose above that normally expected.

One can use dose-rate factors from standard exposure tables to predict the radiation dose from an adherent or retained 131I capsule (15). In this setting, the 131I capsule behaves as an area source, with beta emissions providing the primary radiation exposure to the underlying esophagus. To illustrate this point, a 15-mCi (555 MBq) 131I capsule adherent for 5, 10 and 15 min exposes the underlying esophageal mucosa to approximately 1000, 2000 and 3000 rads, respectively.

CONCLUSION

Standard 131I capsules pose a small spill hazard and low radiation exposure risk to the radiopharmacist and health care providers administering the dosage. We have demonstrated a significant incidence of adherent capsules among routine patients being treated or undergoing diagnosis in an active nuclear medicine clinic. Besides sex, we found no identifiable clinical feature, specific medical history or volume of water ingested with the capsule to predict an increased likelihood for poor transit. Alternatively, absence of dysphagia cannot reliably rule out delayed capsule passage.

Prolonged beta radiation exposure from an adherent or retained capsule may theoretically damage the esophageal mucosa and predispose a patient to short- and/or long-term complications. The unpredictable and asymptomatic nature of delayed transit and the possibility of capsule retention are concerns. Our study used a standard ion chamber survey meter to identify delayed transit among asymptomatic subjects. We established the survey meter’s accuracy with a phantom model prior to subject enrollment.

Although standard survey meters are readily available and simple to operate, we understand that their use may exacerbate already anxious patients. An alternative worth studying is to have each patient eat a bite of food, such as a bagel, immediately after swallowing the 131I capsule. Considering our anecdotal experience from this study, this simple procedure may suffice in ensuring prompt esophageal passage.

Further studies may enhance the current understanding of normal capsule transit among healthy volunteers (14). Scintigraphy provides another means of noninvasive functional correlation with the well-accepted manometric and pH probe monitoring data.

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REFERENCES


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