

Pill Swallowing by Adults With Dysphagia

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Objective: To evaluate differences in swallowing physiology and safety in patients with dysphagia between conventional tablets and a new method of tablet transportation, orally disintegrating technology (ODT) (RapiTab; Schwarz Pharma Inc, Milwaukee, Wis).

Design: The study observed a single group, crossover design.

Setting: Outpatient clinic within an academic teaching hospital.

Participants: A total of 36 adult dysphagic patients referred to the clinic.

Interventions: All subjects underwent simultaneous nasopharyngeal endoscopic evaluation, surface electromyographic (sEMG) measurement, and respiratory monitoring during swallowing. Subjects were evaluated swallowing the ODT and a conventional tablet formulation. Tablets were randomly and blindly presented to each subject. Subjects completed a preference survey subsequent to swallowing both tablets.

Results: Significant differences included greater sEMG amplitude and longer apneic duration when swallowing a conventional tablet compared with the ODT ($P < .001$). Patients with dysphagia demonstrated significantly longer total swallow durations ($P < .001$), a higher number of swallows per tablet ($P < .002$), and the need for fluid to assist in the clearance of the conventional tablet ($P < .001$). No significant difference was noted between the 2 tablet preparations in amount of residue or airway compromise during or following the swallow. On a postevaluation survey, patients reported that they preferred the ODT preparation for most of the parameters assessed.

Conclusions: Patients with dysphagia frequently complain of trouble swallowing medication. In this study, an ODT formulation provided a method of delivery that required less effort to swallow, did not result in increased levels of airway compromise, and was preferred by dysphagic patients. The ODT medication delivery technology may provide benefit to adults with dysphagia in convenience, compliance, and accuracy of dosing.

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DYSPHAGIA (DIFFICULTY swallowing food or liquids) is a common consequence of many health problems and has been associated with complications such as pneumonia, dehydration, and malnutrition. Dysphagia is currently estimated to affect more than 18 million adults in the United States,¹ and it has been proposed that this number is likely to rise in the near future owing to the aging population and a reported association between advancing age and swallowing difficulties.² With impaired swallowing, many patients demonstrate difficulty in transporting substances from the mouth into the pharynx. Hesitation, impaired control of oral materials, incomplete clearance or extended clearance time for swallowed material, and penetration or aspiration of swallowed materials into the airway are all common features of a dysphagic profile.

Swallowing oral medications in the form of pills, tablets, or capsules also presents a

persistent challenge for many individuals. A recent national survey revealed that over 40% of adults in the general community experience problems swallowing pills.³ Of adults who reported difficulty swallowing pills, 14% disclosed that they had delayed taking a dose of their medication, and 8% had skipped a dose completely. Thus, adults who have difficulty swallowing these forms of oral medications may not comply with prescribed regimens. Poor compliance with oral medication regimens may be elevated in the patient with dysphagia. For example, 15% of all residents in surveyed long-term care facilities reported difficulty swallowing tablets and capsules. Of this group, 5% regularly expectorated this medication, while 27% did not even attempt to swallow these medications.⁴ Patients with dysphagia who fail to comply with prescribed medication dosing are likely to encounter increased morbidity and mortality. Thus, health care providers must improve methods to effectively deliver oral medications to the swallowing-impaired patient.

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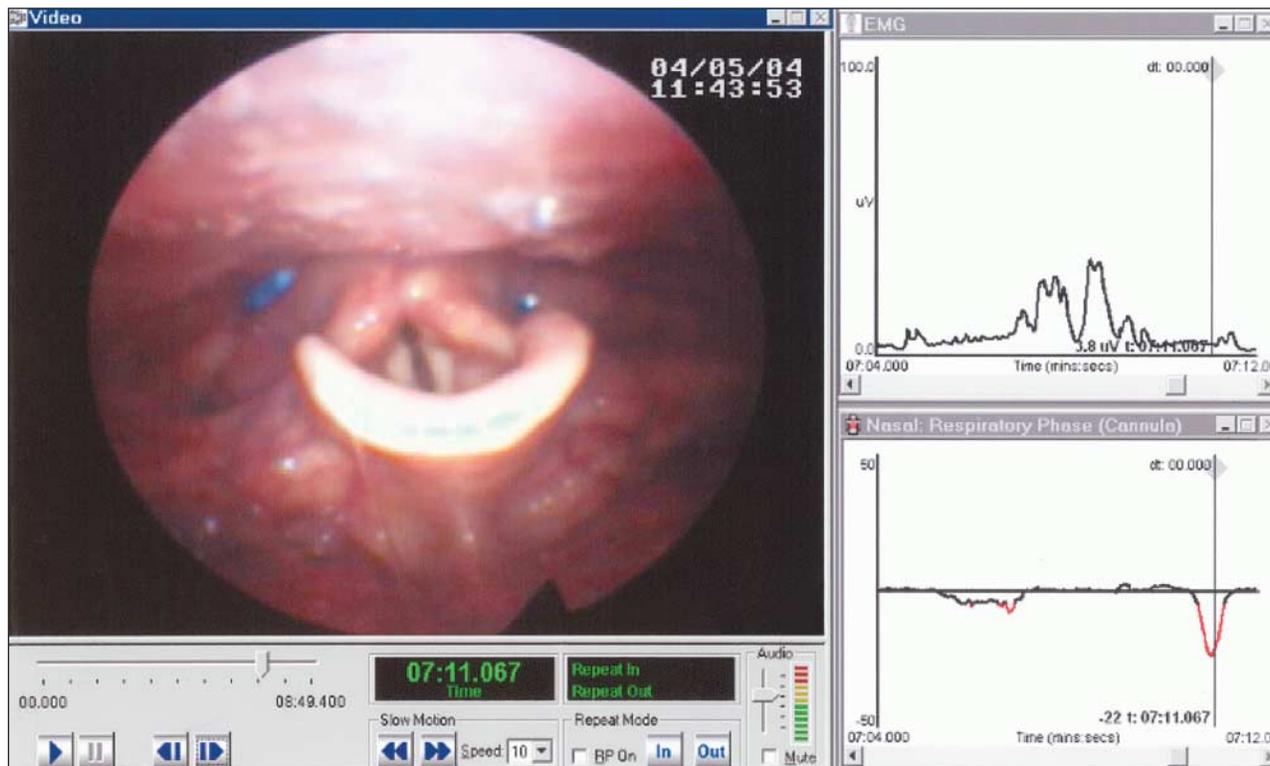


Figure 1. Simultaneous data collection of conventional tablet swallowing. The image displays an example of synchronized data collection using the Kay Digital Swallowing Workstation and signals laboratory (model No. 7100; KayPENTAX, Lincoln Park, NJ).

Recent developments in dosing technology offer an alternative delivery mechanism for medication to patients with oropharyngeal swallowing problems.^{5,6} A form of orally disintegrating technology (ODT), DuraSolv (Cima Labs Inc, Eden Prairie, Minn), which is used in the manufacture of RapiTab (Schwarz Pharma Inc, Milwaukee, Wis), provides a means by which oral medications are delivered via rapid disintegration of a tablet within the mouth facilitating passage through the upper aerodigestive system without the use of water to aid in swallowing. Rapidly dissolving tablets may facilitate safer and more consistent delivery of medication to swallowing-compromised patients.^{7,8} However, advantages of this form of oral medication have not been established in swallowing-impaired adults. Information on the relative effectiveness, safety, and preference of swallowed ODT preparations is a prerequisite to clinical application of this form of oral medication in adults with swallowing impairments.^{9,10}

This study aimed to investigate differences in swallowing effectiveness and safety between ODT and conventional tablet preparations in adults with swallowing impairments. In addition, it sought to evaluate preference for either preparation. The primary null hypothesis for this study was that there would be no difference in the success or safety of bolus clearance between ODT preparations and conventional pill or tablet formulations. Secondary null hypotheses were that there would be no differences in the time to bolus clearance, route of bolus clearance and/or position of residue, number of swallows, and effort attributed to swallowing the 2 formulations.

METHODS

SUBJECTS

We recruited a consecutive sample of patients referred to an outpatient swallowing clinic within an academic teaching hospital between November 2003 and April 2004 for this study. Adults 21 years or older with a complaint of swallowing difficulties based on patient and/or caregiver report were approached for participation in the study. In total, 36 eligible patients participated in this study. This study was approved by the institutional review board of the University of Florida.

PROCEDURES

The study followed a randomized, single-group, crossover design. All swallowing measurements were conducted using the Kay Digital Swallowing Workstation and Swallowing Signals Laboratory (model No. 7100; KayPENTAX, Lincoln Park, NJ). The Kay Digital Swallowing Workstation with signals laboratory is a computer-integrated system of swallowing measurement facilities including videoendoscopy, cervical auscultation, surface electromyography (sEMG), pharyngeal manometry, and respiratory monitoring. The system is specifically designed to evaluate swallowing and permits synchronization, on-line display, recording, and digitization of several physiologic signals during the time of the swallowing evaluation. For this study, nasopharyngeal videoendoscopy was used to visually display all swallowing attempts of each preparation (**Figure 1**).

Simultaneous sEMG was used to evaluate the timing and muscular effort of each swallow event, and simultaneous nasal airflow monitoring was used to measure the apneic duration of swallowing associated with each preparation.

MATERIALS

Each subject was observed videoendoscopically while swallowing 2 tablet preparations, RapiTab (an ODT) and a conventional tablet, both manufactured by Schwarz Pharma Inc. Both tablet types had an average weight of 340 mg and thickness of 4.05 mm. Each tablet preparation was colored blue to maximize visualization during the videoendoscopic study. Tablet order was randomly assigned from a computer-generated random numbers list. The subjects and investigators were blind to the order of presentation of the tablet formulations. To ensure blinding, each preparation was dispensed and arranged by the research assistant according to the randomization schedule prior to the testing session. Subjects were not able to visualize their swallowing attempts during the evaluation.

GENERAL PROCEDURES

During the evaluation, each subject was asked to “place the tablet preparation on his or her tongue, move it around and when able, swallow it completely.” To avoid influencing the subjects’ swallowing behaviors, no other instructions were provided. Once the patients placed the tablet preparation onto their tongue, a “tag” marker was generated on the simultaneous videoendoscopic, nasal airflow, and sEMG traces (Figure 1). All subsequent timing measures were made relative to this marker, which indicated placement of the preparation in the mouth.

VIDEOENDOSCOPIC MEASURES

The nasopharyngeal endoscopic video record was used to visually evaluate the success of all aspects of the swallow attempts, including route of clearance, safety, number of swallows, presence of residue, and extent of bolus clearance. Swallowing success for each trial was defined as clearance of the preparation through the upper esophageal sphincter without residue. Route of clearance was defined as the pathway taken by the bolus during the swallowing attempt. Residue was defined as the presence of some or the entire tablet in the oropharynx following a swallow. Safety of swallowing was defined by entry of swallowed materials or presence of residue in the laryngeal vestibule or proximal trachea during swallowing. Airway compromise was reflected by the penetration of any swallowed material into the endolarynx but not below the vocal folds. Material entering the airway below the true vocal folds was characterized as an aspiration event. The measurement “number of swallows” included a count of swallows required to remove tablet materials from the oropharynx. The extent of clearance of the tablet materials was defined a priori as a composite variable of time to clear, presence of residue, and number of swallows required to clear a bolus. Total time to swallow was measured from the placement of the tablet on the tongue until clearance from the oropharynx on the endoscopic record.

SURFACE EMG MEASURES

Surface EMG was used to evaluate the muscular activity associated with swallowing each tablet. Surface electrodes were positioned in the submental position for each subject. Muscle activity was recorded at a bandwidth of 50 to 250 Hz, with the sampling rate set at 500 Hz. Raw sEMG activity was integrated and rectified and displayed as a graphic trace on a computer screen. Measures derived from the sEMG record included onset of swallow activation, offset of swallow activation, and peak (maximum) amplitude. The effort required to swallow each tablet preparation was inferred from the average sEMG amplitude during the tablet swallow.

NASAL AIRFLOW MEASURES

Respiratory coordination for swallowing was measured using a nasal catheter positioned at the entrance of each subject’s nares. Respiratory information (inhalation/exhalation) displayed as a line tracing was recorded for all swallowing attempts. Respiration points were temporally related to the videoendoscopic physiology such as airway closure and reopening. Respiration measures derived included (1) onset of inspiration, defined as a downward line tracing associated with an open glottis position on the endoscopic trace; (2) swallowing apnea, defined as a horizontal line on the respiratory tracing indicating absence of airflow; and (3) expiration onset, defined as the upward line tracing associated with an open glottic position. Swallow apnea duration was calculated from these measurements. Swallow apnea duration, measured in seconds, reflects the duration of “nonbreathing” during the swallow. Longer apnea durations may reflect more physiologic demands on the subject during swallowing.

RESCUE CRITERIA

If a subject, after multiple attempts, was unable to swallow either preparation successfully, he or she could request a 10-mL aliquot of liquid. Allocation of liquid to assist in swallowing was recorded for each trial.

PATIENT PREFERENCE RATING

On completion of the examination, each subject was asked to rate his or her preference of each preparation on a series of 5-point Likert scales relating to ease of swallowing.

STATISTICAL ANALYSIS

Results were initially described using means, standard deviations, medians, ranges, and statistical tests for significance. Owing to skewed distributions, the Mann-Whitney *U* test for nonparametric data was used for the continuous variables age, time with dysphagia, and sEMG amplitude. Duration of swallow apnea, number of swallows, and total time to swallow were also nonnormally distributed and were transformed using a natural logarithmic transformation. Rank preference data, peak sEMG amplitude, average sEMG amplitude, and duration of swallow apneic pause were reviewed using related-samples *t* tests and the nonparametric equivalent Wilcoxon test; matched pairs were evaluated using the McNemar test. The χ^2 test was used for discrete counts of swallowing events such as number of swallows and provision of a liquid bolus to assist in swallowing. Friedman nonparametric analysis of variance was used to review interactions between age and the other skewed continuous variables by tablet type.

RESULTS

PATIENT CHARACTERISTICS

The characteristics of the patients in the study group are listed in **Table 1**. Most (64%) of the subjects were male with chronic swallowing problems. The mean (SD) age for the group was 64.5 (11.8) years. The median time with a swallowing problem was 9 months (range, 0.75-156 months). Most subjects (89%) were feeding orally, with 11 modifying their diet as a result of the swallowing difficulty. Only 13 (36%) reported a

history of difficulty swallowing tablets. Neurologic impairment (stroke) and head and/or neck cancer were the most frequent underlying causes of dysphagia in this subject group.

An exploratory subgroup analysis was undertaken to descriptively evaluate the role of disease grouping on pill swallowing.

PHYSIOLOGIC SWALLOWING CHARACTERISTICS

Of the 36 subjects, 22 (61%) demonstrated obvious difficulties (defined as visual struggle, coughing, or expulsion of the tablet) swallowing the conventional tablet. Fourteen (39%) demonstrated these difficulties with the ODT tablet. Physiologic swallowing characteristics of the conventional tablet differed significantly from those characteristics associated with the ODT tablet. These physiologic characteristics included number of swallows, timing of swallows, use of liquid to assist with swallowing, airway compromise, effort in swallowing, and respiratory patterns.

Table 1. Demographic Features of Study Subjects

Characteristic	Measure*
Age, mean (SD), y	64.5 (11.8)
Male	23
Female	13
Duration of dysphagia, median (range), mo	9 (0.75-156)
History of pill dysphagia	13
Feeding method	
Oral	32
Nonoral	4
Diagnostic group	
Neurologic	15
Cancer	11
Esophageal	6
Anterior cervical fusion	2
Unknown	2

*Unless otherwise indicated, data are presented as number of subjects (n = 36).

Table 2. Physiologic Characteristics of Swallowing by Tablet Type*

Characteristic	ODT Tablet (n = 36)	Conventional Tablet (n = 36)	Value	P Value
No. of swallows to clear, † median (range)	2 (1-19)	3 (1-20)	3.148	.002‡
Total time to swallow, † median (range), s	49.8 (1.92-323)	56.7 (5.23-323)	-15.700	<.001‡
Use of liquid needed to assist	6	14	5.114	.02§
Residue present following swallow	20	19	0.114	.74
Penetration into the endolarynx	7	5	0.400	.53
Aspiration below true vocal cords	3	5	0.563	.45
sEMG amplitude, mean (SD), µV	55.8 (25.7)	62.1 (26.1)	-18.296	<.001‡
Apneic duration, † median (range), s	1.47 (0.47-4.92)	2.11 (0.62-9.93)	9.775	<.001‡

Abbreviations: NS, nonsignificant finding (P value not available); ODT, orally dissolving technology; sEMG, surface electromyography;

*Unless otherwise noted, data are reported as number or number (percentage) of tablet swallows (NT = 72).

†Log transformation.

‡Paired t test.

§McNemar test.

||χ² Test.

Route of Clearance

No significant association was identified between route of clearance and type of pill preparation.

Number of Swallows

Compared with the ODT tablet, patients with dysphagia required significantly more swallows (P<.002) to clear the conventional tablet from the oropharynx (**Table 2**). Also, a significant association was identified between tablet type, number of swallows, and diagnostic grouping (P<.002). Patients with neurologic impairment required the greatest number of swallows to clear any tablet, followed by patients with head and/or neck cancer.

Total Time to Swallow

The median time to swallow any preparation for the group as a whole was 52 seconds (range, 1.92-323.5 seconds). Subjects required more time to swallow the conventional tablet (median time to swallow, 56.7 seconds; range, 5.2-323 seconds) than the ODT tablet (median, 49.8 seconds; range, 1.9-323 seconds) (P<.001).

Use of Liquid to Assist Swallowing

More subjects requested water to assist in swallowing the conventional tablet than the ODT tablet (14 [39%] vs 6 [17%]) (P=.02). No subject with neurologically based dysphagia requested fluid to assist in swallowing the ODT pill; however, subjects with head and/or neck cancer required water to assist in swallowing both tablet types.

Residue

Overall, residue was present in the hypopharynx after 39 (54%) of 72 tablet swallows. Figure 1 and **Figure 2** present examples of residue accumulation for the ODT and conventional tablets. However, no differences resulted between the 2 tablet types in proportion of subjects showing residue remaining in the hypopharynx after the swallow (Table 2).

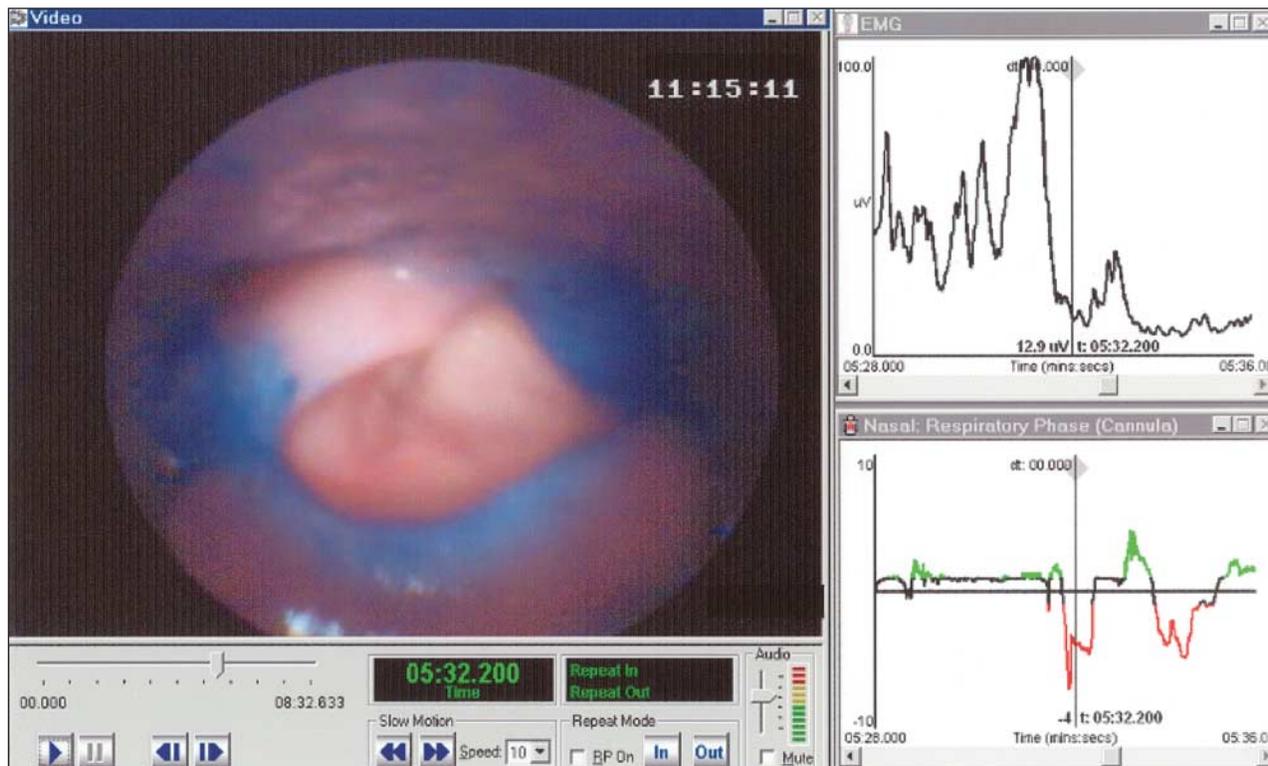


Figure 2. Simultaneous data collection from a subject swallowing an orally disintegrating technology tablet (RapiTab; Schwarz Pharma Inc, Milwaukee, Wis). The image displays an example of synchronized data collection during this process using the Kay Digital Swallowing Workstation and signals laboratory (Kay PENTAX, Lincoln Park, NJ).

Table 3. Patient Preference Data*

Question	Conventional Tablet (n = 36)	ODT Tablet (n = 36)
How easy was the pill to swallow?		
Not difficult	5 (14)	11 (31)
Extreme difficulty	8 (21)	1 (3)
Which pill did you prefer?	8 (22)	27 (76)
How concerned were you when swallowing the pill?	15 (42)	9 (25)
I prefer using water with this tablet.	19 (53)	4 (11)

Abbreviation: ODT, orally disintegrating technology.

*Data are reported as number (percentage) of subjects.

Airway Compromise

From the total of 72 tablet swallows, only 12 (17%) showed penetration of swallowed materials, while 8 (11%) revealed aspiration. No association was identified between aspiration or penetration with either tablet.

Surface EMG Patterns (Effort of Swallowing)

A significant difference resulted between the 2 tablet types in mean sEMG amplitude ($P < .001$). Mean sEMG amplitude was higher when swallowing the conventional tablet, suggesting that greater effort was required to swallow this preparation (Table 2).

Respiratory Patterns

A significant difference in swallow-related apneic duration resulted between the tablet types. Subjects with dysphagia required a significantly longer breath-holding period when swallowing the conventional tablet ($P < .001$) compared with the ODT tablet (Table 2).

A significant interaction also resulted between tablet type, apneic duration, and diagnostic grouping ($P < .001$). Patients with neurologically based dysphagia (2.78 seconds) and dysphagia secondary to anterior cervical spine fusion (2.37 seconds) required significantly longer apneic periods when swallowing the conventional tablet.

PATIENT PREFERENCE

More than 75% (95% confidence interval, 59%-86%) of the sample group found the ODT formulation easier to swallow than the conventional tablet and preferred that preparation as a medication type (Table 3). A significantly greater number of patients with neurologically-based swallowing problems (13/15) found the ODT tablet easier to swallow ($P < .04$) compared with the other disease groups within the sample.

Overall, most subjects experienced some level of concern about swallowing any type of pill. However, a significantly greater number of subjects reported high levels of concern over swallowing the conventional tablet compared with the ODT tablet (42% vs 25%) (Table 3).

Similarly, a significantly larger number of patients preferred to use water to swallow the conventional tablet compared with the ODT tablet and reported dislike at attempting to swallow the conventional tablet without water (53% vs 11%) (Table 3).

This study has identified differences in the physiologic swallowing characteristics and effort related to swallowing an ODT tablet compared with a conventional tablet. The patients with dysphagia in this study required a fewer number of swallows, shorter total swallow duration, shorter apneic duration, reduced muscular effort, and less fluid to assist in swallowing the ODT tablet. Conversely, no difference was found between the 2 tablet types in residue in the oropharynx following a swallow and aspiration or penetration of swallowed materials into the airway. This study has also revealed that patients with dysphagia show a strong independent preference toward the ODT preparation, rating it easier to swallow. These results suggest that ODT may provide benefit to patients with dysphagia by improving both compliance and ease of swallowing while not increasing the risk of airway compromise.

Swallowing tablets is difficult for many patients with dysphagia. Recent surveys suggest up to 40% of the general population may have difficulties swallowing pills or tablets.² Some information on the esophageal transit of pills is available,⁹ but the oropharyngeal aspects of pill swallowing have not been studied. Consequently, the physiologic swallowing characteristics, the influence of different pill characteristics, the impact of different underlying disease processes, and the longitudinal outcomes of pill dysphagia are unknown.

To our knowledge, this is the first study to evaluate the physiologic aspects of tablet swallowing in a group of identified individuals with dysphagia, and it provides preliminary data suggesting that tablet formulation may influence swallowing success. In our study, more than 60% of subjects with dysphagia experienced obvious difficulty swallowing a conventional tablet. However, the evaluation of standard tablet swallowing as part of a dysphagia assessment (either videoendoscopic or videofluoroscopic) is not routinely performed. Traditionally, pills have been used only in the evaluation of esophageal function. Our results suggest that the inclusion of a tablet-swallowing task in oropharyngeal dysphagia evaluations may facilitate comprehensive evaluation and treatment planning.

Our results also suggest that the diagnosed condition underlying the dysphagia may impact the physiologic aspects of tablet swallowing. Patients with neurologically based dysphagia in this study required more swallows to clear a conventional tablet and longer apneic durations, potentially placing them at greater risk for difficulty when taking medication. However, given the size of the study sample and respective disorder subgroups, only limited conclusions can be drawn.

Similarly, the impact of age on swallowing tablets requires consideration. Increasing age is well known to impact swallowing function. A descriptive trend toward increased difficulty swallowing tablets with increasing age was also noted in this study. However, the restricted age range of the sample did not allow meaningful evaluation of this issue. Future studies should include samples with a wider representation of age and sex.

The strengths of this study are the minimization of systematic bias by randomization and minimization of ob-

server bias in outcome evaluation by the blinding of the outcome assessor to the tablet allocation.

A potential weakness of the study is the limited number of subjects and therefore imprecise estimates (ie, wide 95% confidence intervals), introducing the possibility that results could be due to chance. Similarly, such sample size restrictions reduce the ability to generalize these results, and thus our data should be considered pilot in nature.

Patients with dysphagia demonstrate difficulty with the manipulation, control, and clearance of food and/or fluids from the oropharynx. In addition, they frequently report difficulty in swallowing pills. This study has found that an ODT tablet reduced the effort and physiologic stress associated with tablet swallowing in a sample of adults with dysphagia. In addition, patients with dysphagia reported a preference for this tablet. If these results can be replicated in a larger sample, they would suggest that ODT tablets might offer substantial advantages over conventional tablets and enhance compliance in patients who experience swallowing difficulty. Future studies on adults without dysphagia across the age span and focused groups of patients with dysphagia should help to evaluate the physiologic effects, preferences, and clinical application of these preparations.

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