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Swallowing Problems and Dietary Supplements: Data from FDA Adverse Event Reports, 2006-2015

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Background:

To facilitate ease of swallowing and promote patient adherence, the U.S. Food and Drug Administration (FDA) has provided voluntary guidance for the size of generic drug tablets and capsules (1). This guidance recommends that generic products should not exceed 17 millimeters (mm) in a single dimension. If a branded product already exceeds 17 mm, then the generic product should be no larger. No tablets or capsules should exceed 22 mm. Currently, no similar guidance for dietary supplements exists; however, supplements are implicated in swallowing problems, particularly among adults aged 65 years or older (2).

Objective:

To identify and characterize dietary supplement-associated swallowing problems in relation to pill size using data from 10 years of adverse event reports submitted to the FDA Center for Food Safety and Applied Nutrition Adverse Event Reporting System (CAERS).

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Author contributions: The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Wolpert, Budnitz, Geller

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Drafting of the manuscript for important intellectual content: All authors

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Publisher's Disclaimer: Disclaimer: The findings and conclusions in this study are those of the authors and do not necessarily represent the official position of the U.S. Food and Drug Administration (FDA), the U.S. Centers for Disease Control and Prevention (CDC) or the U.S. Department of Health and Human Services (HHS).

Methods and Findings:

The CAERS database contains FDA adverse event and product complaint reports for foods, dietary supplements, and cosmetics (2). The Dietary Supplement and Nonprescription Drug Consumer Protection Act (effective date for compliance: 22 December 2007) requires dietary supplement manufacturers, packers, and distributors to report serious adverse events to CAERS; voluntary reports may be submitted by healthcare professionals, consumers, and other members of the public (3). We used *Medical Data Dictionary for Regulatory Activities* (MedDRA) terminology to identify dietary supplement reports, submitted to CAERS from 1 January 2006 through 31 December 2015, that involved swallowing problems (for example, choking and dysphagia). We extracted sex, age, product, and adverse event outcomes, and excluded 442 reports implicating either multiple supplement products or non-solid oral dose form products (for example, liquids or powders). We classified dietary supplement products by our dietary supplement product categorization, based on ingredients or common reasons for use (4). We measured pill (i.e., tablet or capsule) sizes for the 10 products most commonly identified.

Of 20 791 dietary supplement adverse event reports submitted to CAERS in 2006-2015, 3962 (19.1%) indicated swallowing problems. These reports most commonly involved females (85.6%) (Table 1), representing 25.4% of all CAERS reports among females. Among the 64.5% of swallowing problem reports with age data, 76.8% were adults aged 65 years or older.

Choking was the most frequently reported swallowing problem (86.0%), followed by foreign body trauma (7.8%). Based on CAERS medical reviewer assessment, 14.3% of swallowing problem reports cited serious adverse events, including three deaths attributed to supplement-induced airway obstruction or aspiration (5). Most swallowing problem reports involved multivitamins (72.9%); 17.3% involved calcium supplements.

The 10 most commonly reported dietary supplement products accounted for 3026 (76.4%) of swallowing problem reports (Table 2), with weighted mean pill length, width, and height of 19.3, 9.8, and 7.8 mm, respectively. The proportional reporting ratio (PRR) for swallowing problems from these 10 products was 12.7, indicating that the ratio of swallowing problem reports to reports for other problems was 12.7 times higher for these 10 products than for other dietary supplements. Seven of the 10 products, accounting for 64.5% of all swallowing problem reports, were multivitamins marketed to older adults or calcium supplements. A single multivitamin product marketed to older women was involved in 40.6% of swallowing problem reports.

Discussion:

Most dietary supplement swallowing problem reports involved multivitamins or calcium supplements which are used by up to 35% and 24% of older adults, respectively (5), who have higher rates than others for dysphagia and other swallowing issues (1). The 10 most commonly identified supplement products in swallowing problem reports all exceeded 17 mm in length. Prevention opportunities include modifying supplement dose form

characteristics (e.g., producing smaller dose forms or adding coatings) and educating patients to speak with their pharmacists or physicians about benefits of supplements for them, and, if continued use would be beneficial, discuss ways to address problems swallowing pills.

This study has limitations: frequency of use of specific products was not available, CAERS reports may not be representative of the U.S. population, swallowing problems may be underreported, and completeness of reports can vary. Consequently, patient-specific risk factors for choking could not be fully assessed. Product pill sizes could have changed during or after the study period. Nevertheless, these data identify a specific harm, choking, that may be preventable, particularly for older adult patients who regularly consume dietary supplements.

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Table 1.

Dietary Supplement Swallowing Problem Adverse Event Reports to FDA, 2006-2015*

Case Characteristic	Dietary Supplement Adverse Event Reports Involving Swallowing Problems, n (%) (n = 3962) †	Dietary Supplement Adverse Event Reports Not Involving Swallowing Problems, n (%) (n =16 829)
Sex		
Female	3390 (85.6)	9986 (59.3)
Male	517 (13.0)	6101 (36.3)
Not stated	55 (1.4)	742 (4.4)
Age, y		
<1	0	88 (0.5)
1-4	21 (0.5)	143 (0.9)
5-19	18 (0.5)	503 (3.0)
20-44	103 (2.6)	3575 (21.2)
45-64	450 (11.4)	3698 (22.0)
65-74	643 (16.2)	1775 (10.5)
75-84	825 (20.8)	1295 (7.7)
≥85	495 (12.5)	493 (2.9)
Not stated	1407 (35.5)	5259 (31.3)
Report type‡		
Mandatory	3919 (98.9)	11 834 (70.3)
Voluntary	43 (1.1)	4995 (29.7)
Reported outcome§		
Death	3 (0.1)	351 (2.1)
Non-fatal, serious adverse events	563 (14.2)	6324 (37.6)
Other adverse events	3396 (85.7)	10 154 (60.3)
Swallowing problem type‖		
Choking	3406 (86.0)	
Foreign body trauma	308 (7.8)	
Dysphagia	167 (4.2)	
Other swallowing problem types	81 (2.0)	
Dietary supplement category¶		
Multivitamins	2889 (72.9)	
Calcium/bone health	687 (17.3)	
Pain or arthritis relief	93 (2.3)	
Cardiovascular health	67 (1.7)	
Other specified	67 (1.7)	
Immunity or infection/cold	50 (1.3)	
Single ingredient vitamins or minerals (not calcium)	48 (1.2)	

Case Characteristic	Dietary Supplement Adverse Event Reports Involving Swallowing Problems, n (%) (n = 3962) †	Dietary Supplement Adverse Event Reports Not Involving Swallowing Problems, n (%) (n =16 829)
Other categories	61 (1.5)	

*The term “dietary supplement” means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E) [21 U.S.C. § 321(f)(f)] (4).

†Dietary supplement adverse event reports indicating swallowing problems were identified by the following *Medical Dictionary for Regulatory Activities* (MedDRA) preferred terms: aspiration, choking, choking sensation, drooling, dysphagia, foaming at mouth, foreign body, foreign body aspiration, foreign body trauma, laryngitis, esophageal discomfort, esophageal injury, esophageal obstruction, esophageal spasm, esophagitis, pharyngeal injury, oropharyngeal discomfort, and sensation of foreign body. Reports involving more than one dietary supplement product, or involving non-solid oral dosage forms (e.g., powders, liquids, inhalants), were excluded (n = 442).

‡If both a voluntary and a mandatory report were submitted for the same event, the event was included here as “Mandatory.”

§Serious outcomes are death; a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity; congenital anomaly; and a medical or surgical intervention required to prevent the previous outcomes [Public Law 109-462] (https://www.congress.gov/109/plaws/publ462/PLAW-109publ462.pdf). Other adverse events include non-serious illness/injury; other serious (important medical events); visit to a health provider; and visit to emergency room.

‖Other swallowing problem types: choking sensation (n = 49 reports), pharyngeal injury (n = 11), foreign body aspiration (n = 7), esophageal obstruction (n = 4), esophageal injury (n = 3), foreign body (n = 2), oropharyngeal discomfort (n = 2), sensation of foreign body (n = 2), and aspiration (n = 1).

¶Other dietary supplement categories: bodybuilding, detoxification or cleansing, energy, laxative, microbial additive (probiotics); sexual enhancement; skin or hair health; sleep, sedation or anxiolysis and weight loss (2).

Table 2.

Pill Sizes of 10 Products Commonly Identified in Dietary Supplement Swallowing Problem Adverse Event Reports to FDA, 2006-2015 *

Dietary Supplement Product†	Dietary Supplement Reports Involving Swallowing Problems, n (n = 3962)	Proportional Reporting Ratio (PRR)	Pill Dimensions, mm		
			Length	Width	Height
Multivitamin, Older Females,‡ Product 1	1607	6.8	19.0	10.0	8.0
Multivitamin, Older Persons, Product 1	332	2.7	18.5	9.5	7.3
Multivitamin, Females, Product 1	188	3.2	21.5	9.0	7.8
Calcium Supplement, Product 1	185	3.9	21.0	11.0	8.5
Calcium Supplement, Product 2	161	3.9	20.5	10.0	7.5
Multivitamin, Females, Product 2	145	4.4	18.5	9.5	7.5
Multivitamin, Males, Product 1	138	3.6	19.0	8.5	7.0
Multivitamin, Older Females, Product 2	99	4.1	19.5	10.0	7.5
Multivitamin, Older Males, Product 1	86	2.7	19.5	10.0	7.0
Calcium Supplement, Product 3	85	2.4	20.0	9.8	7.0
All 10 products§	3026	12.7	19.3	9.8	7.8

mm = millimeter.

* Pill sizes were measured by photographing products purchased at a community U.S. pharmacy in 2016-2017 with an adjacent mm ruler using a Nikon 3200 camera secured in a rigid camera stand, magnifying the photographs and measuring dimensions to the nearest millimeter.

† Dietary supplement product description was based on product label.

‡ "Older" refers to ages 50 years and older.

§ Pill dimensions for all 10 products are weighted means.