Osmolality, pH, and Compatibility of Selected Oral Liquid Medications With an Enteral Nutrition Product

Mark Klang, MS, RPh, BCNSP, PhD¹; Veronica McLymont, PhD, RD¹; and Nicole Ng, PharmD¹



Journal of Parenteral and Enteral Nutrition Volume 37 Number 5 September 2013 689-694 © 2013 American Society for Parenteral and Enteral Nutrition DOI: 10.1177/0148607112471560 jpen.sagepub.com hosted at online.sagepub.com



Abstract

When selecting medication for feeding tube administration, the liquid formulation is selected, so as to avoid obstructions that may occur from incompletely crushing a solid dosage form. Liquid medications can present issues of intolerance and compatibility when administered via a feeding tube. A predictor of intolerance is the liquid's osmolarity, and a predicator of compatibility is the liquid's pH value. This study examines 62 liquid formulations for their osmolality, pH, and physical compatibility with enteral nutrition (EN) formulas. These medications were selected as being the most commonly dispensed liquid medications from our outpatient pharmacy department. This study measures osmolality using freezing point depression. Depending on the dose, the osmotic load of a liquid medication may cause cramping and diarrhea. The pH value is predictive of potential interactions with the EN formula. Many drugs are weak bases and require acidic vehicles for optimal stability. The acidic liquids are especially reactive with enteral formulas that contain intact proteins. The result of this interaction can result in an occlusion of the feeding tube as the proteins form a gel-like clog. This study combined the liquid medication directly with the EN formula to determine the potential for feeding tube occlusion. Some drugs formed a solid mass in the test tube immediately, whereas others only presented granules, which may later contribute to obstructing the feeding tube. The prescriber should be aware of the potential impact of their choice in formulation, both in terms of the gastrointestinal tolerance and potential for interaction with coadministered nutrition. (*JPEN J Parenter Enteral Nutr.* 2013;37:689-694)

Keywords

enteral nutrition; drug-nutrient interactions; enteral access

Clinical Relevancy Statement

This study examines 2 physiochemical properties of liquid medications: osmolality and pH. Since liquid medications are often used concurrently in patients requiring nutrition products through enteral feeding tubes, the study also looks at the compatibility of liquid medication with enteral nutrition. Osmolality of oral liquid medications has been linked to causing diarrhea in the feeding tube patient. The clinician can use the data collected here to calculate the appropriate dilution of the medication and improve patient outcome. The acidic pH of liquid medications has been linked to the formation of precipitates, when combined with enteral feeding formulas. The information presented here will alert the clinician to use appropriate flushing before and after drug administration to reduce the risk of obstructing feeding tubes.

Introduction

The patient who receives medications administered through a feeding tube will most likely have nutrition administered by the same route. Medications selected must be compatible with the mechanics of this route. The dosage should be an immediate-release formulation and free of properties that can obstruct the flow through the tube. Solid medication is replaced by a liquid formulation as it is assumed that the liquids would be better tolerated and have less potential obstructing the feeding tube. Some liquid medications are prone to forming obstructions in the feeding tubes when combined with enteral nutrition (EN).¹ It is important to recognize that when selecting a medication, none of the Food and Drug Administration (FDA)–approved liquid medications were designed for feeding tube administration. Liquid medication is designed for those who have difficulty swallowing solid dosage forms orally. Many of these liquids include sugars, flavoring agents, and excipients, which thicken and improve palatability.² Sugars such as sorbitol are often added to enhance solubility and palatability. Sorbitol is a more potent cathartic than lactulose and is responsible for osmotic diarrhea in tube-fed patients who receive their doses undiluted.³ In studies of patients who have contracted diarrhea while receiving EN, many of these cases were found to be caused by the excipients

Received for publication April 17, 2012; accepted for publication November 26, 2012.

This article originally published online on January 17, 2013.

Corresponding Author:

Mark Klang, MS, RPh, BCNSP, PhD, Core Manager, Research Pharmacy, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10065. Email: klangm@mskcc.org.

From the ¹Memorial Sloan-Kettering Cancer Center, New York, NewYork.

Financial disclosure: None declared.

found in the liquid formulations rather than an intolerance to the nutrition. 4,5

The cause of a feeding tube obstruction is dependent on numerous physical and chemical factors of the nutrient, the medication formulation, and the feeding tube being used.⁶ The most validated remedy to unclog a feeding tube is the use of pancreatic enzymes, along with sodium bicarbonate. This combination digests the clabber formed by protein reacting with the acidic gastric fluid.⁷ Based on that observation, it is not surprising that liquid medications formulated as acidic syrups would form an obstruction when in contact with a standard polymeric EN formula.¹ Unfortunately, there is a lack of information on compatibility of liquid medications with an EN product that assist in predicting the next feeding tube obstruction. It is necessary to evaluate each liquid medication individually as even generically equivalent products may have different excipients and formulation properties present.⁸

Since liquids are the preferred medication formulation selected for feeding tube administration,⁹ we decided to examine the most common liquid being dispensed at Memorial Sloan-Kettering Cancer Center. This study was conducted to evaluate the liquid medications being dispensed for pH and osmolality. We also examined if the combination of these liquid medications with the EN formula would result in a deposit sufficient to obstruct a feeding tube.

Methods

A total of 62 commercially available solutions and suspensions (ie, 58 liquid medications and 4 vehicles) were selected from the outpatient pharmacy formulary based on the high volume dispensed.

Osmolalities were measured in mOsm/kg using an osmometer (Osmette III, Natick, MA). This device calculates osmolality from a determination of freezing point depression.

For those medications in which the osmolality exceeded the osmometer capacity of 2000 mOsm/kg, the medication was diluted with sterile water for irrigation (1:5 dilutions). If the osmolality of the diluted sample was still greater than the osmometer capacity, a 1:10 dilution was made in the same manner. A 10- μ L sample was inserted into the device using the device pipette.

The osmometer was calibrated using osmometry reference standards of 100, 500, 1500, and 2000 mOsm/kg (Precision Systems, Natick, MA) at initiation and completion of tests.

The pH value was measured with a pH meter (AB-15, Accumet Basic; Fisher Scientific, Pittsburgh, PA). The pH meter was calibrated using reference buffers of values 4, 7, and 10 (Fisher, Fair Lawn, NJ). Each medication (5 mL in a centrifuge tube) was measured undiluted using the pH meter. The meter probe was rinsed with triple distilled deionized water between measurements.

Five milliliters of each medication, undiluted, was combined with 5 mL of EN formula (Osmolite 1.2; Abbott Nutrition, Abbott Park, IL) in a 10-mL centrifuge tube. This nutrition formula was selected since it is commonly used, is readily available, and consists of intact proteins that have been implicated in several feeding tube obstructions at our institution.

The 2 ingredients were vortexed for 1 minute and then placed for 1 hour inside an incubated shaker at 37°C at 200 rpm. This process was chosen as an attempt to mimic the contact of drug and nutrients if the products were not rinsed appropriately after administration. An attempt was made to pour the contents from the tube through a stem glass funnel (#6180-50, Pyrex; Corning, Corning, NY; 50 mm top diameter, 65 mm stem length, 6 mm internal stem diameter). The obstruction of the glass stem by gravity-flowing contents of the tube was recorded in Table 1 as a clog formation under the "Funnel" column. The stem of the glass funnel is 1.5 times the diameter of a 12 French feeding tube (4 mm). It was assumed that a clog that would obstruct the glass funnels would also obstruct the larger percutaneous endoscopic gastrostomy (PEG) feeding tubes (~20 French). The entire volume (10 mL) that passed through the glass funnel was then poured through a 100-micron nylon screen. Any solid substances found retained on the screen were noted as having a potential for obstructing a finebore feeding tube (~8 French) and noted under the "Screen" column.

Results

The osmolalities and pH measurements of the medications are listed in Table 1. Only 1 medication fell below the upper limit osmolar range of 500 mOsm/kg (guaifenesin solution).¹⁰ Seventeen products had osmolalities >5000 and 3 products produced osmolarity >10,000 with a maximum measured osmolality measurement of 16,100. In the products that required additional dilution, it was assumed that the actual osmolality would be related to a linear function of the dilution. This assumption yielded an underestimate of the actual osmolality of the undiluted product.

The pH measurements ranged from 2.39–9.77. Almost all liquid medications are somewhat acidic, with the exception of antacids and potassium iodide (SSKI). Adequate rinsing of the feeding tube is needed to minimize contact with EN formulas as these acidic fluids have a high potential to contribute to an occluded feeding tube.

Several of the acidic suspensions (pH <4.5) formed solid clogs when combined with enteral formula and could not be removed from the test tube, whereas others produced granules that were trapped by the screen. Not all the acidic liquids formed a precipitate in the test tube or in the screen.

Discussion

Generally, when pharmaceutical drug companies design the formulation of oral liquid medications, minimal consideration is

| | Product | Concentration | μd | Osmolality | / Funnel | Screen | Lot No. | Expiration, Month/Year | Manufacturer |
|--------|---|--------------------|------|-------------------|----------|--------|------------|---------------------------|--------------------------------|
| Liquid | medications | | | | | | | | |
| 1 | Acetaminophen solution | 325 mg/10.15 mL | 4.35 | 4035^{a} | Clog | Clog | 0F10 | 6/12 | PAI (Greenville, SC) |
| 2 | Acetaminophen suspension | 160 mg/5 mL | 4.68 | 6425 ^a | Clog | Clog | 100863 | 11/11 | Precision Dose (Beloit, IL) |
| З | Acyclovir oral suspension | 200 mg/5 mL | 5.8 | 4205 ^a | Passes | Clog | L009104 | 2/12 | Actavis (Morristown, NJ) |
| 4 | Aluminum hydroxide gel | 320 mg/5 mL | 7.21 | 1501 | Clog | Clog | 0B44 | 8/11 | PAI |
| 5 | Al(OH) ₃ , Mg(OH) ₂ , simethicone | 200 mg, 200 mg, 20 | 7.84 | 066 | Passes | Clog | JAN019 | 11/12 | GeriCare (Brooklyn, NY) |
| | N N | mg per 5 mL | | | | | | | |
| 9 | Aminocaproic acid (Amicar) solution | 0.25 g/mL | 6.15 | 3405^{a} | Passes | Passes | H090357A | 7/12 | Xanodyne (Newport, KY) |
| 7 | Atovaquone (Mepron) suspension | 750 mg/5 mL | 5.87 | 135 | Passes | Clog | 0D002 | 10/11 | GSK (Philadelphia, PA) |
| 8 | Azithromycin suspension | 200 mg/5 mL | 9.48 | 3950^{a} | Passes | Passes | MTYG1261 | 3/13 | Greenstone (North Peapack, NJ) |
| 6 | Calcitriol solution | 1 mcg/mL | 7.83 | ٩ | Clog | Clog | 958360A | 10/11 | Boehringer (Ridgefield, CT) |
| 10 | Calcium carbonate suspension | 1250 mg/5 mL | 9.16 | 2490^{a} | Passes | Passes | 059663A | 4/12 | Boehringer |
| 11 | Carbamazepine suspension | 100 mg/5 mL | 3.68 | 4225 ^a | Clog | Clog | 093677 | 2/11 | Taro (Hawthorne, NY) |
| 12 | Dexamethasone intensol | 1 mg/mL | 3.9 | $10,600^{\circ}$ | Clog | Clog | 060548A | 8/12 | Boehringer |
| 13 | Digoxin solution | 0.125 mg/2.5 mL | 6.46 | 5950^{a} | Passes | Passes | 956536C7 | 4/11 | Boehringer |
| 14 | Diphenhydramine HCl | 12.5 mg/5 mL | 3.94 | 3975 ^a | Passes | Passes | L063E10C | 5/12 | Qualitest (Huntsville, AL) |
| 15 | Docusate sodium liquid | 10 mg/10 mL | 6.51 | 6385 ^a | Passes | Passes | 0H21 | 8/12 | PAI |
| 16 | Ergocalciferol (Calciferol) solution | 400 IU/0.05 mL | 5.08 | $16,100^{\circ}$ | Passes | Passes | 00102 | 1/13 | Schwarz (Mequon, WI) |
| 17 | Escitalopram (Lexapro) solution | 5 mg/5 mL | 4.54 | 6030^{a} | Clog | Clog | 1076260 | 4/13 | Forest (St. Louis, MO) |
| 18 | Ferrous sulfate elixir | 220 mg/5 mL | 2.39 | 3445 ^a | Clog | Clog | 601645 | 6/12 | Hi-Tech (Norcross, GA) |
| 19 | Fluconazole suspension | 40 mg/mL | 4.29 | 2185^{a} | Clog | Clog | 0760902 | 5/13 | Greenstone |
| 20 | Furosemide solution | 40 mg/5 mL | 9.77 | 8975 ^a | Passes | Passes | 957332A | 6/12 | Boehringer |
| 21 | Gabapentin (Neurontin) solution | 250 mg/5 mL | 6.31 | 8275 ^a | Passes | Passes | OA9XR | 4/12 | Pfizer (New York, NY) |
| 22 | Guaifenesin solution | 200 mg/10 mL | 2.78 | 278 | Clog | Clog | OF39 | 12/11 | PAI |
| 23 | Guaifenesin DM (dextromethorphan/ | 20 mg/10 mL | 2.78 | 4270^{a} | Clog | Clog | 0083 | 4/12 | PAI |
| | guaifenesin) syrup |) | | |) |) | | | |
| 24 | Hydroxyzine HCl syrup | 10 mg/5 mL | 3.16 | 3540^{a} | Passes | Clog | 30460A | 6/12 | Morton Grove Pharmaceuticals |
| | | | | | | | | | (Morton Grove, IL) |
| 25 | Ibuprofen suspension | 100 mg/5 mL | 3.9 | 2350^{a} | Clog | Clog | L912050 | 12/11 | Actavis |
| 26 | Isoniazid solution | 50 mg/5 mL | 5.86 | 8850^{a} | Passes | Passes | 610152 | 6/12 | Carolina (Savannah, GA) |
| 27 | Lactulose solution | 10 g/15 mL | 4.85 | 4180^{a} | Passes | Passes | 610152 | 9/12 | Morton Grove Pharmaceuticals |
| 28 | Lamivudine (Epivir) solution | 10 mg/mL | 9 | 1460 | Passed | Passes | 0C002 | 3/12 | GSK |
| 29 | Levetiracetam solution | 100 mg/mL | 6.03 | 5075 ^a | Passes | Passes | 0595224 | 3/12 | Boehringer |
| 30 | Levofloxacin (Levaquin) solution | 25 mg/mL | 5.13 | 2115 ^a | Clog | Clog | AEB2V00 | 4/12 | Ortho-McNeil (Raritan, NJ) |
| 31 | Loperamide | 0.2 mg/mL | 4.02 | 6775^{a} | Clog | Clog | M101121-86 | 5/11 | Major (Livonia, MI) |
| 32 | Magnesium hydroxide suspension | 2400 mg/30 mL | 9.44 | 1258 | Passes | Clog | OJ14 | 9/12 | PAI |
| 33 | Megestrol acetate | 40 mg/mL | 4.37 | 3665^{a} | Passes | Clog | 22818401 | 10/13 | PAR (Spring Valley, NY) |
| 34 | Metoclopramide solution | 5 mg/5 mL | 2.74 | 5180° | Passes | Clog | 0C16 | 3/12 | PAI |
| 35 | Metoclopramide solution | 5 mg/5 mL | 2.83 | 4660° | Clog | Clog | 5943A | 4/12 | SilaRx (Spring Valley, NY) |
| 36 | Mineral oil | | 4.89 | ٩ | Passed | Clog | 0E20 | 5/12 | PAI |
| 37 | Multivitamin (Multi-Delyn) liquid | | 3.41 | 3655^{a} | Clog | Clog | 5802A | 12/11 | SilaRx |
| 38 | Neoral (Neo-Fradin) solution | 125 mg/5 mL | 5.76 | 4720^{a} | Clog | Clog | 801820 | 5/11 | X-GEN (Northport, NY) |
| | | | | | | | | | (continued) |

| 39 Ondarasetron solution 4 mg/s mL 3.73 2.95' Clog Clog 6011314 10.12 Bochringer 40 Oxentazpines regension 300 mg/s mL 4.97 Clog Clog 1017 3.13 Scheringer 3.13 Scheringerbundt 3.11 Scheringerbundt 3. | | Product | Concentration | Ηd | Osmolalit | y Funnel | Screen | Lot No. | Expiration, Month/Year | Manufacturer |
|---|---|--|------------------------------------|----------|-------------------|--------------|-----------|--------------------|---------------------------|----------------------------------|
| 40Oxeratbaceprine suspension300 mg/s mL3.041976ClogClog10375/13Standac (Princeton, N41Pherytorin suspension125 mg/s mL4.49309771/2Actavis41Porassium chloride solution10% SF (sugar free)3.294225*PassesPasses1160C10A4/12Qualitest45Porassium chloride solution10% SF (sugar free)3.294225*PassesPasses1106A4/12Qualitest46Prednisolone (Na, PQ) solution10% SF (sugar free)3.294225*PassesPasses107004/12Qualitest47Propranolol HCI solution10% SF (sugar free)3.294225*PassesPasses107004/12Qualitest48Ranitidine solution15 mg/mL6.88637PassesPasses107008/11Visua-Pharm (Birmin49Som SramSrund53320PassesPasses107008/11Visua-Pharm (Birmin40Sem syrupSSem syrup8.8 mg/s mL5.053320Passes107008/11Visua-Pharm (Birmin41Solution10% Srm4.452.56Passes109059/12MajorVisua-Pharm (Birmin42Sem syrupSSen state1.70ClogClog10/12Visua-Pharm (Birmin43Sinchinone (Infants' Drops)2.002.115.05Passes109059/12Major <trr<< td=""><td>39</td><td>Ondansetron solution</td><td>4 mg/5 mL</td><td>3.73</td><td>2935^a</td><td>Clog</td><td>Clog</td><td>0611314</td><td>10/12</td><td>Boehringer</td></trr<<> | 39 | Ondansetron solution | 4 mg/5 mL | 3.73 | 2935 ^a | Clog | Clog | 0611314 | 10/12 | Boehringer |
| 41Phenytoin suspension125 mg/s mL4.493095Passed Clog2097007/12Actavis42Possomazed (Noxafil) suspension200 mg/s mL4.52250°Passes1087NS78/13Schering-Plough (Ke43Potassium chloride solution10% SF (sugar free)3.25Passes1087NS78/13Schering-Plough (Ke46Prednisolone (Na, PO, solution10% SF (sugar free)3.2111,380°Clog209443/12Hi-Tech47Propranolol HC solution5 mg/s mL6.862395°Passes98876A1/12Buehringer48Ranitdine solution5 mg/s mL5.07PassesPasses98876A1/12Buehringer49Sema syrup8 mg/s mL5.07PassesPasses98876A1/12Buehringer50Sema syrup8 mg/s mL5.03330°Passes98876A1/12Major51Sinclinus (Rapamue) solution1 mg/mL6.882395°Passes98876A1/12Major53Sodium citrate, citric acid solution3 g2 gpe 30 mL4.452.56°PassesPasses9/12Major53Suchthoot citrate) suspension1 g10 nL3.32PassesPasses10/12Qualitest54Sodium citrate, citric acid solution3 g2 gpe 30 mL4.452.56°Passes10/12Qualitest55Suchthoot citrate) suspension1 g10 nL3 g2 gpe 30 mL3.32°10/12< | 40 | Oxcarbazepine suspension | 300 mg/5 mL | 3.04 | 1976 | Clog | Clog | H0137 | 5/13 | Sandoz (Princeton, NJ) |
| 42Posaconazole (Noxafil) suspension200 mg/5 mL 4.32 200° PassesPassesRes8/13Schering-Plough (Ke44Potasium oblorde solution1 wL 0% ST (sugar free) 3.29 42.5° Passes 8123 Schering-Plough (Ke45Produsion oblorde solution1 wL 3.44 8145° Passes 81424 612 Upsher-Sinit (Maple47Propratolol HCI solution5 $mg/5$ mL 5.84 537 Passes 81424 512 Upsher-Sinit (Maple48Ranidine solution5 $mg/5$ mL 5.88 537 Passes 81424 512 Upsher-Sinit (Maple49Sema syrup18 mg/mL 6.88 537 Passes 81436 912 Major50Sema syrup88 $mg/5$ mL 5.0397 PassesPasses 910005 912 Major51Solium citrate.88 $mg/5$ mL 5.53 PassesPasses 910005 912 Major53Solium citrate. $3g/2$ gper 30 mL 4.48 170 ClogClog 10012 Qualitest53Solium citrate. $3g/2$ gper 30 mL $3g/2$ PassesPasses 910005 912 Major54Solium citrate. $3g/2$ gper 30 mL $3g/2$ Passes 10005 912 Major55Sucriftate (Stration suspension $1 g/0$ mL $3g/2$ Passes 10005 912 Major55Sucriftate (Carafio) suspension $1 g/0$ | 41 | Phenytoin suspension | 125 mg/5 mL | 4.49 | 3095^{a} | Passed | Clog | 209700 | 7/12 | Actavis |
| 44Potassium chloride solution10% SF (sugar free)3.294.225PasesPasesL160C10A4.12Qualitest45Predassium iodide (SKR) solution1 g/mL9.2111,380°Clog2814246/12Upsher-Smith (Maple46Prednisolner (Na PO5 mg/mL5 mg/s mL6.88637PasesPases5876.6A1/12Boehringer48Ranitidine solution15 mg/mL6.88637PasesPases500059/12Major50Sema concentrate8.8 mg/s mL5.053300°PasesPases100059/12Major50Sema syrup8.8 mg/s mL5.053300°PasesPases10012Qualitest51Sinothione (Infanis' Drops)2.0 mg/0.3 mL5.053300°Pases10012Major53Sodium polystyrene sulfomate15 g/0.01.14.452563°Pases10014210/12Carolina53Sodium fitzet, citric acid solution3 g/2 g per 30 mL4.452563°Pases10014210/12Carolina54Sodium polystyrene sulfomate15 g/00 mL7.892733°PasesPases10/12Carolina55Sucraftate (Carefic suspension1 g/10 mL5.36PasesPases10/12Carolina55Sucraftate (Carefic suspension1 g/10 mL7.892733°Pases10/12Carolina56Suttimethoxazole-trimethoprim20 mg/40 mg per <t< td=""><td>42</td><td>Posaconazole (Noxafil) suspension</td><td>200 mg/5 mL</td><td>4.52</td><td>2050^{a}</td><td>Passes</td><td>Passes</td><td>I0PSN87</td><td>8/13</td><td>Schering-Plough (Kenilworth, NJ)</td></t<> | 42 | Posaconazole (Noxafil) suspension | 200 mg/5 mL | 4.52 | 2050^{a} | Passes | Passes | I0PSN87 | 8/13 | Schering-Plough (Kenilworth, NJ) |
| 45Potassium iodide (SSK1) solution1 g/mL9.2111,380°Clog2814246/12Upsher-Smith (Maple46Predinisolore (Na, PO), solution5 mg/s mL6.886.3395°Passes8.886.9443/12Hi-Tech47Propranolol HCI solution1 mg/s mL6.886.3390°Passes8.886.912Major48Ranitdine solution15 mg/nL6.886.3390°Passes8.886.912Major49Sema concentrate8.8 mg/s mL5.053390°PassesPasses9.12Major50Sema syrup8.8 mg/s mL5.333390°Passes100059/12Major51Seina syrup8.8 mg/s mL5.33330°Passes100160/11Wajor53Solutim polystyrene sulfonate15 g/60 mL7.482565°Passes10014210/12Qualitest53Solutim polystyrene sulfonate15 g/60 mL7.492575°PassesPasses112/12Qualitest54Sulfiamethoxazole-trimethoprim3 g/2 g per 30 mL4.452565°Passes1014210/12Canolina55Sulfiamethoxazole-trimethoprim5 g/60 mL7.892755°PassesPasses113/1010/12Canolina56Sulfiamethoxazole-trimethoprim5 g/60 mL7.492755°Passes113/12Qualitest56Sulfiamethoxazole-trimethoprim5 g/60 mL7.492755°Passes | 44 | Potassium chloride solution | 10% SF (sugar free) | 3.29 | 4225 ^a | Passes | Passes | L160C10A | 4/12 | Qualitest |
| 46Prednisolone (Na, PO ₄) solution5 mg/5 mL6.862395Passes< | 45 | Potassium iodide (SSKI) solution | 1 g/mL | 9.21 | $11,380^{\circ}$ | Clog | Clog | 281424 | 6/12 | Upsher-Smith (Maple Grove, MN) |
| 47Propranolol HCl solution20 mg/5 mL 3.44 8145° PassesPasses 58876 $1/12$ Boehringer48Ranitidine solution15 mg/mL 6.88 637 PassesPasses 210700 8111 Visa-Pharm (Birmin49Semna concentrate $8.8 mg/5 mL$ 5.05 3390° PassesPasses 9120 Major50Senna syrup8.8 mg/5 mL 5.3 3920° PassesPasses 912 Major51Simethicone (Infans' Drops)20 mg/0 3 mL 4.35 2.365° PassesPasses 912 Major53Sodium oritrate, citric acid solution $3 g/2$ g per 30 mL 5.36 Passes 10905 $9/12$ Major53Sodium oritrate, citric acid solution $3 g/2$ g per 30 mL 5.36° PassesPasses 109104 $10/12$ Qualitest54Sodium polystyrene sulfonate $15 g/60$ mL 7.89 2735° PassesPasses 101042 $10/12$ Qualitest55Surelatiato $10 g/10$ mL 3.54 2145° PassesPasses 101042 $10/12$ Qrotina56Sulfamethoxazole-trimethoprim $10 g/10$ mL 3.556° PassesPasses 101042 $10/12$ Qrotina57Valproic acid (Depakene) solution $200 mg/5$ mL 2.556° Passes 10905 $1/11$ Picpethick58Voriconazole (Viend) suspension $10 g/10$ mL 3.54 2145° | 46 | Prednisolone (Na_3PO_3) solution | 5 mg/5 mL | 6.86 | 2395^{a} | Passes | Passes | 604944 | 3/12 | Hi-Tech |
| 48 Ranitidine solution 15 mg/mL 6.88 6.37 Passes Passes 210005 9/12 Major 49 Sema concentrate 8.8 mg/5 mL 5.05 3390° Passes Passes 9/12 Major 50 Sema concentrate 8.8 mg/5 mL 5.05 3390° Passes Passes 10005 9/12 Major 51 Sinethicone (Infants' Drops) 20 mg/0.3 mL 4.85 170 Clog Clog Clog 108110A 10/12 Qualitiest 53 Sodium citrate, citric acid solution 3 g/2 gper 30 mL 4.45 2565° Passes Pass Pass Pass Pass Passes Pass Pass Passes Passes Pass Pass Pas | 47 | Propranolol HCl solution | 20 mg/5 mL | 3.44 | 8145 ^a | Passes | Passes | 958876A | 1/12 | Boehringer |
| 49 Sema concentrate 8.8 mg/s mL 5.05 3390 ^a Passes Passes Passes 9.12 Major 50 Sema syrup 8.8 mg/s mL 5.2 3920 ^a Passes Passes 9.12 Major 51 Simichicone (Infants' Drops) 20 mg/0.3 mL 4.88 170 Clog Clog Clog 109112 Qualitiest 53 Sodium citrate, citric acid solution 3 g/2 g per 30 mL 4.45 2.553 ^a Passes Passes 100142 10/12 Qualitiest 54 Solium polysityme sulfonate 1 g/10 mL 3.54 2145 ^a Passes Passes 100142 10/12 Qualitiest 55 Sucritipes uspension 1 g/10 mL 3.54 2145 ^a Passes Passes 813 Wyeth (Madison, NJ 56 Sulfamethoxazole-trimethoprim 200 mg/40 mg per 5.39 5560 ^c Passes Passes 813 Hio:Tech 57 Valproic acid (Depakene) solution 1 g/10 mL 3.54 2145 ^a Passes 2103 9/12 Hiott (Abbott Park 58 Voric | 48 | Ranitidine solution | 15 mg/mL | 6.88 | 637 | Passes | Passes | 210700 | 8/11 | Vista-Pharm (Birmingham, AL) |
| 50Sema syrup Simetricone (Infants' Drops) $8.8 \text{ mg/5} \text{ mL}$ 5.2 3920^{a} PassesPasses100059/12Major51Simethicone (Infants' Drops) $20 \text{ mg/0.3} \text{ mL}$ 4.88 170 $Clog$ $Clog$ $L08110A$ $10/12$ Qualitest52Sinimus (Rapamune) solution 1 mg/mL 5.36 $-^{\text{b}}$ $Clog$ Cl | 49 | Senna concentrate | 8.8 mg/5 mL | 5.05 | 3390^{a} | Passes | Passes | 100905 | 9/12 | Major |
| 51Simethicone (Infants' Drops)20 mg/0.3 mL4.88170ClogClogL08110.A10/12Qualitest52Sirolimus (Rapamune) solution1 mg/mL5.36 $-^{b}$ ClogClogCMM12/11Wyeth (Madison, NJ)53Sodium citrate, citric acid solution3 g/2 g per 30 mL4.452365 ^a PassesPasses91014210/12Qualitest54Sodium polystyrene sulfonate1 g/10 mL3,542145 ^a PassesPasses10114210/12Carolina55Sucralfate (Carafate) suspension1 g/10 mL3,542145 ^a PassesPasses10114210/12Carolina56Sulfamethoxazole-trimethoprim200 mg/40 mg per5.595560 ^e PassesPasses8/13Myeth57Valproic acid (Depakene) solution250 mg/5 mL2.55510 ^e Passes8/131/13Abbott Park,58Voriconazole (Vfend) suspension40 mg/mL4.192010 ^a Passes703991/11Pitzer/Roerig (New)60Orar Plus5 mL4.192010 ^a PassesClog50961411/11Paddock (Minneapol61Ora Swet61Ora Swet4.234.20 ^a PassesPasses2/9756/11/11Paddock (Minneapol62Syr Spend SF56165 ^a ClogClog5/9952411/11Paddock11/12Paddock60Ora Plus0.73 Syr Spend SF2.756165 ^a </td <td>50</td> <td>Senna syrup</td> <td>8.8 mg/5 mL</td> <td>5.2</td> <td>3920^{a}</td> <td>Passes</td> <td>Passes</td> <td>100905</td> <td>9/12</td> <td>Major</td> | 50 | Senna syrup | 8.8 mg/5 mL | 5.2 | 3920^{a} | Passes | Passes | 100905 | 9/12 | Major |
| 52Sirolimus (Rapamune) solution1 mg/mL 5.36 $-^{b}$ ClogClogClogClogClogS/13PAI53Sodium citrate, citric acid solution $3 g/2$ g per 30 mL 4.45 2563^{a} PassesPasses 676 $5/13$ PAI54Sodium polystyrene sulfonate $15 g/60$ mL 7.89 2735^{a} PassesPasses 101042 $10/12$ Carolina55Sucralitate (Caratate) suspension $1 g/10$ mL 3.54 2145^{a} Passes 1133627 $8/13$ Wyeth56Sulfamethoxazole-trimethoprim 200 mg/40 mg per 5.59 5560^{c} Passes 101042 $10/12$ Carolina57Valproic acid (Depakene) solution 230 mg/40 mg per 5.59 5560^{c} Passes 6102 07399 $1/11$ Piticeh57Valproic acid (Depakene) solution 230 mg/40 mg per 5.59 5500^{c} Passes 6102 07399 $1/11$ Piticeh57Valproic acid (Depakene) solution 230 mg/5 mL 2.56 5010^{c} Passes 6102 07399 $1/11$ Piticeh58Voriconazole (Viend) suspension40 mg/mL 4.19 2010^{a} Passes 6102 07399 $1/11$ Piticeh60Ora Plus0Ora Plus 610^{c} Ora 209^{c} Passes 209^{c} 999524 $11/11$ Paddock (Minneapol61Ora Sweet 4.24 34 Passes 610^{c} 609 | 51 | Simethicone (Infants' Drops) | 20 mg/0.3 mL | 4.88 | 170 | Clog | Clog | L108J10A | 10/12 | Qualitest |
| 53Sodium citrate, citric acid solution $3 g/2 g \text{ per } 3 \text{ mL}$ 4.45 256^3 PassesPassesPasses $5/13$ PAI54Sodium polystyrene sulfonate $15 g/60 \text{ mL}$ 7.89 2735^3 PassesPasses $5/13$ PAI55Sucralfate (Carafate) suspension $1 g/10 \text{ mL}$ 3.54 2145^3 PassesPasses $8/13$ Wyeth56Sulfamethoxazole-trimethoprim $200 \text{ mg/40} \text{ mg per}$ 5.59 5560° Passes 200 secs $8/12$ Hi-Tech57Valproic acid (Depakene) solution $250 \text{ mg/40} \text{ mg per}$ 5.56 5010° Passes $84018WJ$ $1/13$ Abbott (Abbott Park,58Voriconazole (Vfend) suspension 40 mg/mL 2.56 5010° Passes $84018WJ$ $1/13$ Pifzer/Rocrig (New N58Voriconazole (Vfend) suspension 40 mg/mL 2.56 5010° Passes $84018WJ$ $1/13$ Pifzer/Rocrig (New N58Voriconazole (Vfend) suspension 40 mg/mL 2.75 616° 07399 $1/11$ Pifzer/Rocrig (New N59Cherry syrup $82\% w/v$ 2.75 616° 003 9499524 $11/11$ Paddock (Minneapol60Ora PlusOra Plus 4.31 164 $Clog$ $Clog$ 9499524 $11/11$ Paddock (Minneapol61Ora Sweet 4.27 4.20° Passes 200614 $2/17$ $2/07$ Gallipot (St Paul, MI62Syr Spen | 52 | Sirolimus (Rapamune) solution | 1 mg/mL | 5.36 | ٩ | Clog | Clog | CMM | 12/11 | Wyeth (Madison, NJ) |
| 54Sodium polystyrene sulfonate15 g/60 mL7.892735°PassesPassesPasses10/12Carolina55Suralfate (Carafate) suspension1 g/10 mL 3.54 $2145°$ PassesPassesPasses10/12Carolina56Sulfamethoxazole-trimethoprim200 mg/40 mg per 5.59 $5560°$ PassesClog602492 $8/12$ Hi-Tech57Valproic acid (Depakene) solution 250 mg/40 mg per 5.59 $5560°$ PassesPassesR4018WJ1/11Phicthorach57Valproic acid (Depakene) solution 250 mg/5 mL 2.56 $5010°$ PassesPassesR4018WJ1/11Pfizer/Roerig (New Y58Voriconazole (Vfend) suspension40 mg/mL 4.19 $2010°$ PassesPassesR4018WJ1/11Pfizer/Roerig (New Y58Voriconazole (Vfend) suspension40 mg/mL 4.19 $2010°$ PassesR4018WJ1/11Pfizer/Roerig (New Y59Cherry syrup61Ora Plus82% w/v 2.75 $6163°$ ClogClog5328219/12Humco (Texarcana, 160Ora Plus0Ora Plus61Ora Sweet 4.27 $4.20°$ PassesPasses949952411/11Paddock (Minneapol61Ora Sweet 4.24 3.4 PassesClog050961411/12Paddock (Minneapol62Syr Spend SFOra Plus 4.24 3.4 Passes2/07Gallipot (St Paul, MC | 53 | Sodium citrate, citric acid solution | 3 g/2 g per 30 mL | 4.45 | 2565^{a} | Passes | Passes | 0E76 | 5/13 | PAI |
| 55Sucraffate (Carafate) suspension1 g/10 mL 3.54 2145^a PassesPassesRes11336278/13Wyeth56Sulfamethoxazole-trimethoprim $200 \mathrm{mg}/40 \mathrm{mg} \mathrm{per}$ 5.59 5560^c Passes $Clog$ 602492 $8/12$ Hi-Tech57Valproic acid (Depakene) solution $250 \mathrm{mg}/5 \mathrm{mL}$ 2.56 5010^c PassesPasses $84018 \mathrm{WJ}$ $1/13$ Abbott (Abbott Park,58Voriconazole (Vfend) suspension $40 \mathrm{mg/mL}$ 4.19 2010^a Passes $Clog$ 07399 $1/11$ Pffzer/Roerig (New Y59Cherry syrup $610 \mathrm{ora} \mathrm{Pus}$ $07399 \mathrm{mL}$ $1/11$ Pffzer/Roerig (New Y50Ona Plus $82\% \mathrm{w/v}$ 2.75 $6165^a \mathrm{Clog}$ $Clog$ $610 \mathrm{g}$ $9499524 \mathrm{m1}/111$ Padock (Minneapol61Ora SweetOra Sweet $4.24 34 \mathrm{Passes}$ Passes $9509614 \mathrm{m1}/111$ Paddock62Syr Spend SF $4.24 34 \mathrm{Passes}$ Clog $0601254 2/07 \mathrm{Gallipot}(St Paul, M)$ *Results calculated based on 1:5 dilution with sterile water.*Nonolative exceeded capacity of comometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 54 | Sodium polystyrene sulfonate | 15 g/60 mL | 7.89 | 2735^{a} | Passes | Passes | 1010142 | 10/12 | Carolina |
| 56Sulfamethoxazole-trimethoprim200 mg/40 mg per5.595560°PassesClog6024928/12Hi-Tech5 mL5 mL5 mL5 mL100°Passes84018WJ1/13Abbott (Abbott Park,58Voriconazole (Vfend) suspension40 mg/mL4.19 2010^a PassesRasses84018WJ1/11Pfrizer/Roerig (New Y58Voriconazole (Vfend) suspension40 mg/mL4.19 2010^a PassesClog073991/11Pfrizer/Roerig (New Y59Cherry syrup82% w/v 2.75 6165^a ClogClog5328219/12Humco (Texarcana, T60Ora Plus0.730911/11Paddock (Minneapol61Ora Sweet4.214.2434Passes20961411/11Paddock (Minneapol62Syr Spend SF5.976.000.012542/07Gallipot (St Paul, MI ^a Results calculated based on 1:5 dilution with sterile water.4.2434Passes6.0006012542/07Gallipot (St Paul, MI ^b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution.6.006.006.006.006.00 | 55 | Sucralfate (Carafate) suspension | 1 g/10 mL | 3.54 | 2145^{a} | Passes | Passes | 1133627 | 8/13 | Wyeth |
| 57Valproic acid (Depakene) solution250 mg/5 mL2.565010°PassesPasses84018WJ1/13Abbott (Abbott Park,58Voriconazole (Vfend) suspension40 mg/mL4.192010°PassesClog073991/11Pfizer/Roerig (New Y59Cherry syrup82% w/v2.756165°ClogClog5328219/12Humco (Texarcana, T60Ora Plus0.73 Wet4.31164ClogClog94952411/11Paddock (Minneapol61Ora Sweet4.274200°PassesPasses950961411/12Paddock62Syr Spend SF4.2434PassesClog06012542/07Gallipot (St Paul, M) ^a Results calculated based on 1:5 dilution with sterile water.bOsmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 56 | Sulfamethoxazole-trimethoprim | 200 mg/40 mg per 5 mL | 5.59 | 5560° | Passes | Clog | 602492 | 8/12 | Hi-Tech |
| 57 varprote actor (Deparence) solution 2.00 mg/s mg/s 2.00 mg/s mg/s 2.00 mg/s mg/s 2.00 mg/s mg/s $1/11$ Pfizer/Roerig (New Y58Voriconazole (Vfend) suspension40 mg/mL 4.19 2010^a Passes 0.02 0.7399 $1/11$ Pfizer/Roerig (New Y59Cherry syrup82% w/v 2.75 6165^a $Clog$ $Clog$ 532821 $9/12$ Humco (Texarcana, T60Ora Plus0.73 yest 9.99524 $11/11$ Paddock (Minneapol61Ora Sweet 4.27 4200^a Passes 9499524 $11/11$ Paddock62Syr Spend SF 4.24 34 Passes 9609614 $11/12$ Paddock ^a Results calculated based on 1:5 dilution with sterile water. 4.24 34 Passes $2/07$ Gallipot (St Paul, MI ^b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 5 | Welminic and (Danelsone) coluction | <u>1 2/2 5</u> | 73 0 | 50100 | Daggag | Deccar | 04010111 | 61/1 | Abbott (Abbott Douls II) |
| 58 Vorticonazote (Vtend) suspension 40 mg/mL 4.19 2010 Passes Clog 0/399 1/11 Prizer/Koerrg (New Netrols) 76 Cherry syrup 82% w/v 2.75 6165 ^a Clog Clog 532821 9/12 Humco (Texarcana, Texarcana, | 10 | | | 00.7 | 0100 | r asses | L'asses | 04010 W J | C1/1 | AUUUU (AUUUU FAIK, IL) |
| Vehicles59Cherry syrup82% w/v2.756165ªClog5328219/12Humco (Texarcana, T59Cherry syrup4.31164Clog5328219/12Humco (Texarcana, T60Ora Plus4.31164Clog9952411/11Paddock (Minneapol61Ora Sweet4.274200ªPassesPasses950961411/12Paddock62Syr Spend SF4.2434Passes06012542/07Gallipot (St Paul, MI ^a Results calculated based on 1:5 dilution with sterile water. ^b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 58 | Voriconazole (Vtend) suspension | 40 mg/mL | 4.19 | 2010" | Passes | Clog | 07399 | 1/11 | Pfizer/Roerig (New York, NY) |
| 59Cherry syrup82% w/v2.756165aClogClog5328219/12Humco (Texarcana, T60Ora Plus4.31164Clog949952411/11Paddock (Minneapol61Ora Sweet4.274200aPassesPasses949952411/11Paddock (Minneapol62Syr Spend SF4.2434Passes06012542/07Gallipot (St Paul, MIa Results calculated based on 1:5 dilution with sterile water.b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | Vehicl | SS | | | | | | | | |
| 60 Ora Plus 4.31 164 Clog 9499524 11/11 Paddock (Minneapoli 61 Ora Sweet 4.27 4200 ^a Passes Passes 9509614 11/12 Paddock 62 Syr Spend SF 4.24 34 Passes Clog 0601254 2/07 Gallipot (St Paul, MI ^a Results calculated based on 1:5 dilution with sterile water. ^b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 59 | Cherry syrup | 82% w/v | 2.75 | 6165^{a} | Clog | Clog | 532821 | 9/12 | Humco (Texarcana, TX) |
| 61 Ora Sweet 4.27 4200 ^a Passes 9509614 11/12 Paddock 62 Syr Spend SF 4.24 34 Passes Clog 0601254 2/07 Gallipot (St Paul, Mr ^a Results calculated based on 1:5 dilution with sterile water. ^b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 60 | Ora Plus | | 4.31 | 164 | Clog | Clog | 9499524 | 11/11 | Paddock (Minneapolis, MN) |
| 62Syr Spend SF4.243.4PassesClog06012542/07Gallipot (St Paul, MD*Results calculated based on 1.5 dilution with sterile water.*Dosmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 61 | Ora Sweet | | 4.27 | 4200^{a} | Passes | Passes | 9509614 | 11/12 | Paddock |
| ^a Results calculated based on 1:5 dilution with sterile water. ^b Osmolality exceeded capacity of osmometer (2000 mOsm/kg) and product was immiscible with sterile water, thereby preventing further dilution. | 62 | Syr Spend SF | | 4.24 | 34 | Passes | Clog | 0601254 | 2/07 | Gallipot (St Paul, MN) |
| ^c Results calculated based on 1.10 dilution with starila water | ^a Results ^b Osmoli ^c Results | i calculated based on 1:5 dilution with sterile wa ality exceeded capacity of osmometer (2000 mC calculated based on 1:10 dilution with sterile wa | ter. sm/kg) and product was imm | niscible | with sterile v | vater, there | by preven | ting further dilut | ion. | |

Table 1. (continued)

 $\frac{\text{mOsm of Medication}}{\text{Desired mOsm}} \times \text{Volume of dose} = \text{Final diluted Volume}$

Figure 1. Calculation of final diluted volume.

given to its use through an enteral feeding tube. This is clearly evidenced by the hypertonic values recorded throughout the study; some products (eg, dexamethasone, ergocalciferol, furosemide, gabapentin, isoniazid, and potassium iodide) had values even greater than 25 times the osmolar range of the gastrointestinal (GI) tract (127–357 mOsm/kg).² Normally, the osmolality is not a concern because the medication is intended to be taken orally—through which saliva, mucous, and gastric juices act to dilute and buffer the medication to a safe pH and osmolar range when it arrives in the duodenum.¹¹ This is important because the small intestine is exceptionally sensitive to hypertonic solutions and osmolar loads.¹² As a result, administration of hypertonic substances directly into the duodenum or jejunum may result in significant GI intolerance such as osmotic diarrhea. This intolerance may be mistakenly attributed to the feeding formula.⁵

Pharmacists can adjust the osmolarity of a liquid medication by dilution with purified water, just prior to administration. The attached formula may be used to calculate the volume of water that must be added to bring the solution to the optimal osmolarity.¹³ The desired osmolarity for gastric administration should be <700 mOsm, since there is usually adequate residual volume in the stomach to reduce the shift in pressure. However, the goal for jejunal administration should be <300 mOsm as there is less residual volume in the stomach to reduce the shift in reduce the stress of a higher osmolar load (see Figure 1).

Some of the liquid medications with a pH range below 4 (eg, diphenhydramine, sucralfate, and valproic acid) did not produce any precipitate when combined with the EN product. This observation demonstrates that obstruction of a feeding tube due to the interactions of liquid medication and nutrition products is not solely dependent on the pH of the medication. Osmolality and the formulation tested (elixir, solution, or suspension) did not have any relationship to the occurrence of precipitate formation. Nutrition formulas contain ingredients that can contribute to clog formation. The protein component, such as caseinate or whey, will precipitate when exposed to acidic solutions and contribute to an obstruction.¹⁴⁻¹⁶ The higher protein concentration of the Osmolite 1.2 used in this study may yield a higher potential for clog formation than a formula containing a lower concentration of protein. Other causes have been speculated upon for obstruction formation factors, such as soap formation, viscosity of ingredients, and reactions with other excipients. These issues demonstrate the myriad possible causes for a feeding tube to clog. It is important to consider all potential issues when selecting an appropriate agent to prevent clogging the feeding tube.

In some cases, a clog was formed immediately in the test tube and could not be poured through a glass funnel. This reaction occurred with ferrous sulfate elixir, Guaifenesin DM (dextromethorphan/guaifenesin), and loperamide. Based on this, it is anticipated that such a fast reaction would also occur from the direct contact of this drug with nutrition formula within a feeding tube. In other cases, precipitate was noted when particles accumulated on the 100- μ m nylon screen. These precipitates may contribute to clog formation if the tube is not adequately rinsed.

When preparing a medication for enteral tube use, the volume of medication should also be considered. For medications that require a small dosage volume, the effects of the hyperosmolality may be less pronounced.

Conclusion

Most of the oral liquid medications studied were hyperosmolar and prone to forming precipitates. The results gathered can help shed light on the need for proper administration of hyperosmotic medications to reduce the incidence of GI adverse effects and feeding tube clogs. This study also demonstrates the need for more EN compatibility studies with medications, as there is little predictability with these combinations.

The reader should review the EN practice recommendations from the American Society for Enteral and Parenteral Nutrition for more information and recommendations on drug administration through feeding tubes.¹⁹

References

- Cutie AJ, Altman E, Lenkel L. Compatibility of enteral products with commonly employed drug additives. *JPEN J Parenter Enteral Nutr.* 1983; 7(2):186-191.
- Dickerson RN, Melnik G. Osmolality of oral drug solutions and suspensions. Am J Hosp Pharm. 1988;45(4):832-834.
- Eherer AJ, Fordtran JS. Fecal osmotic gap and pH in experimental diarrhea of various causes. *Gastroenterology*. 1992;103(2):545-551.
- Edes TE, Walk BE, Austin JL. Diarrhea in tube-fed patients: feeding formula not necessarily the cause. Am J Med. 1990;88(2):91-93.
- Hill DB, Henderson LM, McClain CJ. Osmotic diarrhea induced by sugar-free theophylline solution in critically ill patients. *JPEN J Parenter Enteral Nutr.* 1991;15(3):332-336.
- Gaither KA, Tarasevich BJ, Goheen SC. Modification of polyurethane to reduce occlusion of enteral feeding tubes. *J Biomed Mater Res B Appl Biomater*. 2009;91(1):135-142.
- Marcuard SP, Perkins AM. Clogging of feeding tubes. JPEN J Parenter Enteral Nutr. 1988;12(4):403-405.
- El-Chaar GM, Mardy G, Wehlou K, Rubin LG. Randomized, double blind comparison of brand and generic antibiotic suspensions, II: a study of taste and compliance in children. *Pediatr Infect Dis J.* 1996;15(1):18-22.
- Gora ML, Tschampel MM, Visconti JA. Considerations of drug therapy in patients receiving enteral nutrition. *Nutr Clin Pract.* 1989;4(3):105-110.
- 10. Niemiec PW Jr, Vanderveen TW, Morrison JI, Hohenwarter MW. Gastrointestinal disorders caused by medication and electrolyte solution

osmolality during enteral nutrition. JPEN J Parenter Enteral Nutr. 1983;7(4):387-389.

- Dawes C, Wood CM. The contribution of oral minor mucous gland secretions to the volume of whole saliva in man. *Arch Oral Biol.* 1973;18(3): 337-342.
- Ladas SD, Isaacs PE, Quereshi Y, Sladen G. Role of the small intestine in postvagotomy diarrhea. *Gastroenterology*. 1983;85(5):1088-1093.
- Estoup M. Approaches and limitations of medication delivery in patients with enteral feeding tubes. *Crit Care Nurse*. 1994;14(1):68-72, 77-79; quiz 80-81.
- Nicholson LJ. Declogging small-bore feeding tubes. JPEN J Parenter Enteral Nutr. 1987;11(6):594-597.

- Hofstetter J, Allen LV Jr. Causes of non-medication-induced nasogastric tube occlusion. Am J Hosp Pharm. 1992;49(3):603-607.
- Frankel EH, Enow NB, Jackson KC, II, Kloiber LL. Methods of restoring patency to occluded feeding tubes. *Nutr Clin Pract.* 1998;13(3):129-131.
- Mateo MA. Nursing management of enteral tube feedings. *Heart Lung*. 1996;25(4):318-323.
- Klang M. Recommendations for compounding medications for feeding tube administration. Int J Pharm Cmpd. 2010;14(4):276-282.
- Bankhead R, Boullata J, Brantley S, et al. Enteral nutrition practice recommendations. *JPEN J Parenter Enteral Nutr.* 2009;33(2):122-167.