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Pharmacology and Swallowing

Angela Mansolillo, MA, CCC-SLP, BCS-S

Moderated by:
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Pharmacology and Swallowing

Angela Mansolillo, MA, CCC-SLP, BCS-S

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Objectives

- Explain concepts of pharmacokinetics and pharmacodynamics as they impact people with dysphagia.
- Describe medication effects and side effects and their impact on swallow function.
- Identify strategies to reduce medication errors for people with dysphagia.

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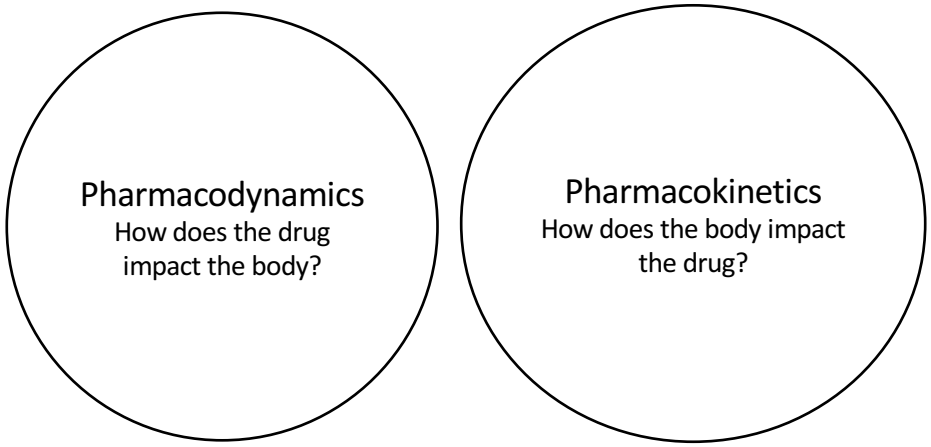
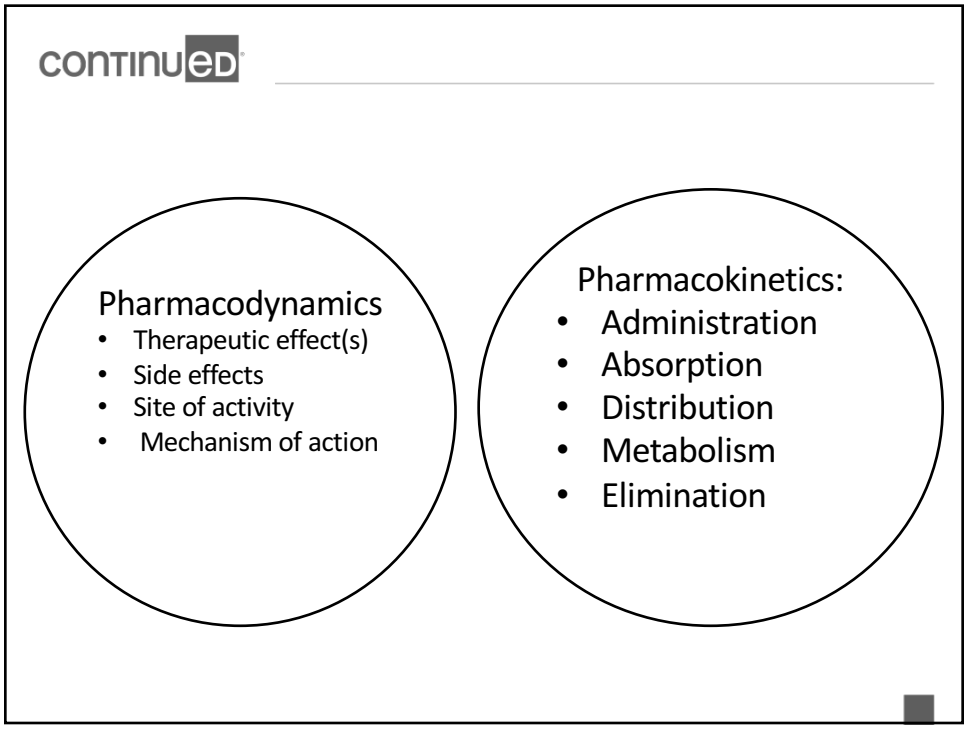
Pharmacology





Medications and Aging

As we age:

- More prescribed medications
- Higher likelihood of esophageal dysmotility at baseline
- Decreased saliva production at baseline
- Altered absorption and metabolism of medications
- Neurotransmitters may become less balanced as we age

CONTINUED

Medications and Aging

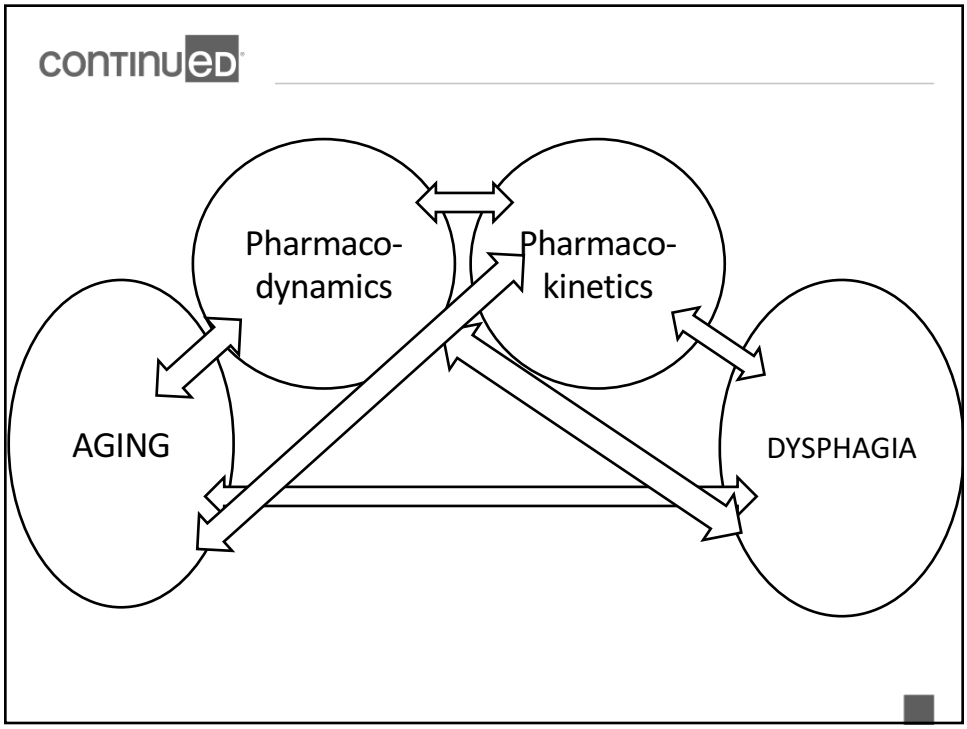
So…

- Increased drug sensitivity
- Medications metabolized more slowly
- Higher likelihood of side effects
- Increased risk of drug-induced delirium

CONTINUED

And…

- **What about Dysphagia?**
- Difficulties with pill swallowing
- Increased aspiration/choking risk when taking medications
- Increased susceptibility to swallow-related side effects
- Thickeners/Foods potentially impact absorption of drugs



Pharmacokinetics

- ***(Administration*** – Drug enters the body)
- ***Absorption*** – Drug moves into/through the bloodstream
- ***Distribution*** – Drug is transported to target site(s)
- ***Metabolism*** – Drug is chemically altered
- ***Elimination*** – Drug is eliminated from the body

CONTINUED

Administration

- Manner by which the drug enters the body:
  - Topical
  - Sublingual
  - Transdermal
  - Rectal
  - Inhalation
  - Intravenous
  - Subcutaneous
  - Intrathecal

And of course…

  - Oral

CONTINUED

Administration

- *10-44% of general population* report difficulty swallowing pills – in the absence of other swallowing problems (Carnaby-Mann et al, 2005; Marquis et al, 2013; Schiele, et al, 2013)
- *14% of patients with PD* report difficulty with pills (Walker, et al, 2011)
- Patients with *dysphagia* and patients with *mental illness* more likely to have difficulty (Schiele, 2013)

CONTINUED

And here's the other problem…

- 70% of interviewees reported that their MD was not aware of their difficulty (Schiele, 2013)
- Respondents reported that doctors and pharmacists ***rarely*** asked about swallowing difficulties (Marquis et al, 2013)
- ***In response to difficulties, people reported non-adherence, altering formulation***

Dysphagia and Pain Medication

Survey of 1021 patients and 34 MD's

- MD's estimated that 5-20% of their patients had difficulty swallowing; 29% of patients reported difficulty
- Among patients who reported crushing or cutting medications, 65% did not know that this could alter drug release
- Alternatives prescribed by MD's included liquids, patch

Pergolizzi, et al, 2014.

Tablet/Pill Swallowing

Normal Subjects:

- ***Oral retention*** not uncommon (difference in flow rates of solid and liquid?)
- Increased ***muscular activity*** as compared to water alone
- ***Non-coated tablets, larger tablets*** resulted in more muscular activity then small, coated tablets.

Yamamoto, et al, 2013

Tablet/Pill Swallowing

People with Dysphagia:

- Report that ***coated tablets*** are easier to swallow than non-coated; ***capsules or torpedo-shaped*** tablets are easier than round tablets; ***smaller pills*** generally easier than larger.
- Also report that their pharmacist did not know that they had swallowing difficulties.

Kelly et al, 2009

Tablet/Pill Swallowing

Patients with Stroke-Induced Dysphagia

Compared pill swallows (placebos – round, oval, and oblong) to thin liquid, thick liquid, and pudding swallows during Videoendoscopy

- Higher incidence of aspiration/penetration with pill swallows with liquid as compared to liquid alone
- More residue with pills swallows with liquids/purees than with liquids/purees alone
- Pill shape was not a significant factor in this study

Schiele, et al, 2015

Tablet/Pill Swallowing

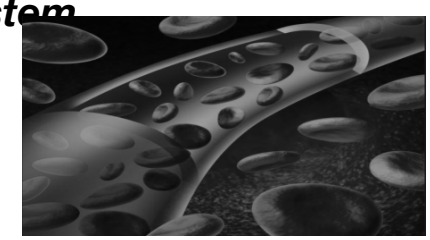
Esophageal Transit:

- ***Oval*** tablets have faster esophageal transit than round; ***lighter*** faster than heavier; ***coated*** faster than non-coated (Channer and Virjee, 1986; Channer and Virjee, 1985)
- ***Upright posture*** facilitates transit (Channer and Virjee, 1986; Osmanoglou et al, 2004)
- ***50ml*** of water facilitates transit (Osmanoglou et al, 2004)

Absorption

- ***Rate and/or extent*** at which the medication leaves the site of administration and ***moves into the circulatory system***

Smith, et al, 2012



Absorption

- **Important Concepts:**
- **Bioavailability** – fraction of the drug that reaches systemic circulation (varies with administration form)
- **Time to peak concentration** – time required to reach maximal serum concentration

Absorption

Has implications for…

- Choice of formulation
- Crushing
- Thickening
- GI function
- Enteral feeding

Medication Formulations

Many different types of formulations…but for our purposes:

- Liquids
- Tablets/Capsules

CONTINUED

Medication Formulations

Liquid Medications

- Drug must be distributed throughout the liquid evenly (implications for thickening)
- Flavoring added which may contain sugars (implications for diabetes management)
- Dose often different from tablets
- Side effects different from tablets

CONTINUED

Medication Formulations

Tablets/Capsules

- Contain multiple additives - binders, disintegrants, coloring, etc.
- Capsule granules may be coated differently to affect release

CONTINUED

Medication Formulations

Coatings May:

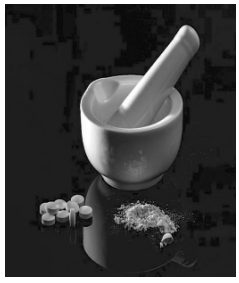
- Facilitate timed release; slow release
- Protect stomach
- Improve taste; enhance appearance
- Ensure delivery of medication beyond the stomach
- Provide physical and/or chemical stability
- Add an active compound
- Allow for imprinting of info

CONTINUED

Medication Formulations

Consequences of Crushing/Capsule Opening

- Spill, Contamination, Morter and Pestle residue
- Alteration of peak effect
- Alteration of absorption site
- Sensitivities/allergies (aerosolization)
- Inappropriate mixing of additives
- Stomach upset
- Bad taste(!)



Also…Impact on pharyngeal mucosa for patients with long dwell times or post-swallow residue not studied

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Thickeners and Medications

- Thickeners may decrease medication availability
- Increasing viscosity impedes drug dissolution and disintegration
- Thickeners slow transit – effect on absorption site?

Cichero, J, 2013; Manrique, et al, 2016; Tomita, et al, 2017

And…

Addition of thickeners to liquid medications is considered “off license”

Legal implications, responsibilities are unclear

What about Food?

"Whole or Crushed in Puree"

- Can impact coating – may slow or speed up disintegration
- Effects often unknown on medication availability
- What about meds that should be taken "on an empty stomach"?

Absorption and GI Function

Gastric pH:
Medications that alter pH (e.g PPIs) may impact absorption

GI motility:
Delayed emptying slows time to peak concentration and delays onset of action of drug

Aging:
Normal changes in GI system as we age slow transit and potentially absorption

CONTINUED

Absorption and Enteral Feeding

- **Gastric pH**
- Formulas increase pH; reduce absorption of meds that need acidic environment
- Ingredients in formula bind to drug and reduce absorption

Common Errors - Medications Via Tube Feed

- Feeding not turned off
- Tube not flushed before/after medication administration to avoid medication interactions
- Crushed meds via tube (blockages, GI upset, interactions with feeding)
- Medication admin immediately before/after feeding

CONTINUED

Distribution

- Process by which the drug moves ***from the bloodstream to the body tissue***
- Process is ***protein dependent*** in part – drugs bind to proteins in the bloodstream; some drugs more tightly than others
- The unbound drug (or portion of the drug) is distributed to tissues

CONTINUED

Distribution

Uneven process…drugs concentrate in the tissues that have an affinity for retaining them

- *Water soluble drugs* – tend to stay in plasma and interstitial spaces
- *Lipid soluble drugs* – concentrate in fatty tissue

CONTINUED

Distribution

- **Important Concepts:**
- **Plasma Protein Binding** – Process by which a drug binds to proteins in the plasma

Volume of Distribution – Relationship of the plasma concentration to the administered dose; not an actual volume. Drugs that are highly tissue-bound have high VOD while those that remain in circulation have low VOD

CONTINUED

Distribution

- **Implications for…**
- **Hydration** – Decreased total body water increases drug concentrations for water soluble medications
- **Aging –** As we age, fat to muscle ratio increases; implications for lipid-soluble medications
- **Protein levels** – Highly protein-bound drugs will be more readily released in patients with low albumin levels; may lead to higher than therapeutic levels

CONTINUED

Metabolism

Chemical alteration of the drug; occurs in a variety of body tissues – GI tract, kidneys, lung, brain, most commonly the liver

Varies with drug, liver function, individual

Goal is to facilitate excretion

CONTINUED

Metabolism

- **Important Concepts:**
- **First Pass Effect** – Hepatic metabolism of meds absorbed from the GI tract; resulting reduction in bioavailability
- **Half-Life** – Amount of time required for drug concentration to decrease by half

CONTINUED

Metabolism

- **Implications for…**
- **Aging** – Hepatic metabolism decreases with age so maintenance drug doses are generally lower in the elderly.
- Also, First Pass metabolism decreases with aging; i.e elderly have higher circulating drug levels
- **Polypharmacy** – One drug has the potential to enhance the toxicity or reduce the therapeutic effect of another drug; this impact is enhanced by polypharmacy

CONTINUED

Elimination/Extraction

- Removal of the drug from the body
- Typically via kidneys or liver but also… skin, lungs (e.g. alcohol), salivary glands, lacrimal glands, feces, milk
- Fluctuating renal function in ill patients may limit elimination

CONTINUED

Elimination/Extraction

Important Concepts

Clearance – Volume of blood cleared of the drug over a specified unit of time

Extraction Rate – Percentage of drug removed from blood as it passes through the eliminating organ

CONTINUED

Elimination/Extraction

- **Implications for Aging Clients**
- Reduced blood flow through the liver, kidneys
- Kidney shrinkage
- Undernutrition – impact protein binding
- Loss of muscle mass – more fat; decreased body water
- Changes in immune function
- Polypharmacy

CONTINUED

Pharmacodynamics

- 1. Therapeutic effect(s)
- 2. Side effects
- 3. Site of activity
- 4. Mechanism of action

Pharmacodynamics

- **Potency**: Amount of drug needed to produce an effect
- **Efficacy:** Drug's capacity to produce an effect
- **Effectiveness:** How well the drug works in real-world use; typically lower than efficacy

Pharmacodynamics

- **Site Selectivity –** Degree to which a drug acts on a given site relative to other sites
- *Some drugs are relatively less selective than others; work on multiple sites simultaneously*

CONTINUED

Pharmacodynamics

- ***How do drugs find their site?***
- **Receptors:** Molecules on cells which allow substances to attach to cells
- Agonists – activate receptors
- Antagonists – block access to receptors

Enzymes: Regulate rate of chemical reaction

- Inhibitors vs. Activators/Inducers

Chemical Interactions

CONTINUED

Therapeutic Effects

Medications That May Improve Swallowing?

- Pain medications
- Dopamine
- ACE inhibitors
- Beta blockers
- Angiottensin II Receptor Blockers (ARBs)/Antagonists of Angiotensin

CONTINUED

Therapeutic Effects

HNC Patients and Pain Management – Gabopentin (Neurontin) use associated with….

During treatment: Better pain management; Less reliance on opioids

At completion of treatment: Better pain management, decreased G-tube use; less weight loss; higher FOIS scores; Improved swallow function

One year later: Reduced PEG dependence; High FOIS scores; Low frequency of persistent dysphagia

Bar, et al, 2010; Starmer, et al, 2014; Starmer, et al, 2017

CONTINUED

Therapeutic Effects

Swallowing and Dopamine

Relationship is unclear…

L-Dopa improves swallow function in *some but not all* patients with PD

Dysphagia, therefore, not caused by a lack of dopamine only

So…implications for medication scheduling?

L-Dopa does improve UE function for self-feeding

CONTINUED

Therapeutic Effects

Angiotensin-converting-enzyme (ACE) inhibitors

- Used to treat HTN, CHF (e.g. Capoten/captopril, Vasotec/enalapril, Altace/ramipril)
- Reduce tension in blood vessels, reduce blood flow
- Increase cough sensitivity; lower cough threshold; i.e. people who take them cough with less stimulation
- Some evidence to suggest that they could prevent aspiration and aspiration pneumonia (Marik and Kaplan, 2003); Effect more pronounced in Asian populations (Miarons, et al, 2016)

CONTINUED

Therapeutic Effects

Substance P

Peptide that transmits signals from sensory nerves to CNS

- Binds to molecules to relay signals
- Important for pain transmission, emotional responses, ***cough and swallow***
- Reduced in patients with dysphagia

Kishida, et al, 2013

CONTINUED

Therapeutic Effects

Retrospective review of older patients to determine which medications were associated with dysphagia and which had protective effects:

ARBs/Antagonists of Angiotensin:

Used to control hypertension in patients intolerant of ACE inhibitors May protect against disuse atrophy in the elderly

Beta blocker agents:

Block norepinephrine and epinephrine; used to treat hypertension, heart disease

Thin oral, nasal and pulmonary secretions which may explain protective effect

Miarons, et al, 2016

CONTINUED

Pharmacokinetics

- **Side Effects**
- Unwanted or unexpected events or reactions to a drug
- May occur when treatment goes beyond the desired effect or in addition to the desired therapeutic effect.
- Vary in severity
- Vary with age, gender, presence of allergies, polypharmacy

Anti-Cholinergic Medication

Purpose: Used to treat allergy, nausea, incontinence, excess secretions

Mechanism: Block acetylcholine; inhibit parasympathetic nerve impulses

Examples*:* Doxylamine (Unisom); Dimenhydrinate (Dramamine); Diphenhydramine (Benadryl)

Anticholinergics and Dysphagia

Potential Effects on Swallowing:

- Reduced GI motility (suppress GI secretions, GI motility)
- Xerostomia (suppress oral secretions)
- Dizziness
- Altered mental status (delirium, sedation, confusion)

CONTINUED

Anti-Psychotic Medication

Purpose: Control of psychotic symptoms; treat bi-polar depression

Typical (or First generation) anti-psychotics have higher risk of side effects as compared to atypical (or Second Generation)

Mechanism: Alter levels of neurotransmitters; Block dopamine receptors; Atypical anti-psychotics also act on serotonin

CONTINUED

Anti-Psychotic Medications

Examples:

First Generation (Typical) – Haloperidol (Haldol); Chlorpromazine (Thorazine)

Second Generation (Atypical) - Clozapine; Risperidone; Aripiprazole (Abilify); Quetiapine (Seroquel)

Anti-Psychotics and Dysphagia

Potential Impact on Swallowing:

- Prevalence of dysphagia in patients taking anti-psychotics = 21.9 to 69.5% depending on the study

Miarons Font and Rofes Salsench, 2017

- Comparison of patients with dysphagia exposed to anti-psychotics to those without exposure: Significantly more impaired dysphagia in patients with exposure…
- And the higher the dose, the more the severe the swallowing problems

Rudolph, et al, 2008

Anti-Psychotics and Dysphagia

Potential Impact on Swallowing:

- Pseudoparkinsonism; dystonia
- Sedation
- Tardive-dyskinesia
- Xerostomia
- Reduced GI motility
- Impaired swallow response

CONTINUED

Mood Stabilizers

Purpose: Used to treat Bi-Polar Disorder and schizo-affective disorder

Mechanism: Unknown

Examples: Lithium (occasionally anti-convulsant medications are utilized as mood stabilizers as well)

CONTINUED

Lithium and Dysphagia

Potential Impact on Swallowing:

- Xerostomia
- Sedation
- Decreased motor coordination
- Decreased peristalsis

CONTINUED

Anti-Depressants

Purpose: Treatment of depression, anxiety, sleep disorders, obsessive-compulsive disorders

Mechanism: increase concentrations of neurotransmitters by interfering with cellular reabsorption

Selective serotonin reuptake inhibitors (SSRIs) – increase availability of serotonin

Serotonin norepinephrine reuptake inhibitors (SNRIs) – increase serotonin and norepinephrine

Monoamine oxidase inhibitors (MAOIs) – increase availability of monoamine

CONTINUED

Anti-Depressants

Examples:

SSRIs: Fluoxetine (Prozac); Sertraline (Zoloft); Citalopram (Celexa); Escitalopram (Lexapro)

SNRIs: Duloxetine (Cymbalta); Venlafaxine (Effexor)

MAOIs: Phenelzine (Nardil)

Anti-Depressants and Dysphagia

Potential Effects on Swallowing:

- Sedation
- Impaired cognition
- Impaired motor function (chewing, swallowing)
- Alterations in taste
- Reduced GI motility
- Dry mouth, constipation, urinary retention

Anti-Convulsant Medications

Purpose: Seizure control; neuropathic pain control; also used as mood stabilizers

Mechanism:

- Decrease brain activity; suppress rapid firing of neurons
- Block calcium and sodium channels in brain
- Bind to the neurons that create anxiety and soothe excitability

Examples:

Phenytoin (Dilantin); Carbamazepine (Tegretol); Levatiracetam (Keppra)

CONTINUED

Anti-Convulsant Medications

Potential Effects on Swallowing:

- Mucosal hypersensitivities
- Gingival hyperplasia
- GI upset
- Sedation
- Ataxia,
- Xerostomia
- Altered taste/smell

CONTINUED

Anti-Anxiety Medications

Purpose: Utilized to reduce anxiety and its symptoms (e.g. tachycardia, palpitations)

Mechanism: Reduce brain activity via sedation (barbiturates) or via Gamma-aminobutyric acid (GABA) enhancement (benzodiazepines).

Examples: Buspirone (Buspar); Clonazepan (Klonopin)

CONTINUED

CONTINUED

Anti-Anxiety Medications

Potential Effects on Swallowing:

- Sedation, lethargy
- Altered mental status
- Reduction in motor control, coordination
- Altered taste
- Xerostomia
- GI upset

CONTINUED

Chemotherapy Agents

Purpose: Intra-cellular toxins used for cancer treatment

Mechanism: Cytotoxins attack rapidly dividing cells

CONTINUED

Chemotherapy and Dysphagia

Potential Effects on Swallowing:

- Xerostomia
- Altered taste, smell
- GI upset
- Mucosal injury (oral cavity, pharynx, esophagus, GI tract)
- Fungal infections

CONTINUED

Botulinum-A Toxin (Botox)

Purpose: Utilized to decrease spasm in CP, dystonia, achalasia, migraine, torticollis; also used cosmetically

Mechanism: Neurotoxic protein that induces weakness, paralysis; can spread from injection site

CONTINUED

Botox and Dysphagia

Potential Effects on Swallowing:

- Oral muscle weakness
- Pharyngeal muscle weakness
- Laryngeal weakness

CONTINUED

To summarize…

Medications can…

- ***Impact motor function*** – anticonvulsants; antipsychotics; anti-anxiety medications
- ***Impact GI function*** – antihistamines; antipsychotics
- ***Impact arousal*** – anticonvulsants; narcotics; muscle relaxants

CONTINUED

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To Summarize….

- ***Medications Can..***
- ***Impact salivation*** – anticholinergics; antihistamines; anti-depressants; anti-psychotics; anti-Parkinson agents…
- ***Impact taste/smell*** – anticholinergics; antibiotics; cardiac medications; chemo therapy agents; ….
- ***Impact pharyngeal swallow*** - anticonvulsants; antipsychotics; anti-anxiety medications

CONTINUED

Also…Pill Esophagitis

- **Mucosal injury**
- More likely with dry mouth, insufficient fluids, recumbence following ingestion, larger pills
- Iron, potassium, aspirin, steroids, tetracycline, antibiotics, NSAIDs are particularly risky
- Patients with abnormal esophageal structure or function are at higher risk
- Elderly at higher risk (reduced esophageal motility)

Pill Esophagitis

Prevention of Esophagitis

- All meds with at least 3 ounces of fluid
- All medications in upright position; maintain upright at least 10 minutes
- Avoid medication administration just before bedtime
- Substitute liquid meds for bedbound patients or patients with esophageal motility issues
- Take larger medications earlier in day

Medications and Dysphagia

Prevention of Dysphagia:

- Start with lower doses
- Increase dose slowly
- Avoid prolonged use
- Avoid multiple psychotropic and anticholinergic medications
- Avoid meds with side effects that exacerbate current symptoms

Medications and Dysphagia

Treatment:

- ***For xerostomia***: Ice chips, water sips, sugarless candy, saliva substitutes
- ***For sedation***: Schedule medications after mealtimes; consider change in medication
- ***For motor impairments:*** Consider change in medication

Medications and Dysphagia

Treatment:

- ***For GI issues****:* Bowel regimens for GI motility (fiber, fluid, laxatives); monitor for dehydration, nutritional compromise
- ***Treating GI upset*** – meds with food or milk, split doses; monitor for dehydration, nutritional compromise
- ***Mucositis*** – topical anesthetics, rinses

CONTINUED

Medication Errors

Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.

- Occur in all settings
- May or may not cause an adverse drug event
- Most commonly involve wrong drug, wrong dose, or wrong route of administration

Hughes, 2008

CONTINUED

Medication Errors – People with Dysphagia

- **Includes…**
- **Oral Administration:**
- Crushing
- Capsule opening

Medications Via Tube Feed:

- Feeding not turned off
- Tube not flushed before/after medication administration to avoid medication interactions
- Crushed meds via tube (blockages, GI upset, interactions with feeding)

CONTINUED

Also…

Medication Not Administered/Not administered on time:

- Patient unable
- Patient requires additional time
- Patient requires additional supervision
- RN judged unsafe

Not medication error per se, but more likely with dysphagia patients…

CONTINUED

Improving Medication Administration for People with Dysphagia

Medication Administration Process

- Ordering/Prescribing
- Transcribing and Verifying
- Dispensing and Delivering
- Administering
- Monitoring and Reporting

Ordering/Prescribing

Communication with MD

- Nature of dysphagia
- Safest medication type
- Safest medication route
- Need for crushing, mixing with food
- Patient preferences
- Review medications regularly in light of changing dysphagia status

Verifying/Dispensing and Delivering

Communication with Pharmacist

- Alert to dysphagia
- Consider alternative formulation
- Dispense smallest tablet/capsule possible

CONTINUED

Administering

RN education yes, but patient/family too

Issue of covert admin?

Specific protocols for administration of medications for each patient

"DO NOT CRUSH" lists

Clear instructions/alerts via MAR

Interventions for dry mouth prior to med administration

One at a time!

CONTINUED

Administering

Compensatory Strategies

- Volitional swallow
- Effortful swallow
- Pacing (one at a time!!)
- Carbonation

CONTINUED

Administering

Chin Down Head Position

- Reduces aspiration by reducing space between tongue base and pharyngeal wall, epiglottis and arytenoid; narrows laryngeal vestibule
- And…requires more effort

But…

- Positions airway below pyriform sinuses – may increase aspiration of post-swallow residue

Administering

Direct Interventions?

Can we improve swallowing for pills?

Practice with placebo pills of increasing size?

Monitoring and Reporting

- Assess success with various meds, routes
- Assess for fluctuations in performance

New Directions

Disintegrating Medications

- Trialed with oral chemotherapy and anti-depressant medications

Liorca, 2011; Siden and Wolf, 2013

CONTINUED

New Directions

Aqueous mixtures in gels

- Thicken in stomach to ensure time release

Hoh, et al, 2010; Shimoyama et al, 2012

CONTINUED

Questions to Consider…

- What is the risk/benefit for *this patient* at *this time* with this *medication?*
- Do the benefits of this medication outweigh the potential impact on swallowing? The potential for aspiration?
- Can the dosage or formulation be modified?
- Can the medication be changed?
- How can we facilitate swallowing of this medication?

CONTINUED

CONTINUED

To conclude…

- Pill swallowing should be part of swallow assessment
- Review current medications and potential impact on swallow function
- Understand implications of “off license” administration
- Safe administration requires a team