



PILL SWALLOWING

Dr Melanie Elaine Collins (MBChB) (DipHIVMan)
24 October 2018





ORGANIC/PHYSIOLOGICAL CAUSES OF DYSPHAGIA WILL NOT BE DISCUSSED IN THIS TALK AND ANY PATIENT WITH NEW ONSET DIFFICULTY SWALLOWING OR OTHER DANGER SIGNS SHOULD BE INVESTIGATED USING STANDARD PROTOCOLS

Why is this talk important?



- Limited paediatric ART formulations
- Syrups/Solutions
 - Kaletra[®]
 - Requires cold-chain transportation
 - Requires refrigeration in the facility
 - Difficult to measure
 - Unpalatable
 - Norvir[®]
 - As above
 - Short half-life
- Crushing of ARVs is not recommended – especially PIs
- Affects both adult and paediatric patients – surprisingly common
- Impacts on adherence



IS IT SAFE TO CRUSH ARVS?



Administration of crushed 200/50mg lopinavir/ritonavir tablet decreased the AUC of lopinavir and ritonavir by approximately 40%

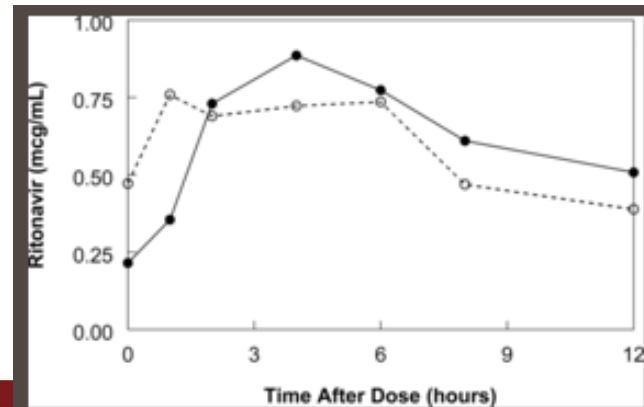
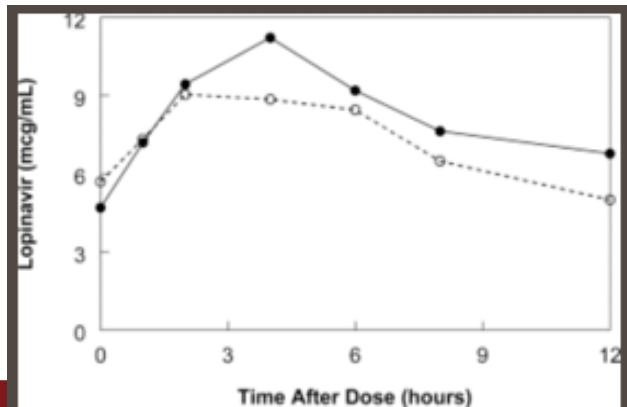


Pharmacokinetics of Lopinavir/Ritonavir Crushed versus Whole Tablets in Children

Brookie M. Best, Pharm.D., M.A.S.^{1,2}, Edmund V. Capparelli, Pharm.D.^{1,2}, Huy Diep, B.S.¹, Steven S. Rossi, Ph.D.², Michael J. Farrell, R.N.², Elaine Williams, R.N., M.S.N.^{3,4}, Grace Lee, B.S.³, John N. van den Anker, M.D., Ph.D.^{3,4}, and Natella Rakhmanina, M.D., Ph.D.^{3,4}

The magnitude was highly variable and unpredictable between subjects, ranging from 5 to 75% reduction in AUC

Increased doses and therapeutic drug monitoring are needed to ensure adequate lopinavir/ritonavir exposure in patients requiring crushed Kaletra[®] tablets



DOES TEACHING CHILDREN HOW TO SWALLOW TABLETS IMPROVE OUTCOMES?



A retrospective chart review of 23 paediatric patients with HIV aged 4 to 21 years who were clinically referred for pill-swallowing either for noted difficulties with currently prescribed antiretroviral regimens and/or desire to change the child's regimen/formulary



Efficacy of a Pill-Swallowing Training Intervention to Improve Antiretroviral Medication Adherence in Pediatric Patients With HIV/AIDS

Patricia A. Garvie, PhD^{a,b}, Shelly Lensing, MS^c, Shesh N. Rai, PhD^c

^aDivision of Behavioral Medicine, ^cDepartment of Biostatistics, St Jude Children's Research Hospital, Memphis, Tennessee; ^bDepartment of Pediatrics, University of Tennessee Health Sciences Center, Memphis, Tennessee


The number of sessions required to complete training increases with age:

- 40% aged between 4-5 years required 1 session
- 50% of participants ≥ 8 years required ≥ 4 sessions



Most likely because they were naïve to pill swallowing and therefore were not influenced by previous negative experiences.

Children as young as 4 years can readily acquire the ability to swallow pills regardless of target size required



FLUOROSCOPIC STUDIES HAVE SHOWN THAT PATIENTS EXPERIENCE
OESOPHAGEAL SPASM WHEN PROMPTED TO RECALL UNPLEASANT
TOPICS, ILLUSTRATING THAT THE POTENTIAL ROLE OF ANXIETY MUST
BE CONSIDERED, EVEN WHEN ANXIETY IS NOT THE PRIMARY
PRESENTING PROBLEM

Efficacy of a Pill-Swallowing Training Intervention to Improve Antiretroviral Medication Adherence in Pediatric Patients With HIV/AIDS



TABLE 2 Time-Point Comparisons for Adherence

| Pairs | <i>n</i> | Mean (SD) | Median (Range) | <i>P</i> ^a |
|-------|----------|-------------|---------------------|-----------------------|
| T1–T2 | 17 | 2.4 (11.7) | 0.0 (–10.4 to 31.0) | .689 |
| T2–T3 | 15 | 3.8 (14.9) | 6.0 (–33.0 to 34.0) | .149 |
| T1–T3 | 14 | 10.9 (14.0) | 9.8 (–14.3 to 34.5) | .014 |

Adherence was significantly improved and reported improved adherence in 71.4% of patients

TABLE 3 Time-Point Comparisons for CD4⁺ T-Cell%

| Pairs | <i>n</i> | CD4 ⁺ T-Cell% Category, <i>n</i> (%) Patients at Specified Time Points | | | | | | <i>P</i> ^a |
|-------|----------|---|---------|----------|----------|-----------|-----------|-----------------------|
| | | 0%–14% | | 15%–24% | | ≥25% | | |
| T1–T2 | 21 | 4 (19.1) | 2 (9.5) | 7 (33.3) | 6 (28.6) | 10 (47.6) | 13 (61.9) | .063 |
| T2–T3 | 21 | 2 (9.5) | 2 (9.5) | 6 (28.6) | 2 (9.5) | 13 (61.9) | 13 (81.0) | .125 |
| T1–T3 | 22 | 4 (18.2) | 2 (9.1) | 7 (31.8) | 2 (9.1) | 11 (50.0) | 18 (81.8) | .004 |

A significant improvement in CD4 T-cell% emerged from baseline to 3 months (T2; *P* .063) and from baseline to 6 months (*P* .004; Table 3)

TABLE 4 Time-Point Comparisons for VL (copies per mL)

| Pairs | <i>n</i> | Mean (SD) | Median (Range) | <i>P</i> ^a |
|-------|----------|-----------------|---------------------------|-----------------------|
| T1–T2 | 22 | 14 369 (56 194) | 0 (–110 800 to 187 396) | .241 |
| T2–T3 | 22 | 9424 (30 556) | 0 (–36 090 to 115 271) | .241 |
| T1–T3 | 22 | 23 793 (58 757) | 1258 (–36 090 to 188 543) | .093 |

Decrease in VL by 6 months, with a median decrease in VL of 1258 copies per mL (*P* = .093; Table 4)



DIFFICULTY SWALLOWING PILLS IS COMMONLY ASSOCIATED WITH PAEDIATRIC PATIENTS, BUT IS IT A COMMON PROBLEM FOR ADULT PATIENTS?



Pill phagophobia, a form of psychogenic dysphagia, is the inability to swallow pills in the absence of a physiologic explanation



“Doc, I Just Can’t Swallow Pills”: HIV Infected Patients and Pill Phagophobia

Joan M. Duggan^{1*}, Vipul Shukla², Barbara Akpanudo¹, Glen Gutterson², Lindsey Eitniece³ and Eric Sahloff⁴

¹Department of Medicine, Division of Infectious Diseases, University of Toledo, HSC, Toledo, OH 43614, USA

²College of Medicine, University of Toledo, HSC, Toledo, OH 43614, USA

³Department of Pharmacy, University of Toledo Medical Center, Toledo OH 43614, USA

⁴College of Pharmacy, University of Toledo, HSC, Toledo, OH 43614, USA

Over 50% of adults may experience difficulty in swallowing large oral pills and if given a choice, over 80% would choose an inconvenient dosing regimen in order to have a smaller pill formulation

Head posture training, shaping, and positive reinforcement are methods that can be utilized to help patients swallow pills

Of all participants ($N = 1,051$), 37.4 % reported having had difficulties in swallowing tablets and capsules



The majority (70.4 %) of these patients was not identified by their GP

[European Journal of Clinical Pharmacology](#)

April 2013, Volume 69, [Issue 4](#), pp 937–948 | [Cite as](#)

Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms

Authors

[Authors and affiliations](#)

Julia T. Schiele, Renate Quinzler, Hans-Dieter Klimm, Markus G. Pruszydlo, Walter E. Haefeli 

Therefore, physicians should rule out swallowing difficulties regularly to avoid non-adherence and inappropriate drug modifications

Pill Properties that Cause Dysphagia and Treatment Failure

Jeremy Fields, MD^{1,2}, Jorge T. Go, MD, MSc^{1,3}, Konrad S. Schulze, MD^{1,4,*}

¹ Department of Medicine, University of Iowa; Iowa City, Iowa

² McFarland Clinic, Ames, Iowa

³ Mercy Gastroenterology Clinics, Clive, Iowa

⁴ VAMC, Iowa City, Iowa



Pill Properties that Cause Dysphagia and Treatment Failure

Jeremy Fields, MD^{1,2}, Jorge T. Go, MD, MSc^{1,3}, Konrad S. Schulze, MD^{1,4,*}



Table I

Interview participant characteristics and experiences with pills.*

| | |
|--|----|
| Sometimes experienced difficulties with pills (%) | 54 |
| Frequent ongoing pill sticking/globus sensation (%) | 13 |
| Solid food dysphagia (%) | 8 |
| Pills as bad as food (%) | 5 |
| Pills worse than food (%) | 2 |
| Clinical complications from pill swallowing [†] (%) | 4 |
| Measures to ensure effective swallowing (%) | |
| Plenty of water | 55 |

This survey suggests that 4 out of 5 Americans take pills on a daily basis and that about half have encountered pills that are hard to swallow

| | |
|------------------------------------|----|
| Cut, break, or crush large tablets | 30 |
|------------------------------------|----|

| | |
|---|---|
| Swallow in viscous medium (eg, apple sauce or chewed bread) | 7 |
|---|---|

| | |
|---------------------------------|---|
| Stop hard-to-swallow medication | 6 |
|---------------------------------|---|

| | |
|---|---|
| Position pill to back of tongue, turning head | 2 |
|---|---|

| | |
|--------------------------------|---|
| Open capsule, swallow contents | 1 |
|--------------------------------|---|

| | |
|----------------------------|---|
| Request easier preparation | 1 |
|----------------------------|---|

Pill Properties that Cause Dysphagia and Treatment Failure

Jeremy Fields, MD^{1,2}, Jorge T. Go, MD, MSc^{1,3}, Konrad S. Schulze, MD^{1,4,*}



Table II

Pill properties, problems, and preferences revealed during structured interviews

| | |
|--|----------|
| Pills too large or bulky | 20 |
| Difficulties with specific large capsules* | 6 |
| Difficulties with specific large tablets [†] | 6 |
| Small pills or pill fragments [†] | 7 |
| Pills too dry, rough, sticky or hard | 12 |
| Pill of odd shape, with sharp edges | 3 |
| Pills smell/taste bad | 3 |
| Preferences regarding pill properties (%) | |
| Capsules vs tablets | 50 vs 49 |
| Round vs oblong (oval) | 50 vs 49 |
| Coated vs chewable | 90 vs 9 |
| Anticipated swallowing effort [§] | |
| Jumbo tablets or capsules ($>13 \times 4 \times 4$ mm) [†] | 3.6 |
| Small coated tablet (low-dose aspirin) | 1.2 |
| Medium-sized tablets with smooth coating | 1.3-1.6 |

Participants were asked to place pills into score boxes labelled according to swallowing effort:
1 = easy ; 2 = slight ; 3 = considerable ; 4 = hard/impossible

Jumbo tablets and capsules were widely loathed, and 4 out of 5 participants would rather take the requisite amount of drug in several medium-sized preparations.

Pill Properties that Cause Dysphagia and Treatment Failure

Jeremy Fields, MD^{1,2}, Jorge T. Go, MD, MSc^{1,3}, Konrad S. Schulze, MD^{1,4,*}



Jumbo = >13 x 4 x 4 mm

Currently available ARVs

| Paediatric Aluvia® (100/25) | Adult Aluvia® (200/50) | Dumiva® (ABC/3TC) | FDC (TDF/FTC/EFV) |
|---|---|---|---|
|  |  |  |  |
| 16mm | 21mm | 23mm | 25mm |



DOCUMENTED TECHNIQUES

Twenty-nine 3- to 13-year-old children with HIV infection who were naïve to pill swallowing or who had difficulty with pill swallowing were seen for training.



Teaching and Maintaining Pill Swallowing in HIV-Infected Children

Danita I. Czyzewski, PhD, R. Duane Runyan, PhD, Molly A. Lopez, PhD, Nancy R. Calles, RN, BSN

AIDS Read. 2000;10(2)

Seventeen children learned to swallow large capsules and were able to comply with their PI regimen for at least 6 months

Fourteen of these children learned with one 30-minute training session

Teaching and Maintaining Pill Swallowing in HIV-Infected Children

Danita I. Czyzewski, PhD, R. Duane Runyan, PhD, Molly A. Lopez, PhD, Nancy R. Calles, RN, BSN

AIDS Read. 2000;10(2)



- Difficulties with pill swallowing include children being unable to swallow a large capsule even once, as well as swallowing medication with such coercion, discomfort, or anxiety that each administration is a struggle
- Immediate solutions including bribery or punishment can cause long-term problems
- No other paediatric regimen so consistently lacks alternative dosage forms (liquid, chewable, non-oral)
- Capsules are too big to be hidden in foods, and hiding medications in food frequently produces problems such as food aversion and lack of trust in the caregiver

Pill-Swallowing Training Procedure



Important to minimise negative experience

If the pill is swallowed, the trainer praises the child's success but no extrinsic rewards are given

Trainer meets child in a distraction-free room without the parent/caregiver

Series of 7 placebo pills ranging from "sprinkle" size to 1000-IU gelatin capsules
Only shows child 1 size of placebo at a time

1st the trainer may ask the child to take a drink of water to provide a successful experience and increase confidence

Difficulty swallowing this tiny placebo is usually a poor prognostic sign

The trainer then models the behaviour with the smallest placebo and the asks the child to practice swallowing with the sprinkle-sized placebo

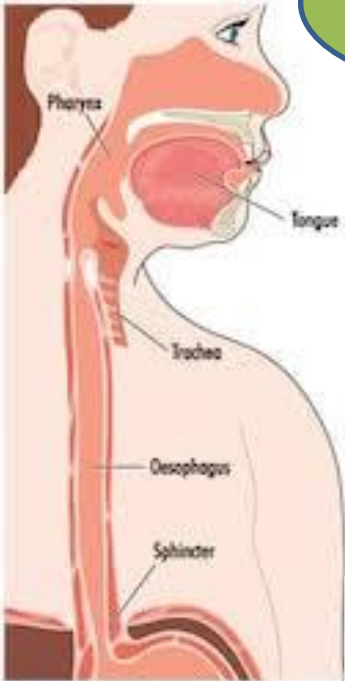
After a success the trainer quickly moves to the next pill, using the term "next pill", never "bigger pill"

When the child successfully swallows the largest pill, the trainer brings the parent/caregiver into the room and the child demonstrates for the parent/caregiver

After 2 consecutive failures the trainer has the child swallow the largest pill that was successfully swallowed to end the session with a success

Forty-one children (24 girls and 17 boys, aged two to 17 years)

NGUNK



Shown diagrams and taught about oesophageal flexibility
Taught the funny 'ngunk' noise their throat makes when they swallow water with their heads turned off centre
The five head positions were introduced

Practice at home for 14 days

Successful treatment of pill-swallowing difficulties with head posture practice

Bonnie J Kaplan PhD^{1,2}, Roberta A Steiger MD¹, Jamie Pope MSc³,
Ashley Marsh BA³, Maegan Sharp BA³, Susan G Crawford MSc²

Traditional behavioural techniques of stimulus shaping, positive reinforcement and relaxation training were not used

The investment of staff time was generally approximately 45 min per patient for the initial interview, but most of that time was for reviewing the research consent forms, which would not be needed in other settings

Eight children did not practice, and withdrew from the study
All 33 children who carried out the practice sessions were successful; 29 succeeded in all five positions, and the other four could swallow in at least a few of the positions.



Successful treatment of pill-swallowing difficulties with head posture practice

Bonnie J Kaplan PhD^{1,2}, Roberta A Steiger MD¹, Jamie Pope MSc³,
Ashley Marsh BA³, Maegan Sharp BA³, Susan G Crawford MSc²

TABLE 1
Final preferred head position

| | Study 1 (n=106), % | Study 2 (n=134), % | Study 3 (n=108), % | Study 4 (n=33), % |
|---------------|-----------------------|-----------------------|-----------------------|----------------------|
| Centre | 27.4 | 44.8 | 33.3 | 24.2 |
| Up | 7.6 | 9.7 | 11.1 | 36.4 |
| Left or right | 22.6 | 30.6 | 22.2 | 18.2 |
| Down | 19.8 | 14.2 | 33.3 | 3.0 |
| No preference | 22.6 | 0.7 | 0 | 18.2 |

Follow-up phone calls after 30 days confirmed that the children had successfully transferred their skill to prescribed medications

A training video can be viewed at
www.ucalgary.ca/research4kids/pillswallowing



DANGER SIGNS WHEN LEARNING PILL SWALLOWING



- Choking
- Difficulty breathing, crying or talking
- Stridor
- New Wheeze
- New cough
- Trouble swallowing
- Drooling or bring up saliva
- Halitosis
- Decreased level of consciousness



Pill may have been aspirated

Practical Points for Paediatric Patients



- Teach children to swallow tablets prior to non-adherence
 - To avoid a high pressure situation
- Where placebo pills are not available
 - Make use of different sized sweets
- Children can practice with formulations that can be crushed or halved if they are not able to swallow them
 - 3TC 150mg tablet
 - ABC 60mg tablet
 - MVT
- Make use of available resources
 - See resources slide

| Size | Sweet |
|------------|--------------------|
| Very Small | Cake decorations |
| Small | Smint |
| Medium | Tic Tac |
| Big | Skittle or Smartie |
| Very Big | Jelly Bean |



DEVICES TO ASSIST PILL SWALLOWING



Allows pills and water to be poured into the mouth simultaneously



Same function as above, but can fit onto most water bottles

TAKE HOME MESSAGES



- Difficulty swallowing pills is a common problem that affects both paediatric and adult patients
- Difficulty swallowing pills negatively impacts on adherence and in the case of ARVs can result in the development of drug resistance which may limit future treatment options
- Various techniques are described
 - Behavioural/Modeling
 - Head posturing
- Actively enquire about pill swallowing, especially in patients with unsuppressed HIVVL
- Teach children to swallow pills prior to non-adherence and treatment failure


RESOURCES



- Training Videos
 - www.ucalgary.ca/research4kids/pillswallowing
 - MSF
 - South African HIV Clinicians Society

Acknowledgements

- Jackie Dunlop
- Leon Levin



THANK YOU

QUESTIONS?