



Formulations, Packaging and Medication Practices Considerations

Michael J. Theodorakis – Aðalsteinn Guðmundsson

EMA, Geriatric Expert Group



Current facts about drug use in older people

- The number of drugs used increases almost linearly with age
- Several studies in different settings have shown that older adults use an average of 2 - 6 prescribed medications and 1 - 3 non - prescribed medications (30% of all prescription drugs – 40% of OTCs)
- At least 80% of people aged >65 are using one or more drugs on prescription
- More than 40% of the elderly are using 5 or more drugs each week
- The process of ageing, the high prevalence of co - morbidities, the large numbers of drugs used and the complexities related to the use of medicines in this section of the population, constitute a solid basis for trouble!



Why are formulations and packaging important?

A. Directly impact upon impairment of or conditions seriously affecting ability to take medications, specifically to :

- **remember** (what - when - where - how)
- **reach** (overall mobility - frailty - arthritis)
- **see** (visual acuity - cognitive decline)
- **open** (manual dexterity, musculoskeletal disorders)
- **swallow** (taste – sialorrhea, xerostomia, dysphagia)
- **pay** (acquire - access)



Why are formulations and packaging important?

B. Cross-react - synergistically or antagonistically, directly or indirectly - with factors influencing pharmacokinetics and/or pharmacodynamics (thus predisposing to ADRs):

- gastrointestinal qualitative characteristics and motility
- malnutrition
- dehydration
- dose adaptation – related formulation modifications
 - body weight
 - renal / liver / heart insufficiency
 - altered cutaneous physiology (transdermal applications)
- underlying disorders - comorbidities
- polypharmacy (concurrent use – overdose)
- socio-cultural / economic / psychological distress



How to improve patient compliance and adherence?

A. Geriatric populations require specifically tailored formulations

- Older people often self-adjust dosage and frequency
- Appropriate packaging or information on repackaging
- If gastroprotected then it cannot be a large tablet
- Colour and shape recognition (generics / substitution)
- Innovations and/or “smart” formulations
- Adaptations to / reductions of pill burden to enhance compliance and improve safety



How to improve patient compliance and adherence?

B. Physician, Pharmacist and Health care provider initiatives

- prescribing combination drugs or long-acting forms
- fewer pills to remember
- often re-evaluation of medications
- encourage patients to use one pharmacy
- encourage follow up



How to improve patient compliance and adherence?

C. Medication aids

Remove cotton packing

Store in original container

Dry place - away from heat/light

Follow dosing instructions

Get rid of outdated medications

Avoid sharing medications

For those with vision problems

- Large print labels
- Color coded labels



Polypharmacy and drug formulations

Means to reduce high pill burden in older population

- Fixed dose combination drug products, products
- Long-acting active ingredients
- Sustained release/extended release formulations when appropriate
- Alternative routes of administration (consider cost)
- Nonpharmacologic alternatives or interventions



Pill splitting is common among older patients: A risky practice?

Practice increased during downturn in economy

FDA warns against unless specified in manufacturer's drug application

- FDA's Consumer Updates: July 2009

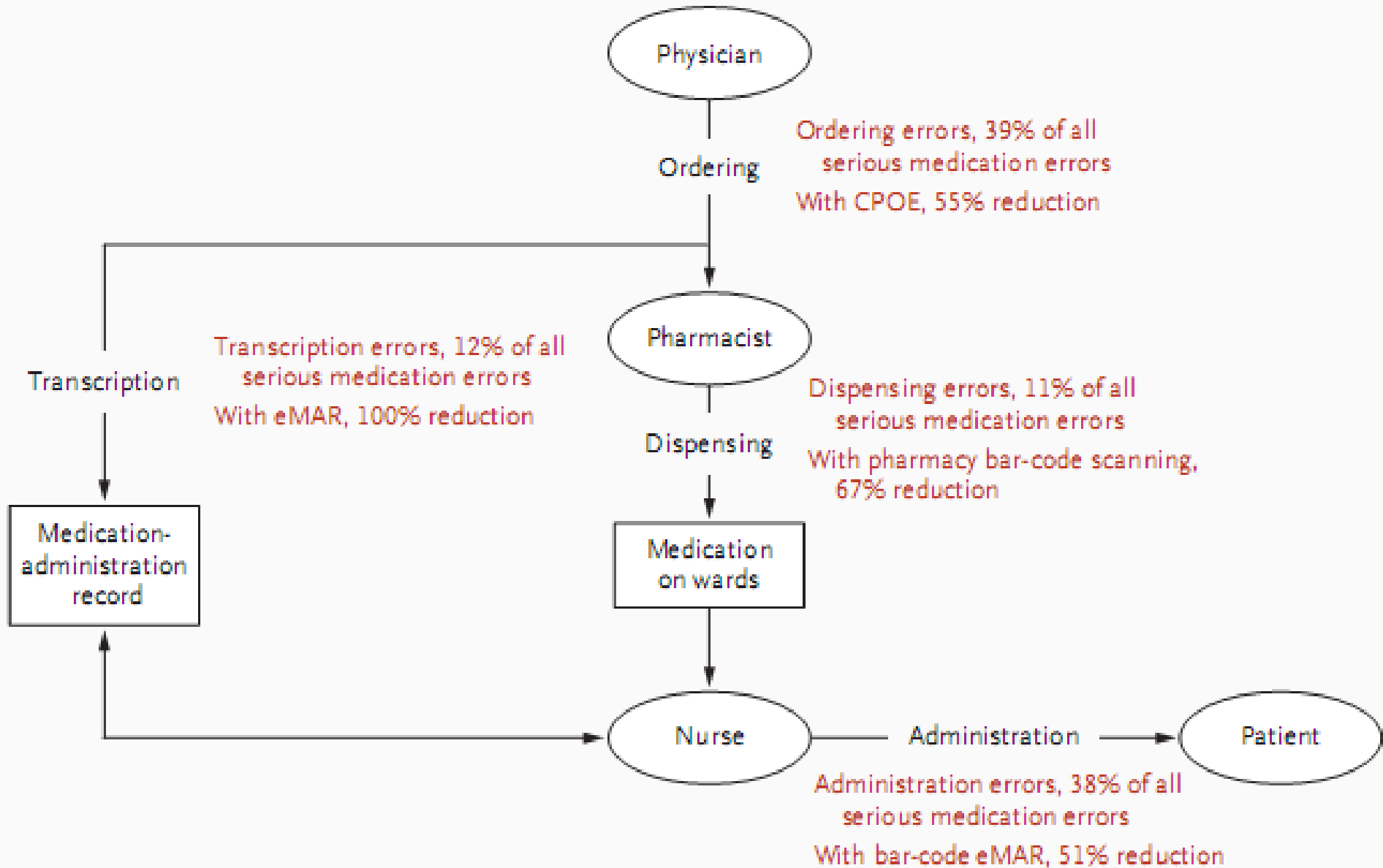
49% of primary care patients in Germany split ≥ 1 drug and 8,7% are unscored pills

- Quinzler et al. Eur J Clin Pharm 2006

In nursing homes manufacturing limitations (dose) accounted for 80.5% of pill-splitting

- Fischbach et al CMAJ Mar.20,2001;164

Bar code technology and safer drug treatment





Effect of formulation and delivery system on administration errors in UK nursing and residential care homes

Odds of errors compared with Tab/Caps monitored dosage systems:

- liquids **4.31** (CI 2.02 - 9.21)
- topicals/transdermals/injections **19.61** (CI 6.90 - 55.73)
- inhalers **33.58** (CI 12.51 - 90.19)
- tablets and capsules not in MDS **2.14** (CI 1.02 - 4.51)

Allred et al. *BMJ Qual Saf* 2011;20:397-401



Formulations, delivery methods and alternative administration options in dementia

- Neuropsychiatric symptoms occur in 90% of patients with dementia
- Adherence, agitation or inability to swallow are example of challenges
- Examples of alternate (lower) strength, forms, routes or “covert” administration discussed
- Crushing of pills is particularly common in nursing home dementia units (even 50%)

– Muramatsu et al. Am J Ger Pharm 2010;8:98-114



Crushing tablets or opening capsules: Risks of inadequate or improper dosing

Examples

1. Partial administration of medication
2. Destruction of extended release properties
3. Neutralization (drug-drug, incompatible media mixing)
4. Health hazards for staff
5. Feeding tubes-drug administration interactions!



Dysphagia and medication administration errors

- Dysphagia increasingly common problem among aging population
- Multiple causes of dysphagia, even drugs
- Increases drug administration error rate
- Guidelines and input from pharmacists is often lacking
- **Discussion:** Alternative methods of administration, dosage forms, or therapeutic agents





Special situations to discuss

- Palliative care and non-oral drug administration
- Cost of drug formulation overvalued compared to cost of administering drug(formal support)?
- Comparisons of same drug in different formulations are lacking re efficacy and safety
- Independant role of drug (formulations, pill burden) causing malnutrition??



Take – home messages

- Age associated changes in pharmacokinetics and multimorbidity frequently reduce the dose tested for evidence and safety in nongeriatric populations
- Visual impairment, swallowing difficulties, lack of dexterity, dementia and palliative care are increasingly common examples of situations where increased flexibility in packaging, formulations or delivery-/administration options are needed
- The common practice of medication alteration (crushing pills) in nursing homes needs attention



Take – home messages

- Drug industry should tailor to the special needs of older populations by increasing their enrollment in trials and enhance the development of “smart” novel formulations or alternative delivery forms and doses.
- Increased pharmacological training and interventions are needed to reduce dosing error risks and ADRs associated with drug formulations.