MOOC 15 Medication Management for Older Adults
Chapter 2 Case Study on Medication Management

In this Chapter, we will discuss the medication management through a few case studies in the following items:

- Common medication issues
  - Adverse drug reactions (ADRs)
  - Drug-drug interaction (Can be pharmacokinetic or pharmacodynamic)
- Strategies for improving drug regime and adherence
- Medication errors in institutional setting
- Consideration in medical management in dementia person

Let's start!

Common medication issues

Adverse drug reactions (ADRs)

Case 1

- A 74-year-old lady, live at home, cared by maid.
- Past history: Chronic insomnia, HT, hyperlipidemia, minor stroke.
- Admitted to hospital due to urinary tract infection with fever.
- Investigation: WBC 23, creatinine 140 (baseline 90) & Urine culture grew E Coli.
- Medical order: Started Augmentin IV, kept nil by mouth, all oral medications withheld.
- Fever subsided Day 2.

However, this lady developed ***acute confusion (delirium)*** Day 3 after admission.

- Further assessment: No focal CNS sign, no neck rigidity.
- Extensive investigations essentially unremarkable.
    - CT brain normal
    - Blood test – WBC down to 10
    - RFT – creat 100
- Drug history:
    - Amlodipine 10 mg om
    - Lipitor 10 mg nocte
    - Aspirin 80 mg daily
    - 15 tables of Zopiclone (bought over the counter) per night for 10 years
    - Gingo Biloba
- No history of TCM taken.

Can you guess WHY?

The answer is **Zoplicone withdrawal**.

- Diagnosis: Zoplicone withdrawal with delirium.
- Treatement: Zoplicone resumed and titrate down → Delirium subsided.

Further information:

Age and Ageing 2005; **34:** 526–527
doi:10.1093/ageing/afi132
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Zopiclone withdrawal: an unusual cause of delirium in the elderly

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Lessons to learn

- Careful drug history.
- Withdrawal symptom may occur if stopping some drugs (e.g. drugs acting on CNS) abruptly.
- A high degree of suspicion is needed.

Case 2

- A 90-year-old lady, bedbound, ADL dependent with Clinical Frailty Scale 7.
- Past history: History of hip fracture and vertebral collapse, esophagitis and hiatus hernia, dementia.
- Drug history:
  - Denosumab 60 mg every 6 months SC
  - Calcichew 1 tab daily
  - Lansoprazole 15 mg daily
  - Senokot 15 mg nocte prn
- She was admitted to hospital due to UTI.
- Treated with antibiotics but complicated by coffee ground vomiting → Lansoprazole increased to 30 mg QD.
- Complained of constipation → Calcichew stopped.
- Upon discharge:
  - Lanzoprazole 30 mg daily
  - Senokot 15 mg nocte prn
  - Denosumab 60 mg every 6 months SC
- At follow up:
  - She has nil complaint.
  - Due for another dose of q6m Denosumab, RLFT and Bone profile recheck.

Collect Date :	14/08/22	14/08/22	14/08/22	15/08/22	**01/11/22**		
Collect Time :	00:16	08:30	11:27	09:15	**10:25**		
Request No. :	C8141256	C8141563	C8141815	C8152395	**CB012329**		
Remark :	chest infection	chest infection	chest infection	chest infection	OSTEOPOROSIS	Ref. Interval	Units
Comment					Below		
Na		147	145	148		136 - 148	mmol/L
K		3.7	3.5 L	3.8		3.6 - 5.0	mmol/L
Chloride		111 H	108	111 H		100 - 109	mmol/L
Urea		10.6 H	11.3 H	12.6 H		2.9 - 8.0	mmol/L
Creatinine		126 H	125 H	130 H		49 - 82	umol/L
Estimated GFR		31 L	31 L	30 L		>90	unit
Calcium		2.06 L			1.61 L	2.24 - 2.63	mmol/L
Adjusted Calcium		2.38			1.93 L	2.24 - 2.63	mmol/L
Phosphate		1.03			0.77 L	0.88 - 1.45	mmol/L
Total Protein		62 L	60 L			67 - 87	g/L
Albumin		26 L	24 L		26 L	39 - 50	g/L
Globulin		36	36			26 - 40	g/L
Total Bili		6	6			4 - 23	umol/L
ALP		107	102		121	47 - 124	U/L
ALT		16	15			8 - 45	U/L
AST		22	21			15 - 37	U/L
Troponin T	40					See Below	ng/L

- Diagnosis: Hypocalcaemia due to denosumab in a patient with renal impairment and stopping calcium supplement.

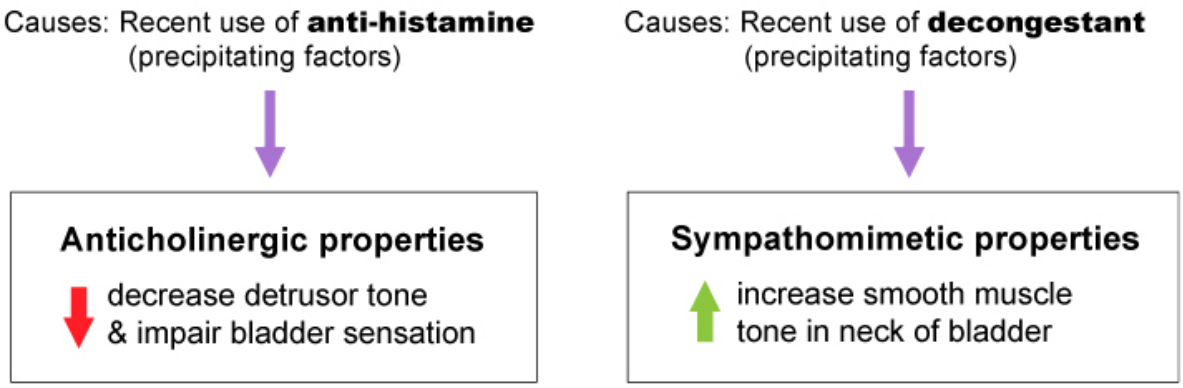
Lessons to learn

Denosumab and hypocalcaemia

- Hypocalcemia is a recognized S/E of Denosumab.
    - Denosumab inhibits osteoclastic bone resorption, leading to hypocalcemia by reducing calcium mobilization from bone into bloodstream.
    - Risk factor:
        - Renal impairment
        - Vitamin D deficiency
        - Lack of prophylactic supplementation of calcium and/or vitamin D

Case 3

- 78 years old, male.
- Past health: BPH, HT, DM.
- Drug history:
    - Terazosin
    - Amlodipine
    - Metformin
- Suffered from flu with cough, fever, nasal congestion, running nose.
- Seen by GP → Given Panadol, Piriton, nasal decongestion medications.
- Complained of abdominal distension and difficult to urinate for 1 day, leakage of small amount of urine continuously.
- Diagnosis: acute urinary retention with overflow incontinence, ***but why?***
- Causes: Recent use of **anti-histamine** and **decongestant**.



- Dx : Acute Retention of Urine

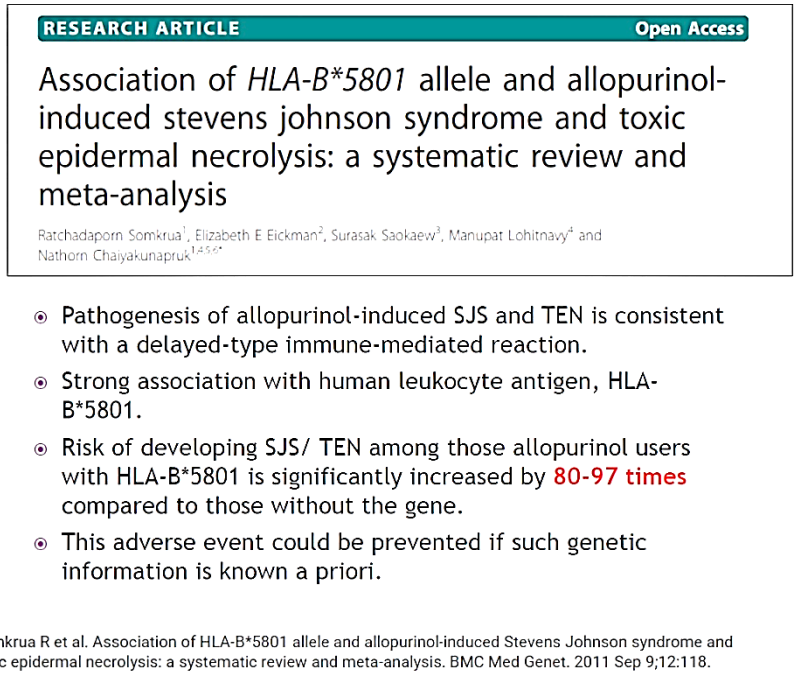
Lessons to learn

Examples of important drug-disease interactions

Disease / Condition	Drugs
BPH	Anticholinergics; TCA
CRF	NSAID
Constipation	Anticholinergics; Opioid analgesics; TCA
DM	Corticosteroids
Falls	Anticholinergics; Sedative-hypnotics; TCA; Benzodiazepines
Heart block	Digoxin; TCA
Narrow-angle glaucoma	Anticholinergics
Parkinson's disease	Metoclopramide
Peptic ulcer disease	Aspirin; NSAID
Syncope	Alpha-blockers

Case 4

- 76 years old lady received a prescription for **Allopurinol** from the GOPC for Hyperuricemia.
- However, she began to experience serious side effects one month after taking the drug, including head swelling, fever and allergic reactions such as skin rashes.
- She was worsened into "Toxic Epidermal Necrolysis", where the skin ulceration, like a severe burns.
- She died after two months.



RESEARCH ARTICLE Open Access

Association of *HLA-B*5801* allele and allopurinol-induced stevens johnson syndrome and toxic epidermal necrolysis: a systematic review and meta-analysis

Ratchadaporn Somkrua[1], Elizabeth E Eickman[2], Surasak Saokaew[3], Manupat Lohitnavy[4] and Nathorn Chaiyakunapruk[1,4,5,6*]

- Pathogenesis of allopurinol-induced SJS and TEN is consistent with a delayed-type immune-mediated reaction.
- Strong association with human leukocyte antigen, HLA-B*5801.
- Risk of developing SJS/ TEN among those allopurinol users with HLA-B*5801 is significantly increased by 80-97 times compared to those without the gene.
- This adverse event could be prevented if such genetic information is known a priori.

Somkrua R et al. Association of HLA-B*5801 allele and allopurinol-induced Stevens Johnson syndrome and toxic epidermal necrolysis: a systematic review and meta-analysis. BMC Med Genet. 2011 Sep 9;12:118.

You may read this local news for your information.

Lessons to learn

- Carbamazepine (Tegretol) – another drug also needs to check HLA before prescription.
  - All Asians given carbamazepine should be tested HLA 1502 due to the risk of Steven Johnson Syndrome (SJS) and toxic epidermal necrosis (TEN) as advised by FDA.

Drug-drug interaction (Can be pharmacokinetic or pharmacodynamic)

Pharmacokinetic nature of drug-drug interaction

- Effects of one drug on the absorption, distribution, metabolism, or excretion of another drug.
- Interactions → changes in serum drug concentrations → change clinical response.
- The most frequent pharmacokinetic drug-drug interactions involve several isoenzymes of the hepatic cytochrome P450 (CYP) and drug transporters e.g. the P-glycoprotein.

Drugs which affect cytochrome p450 isoezymes

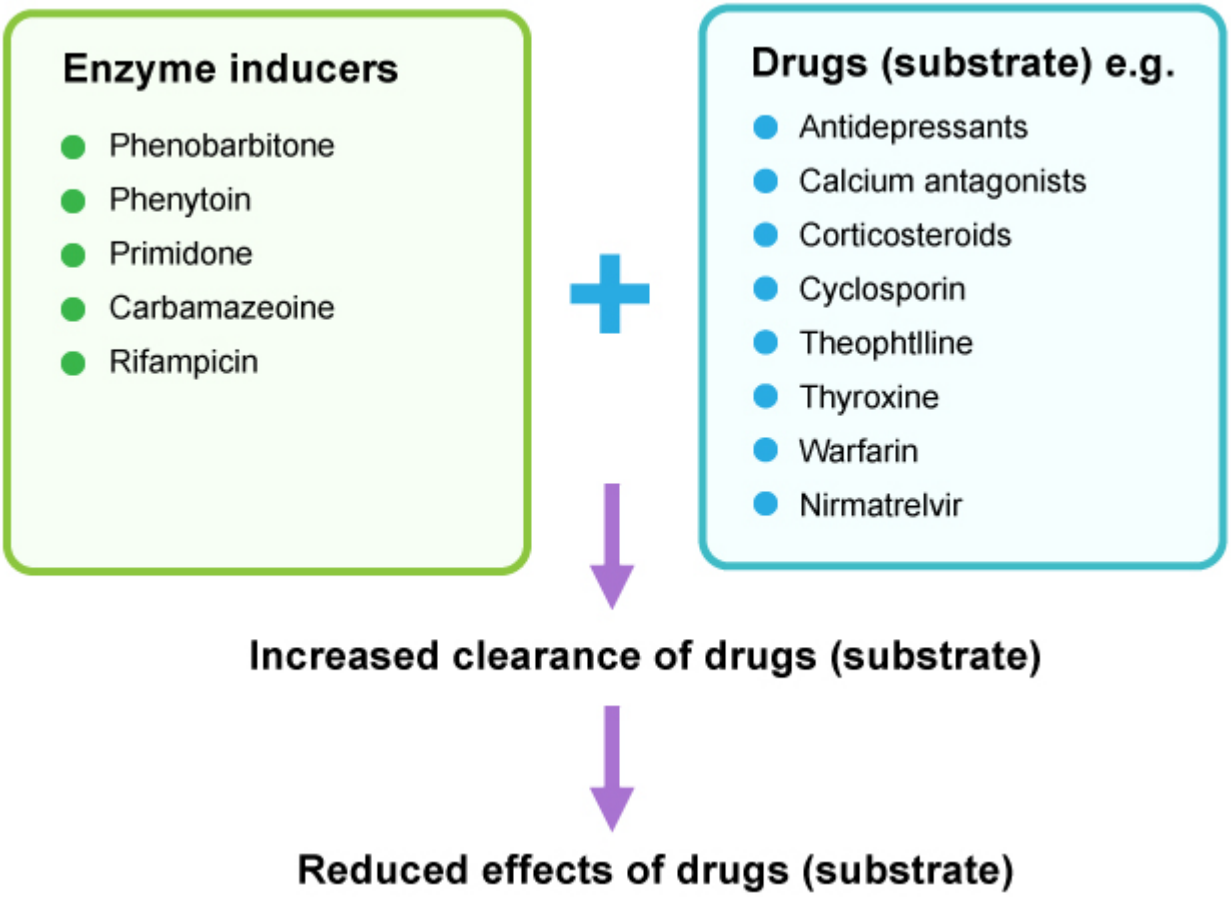
Drugs which increase the activity of Cytochrome P450 isozymes:

- Phenobarbitone
- Phenytoin
- Primidone
- Carbamazeoine
- Rifampicin

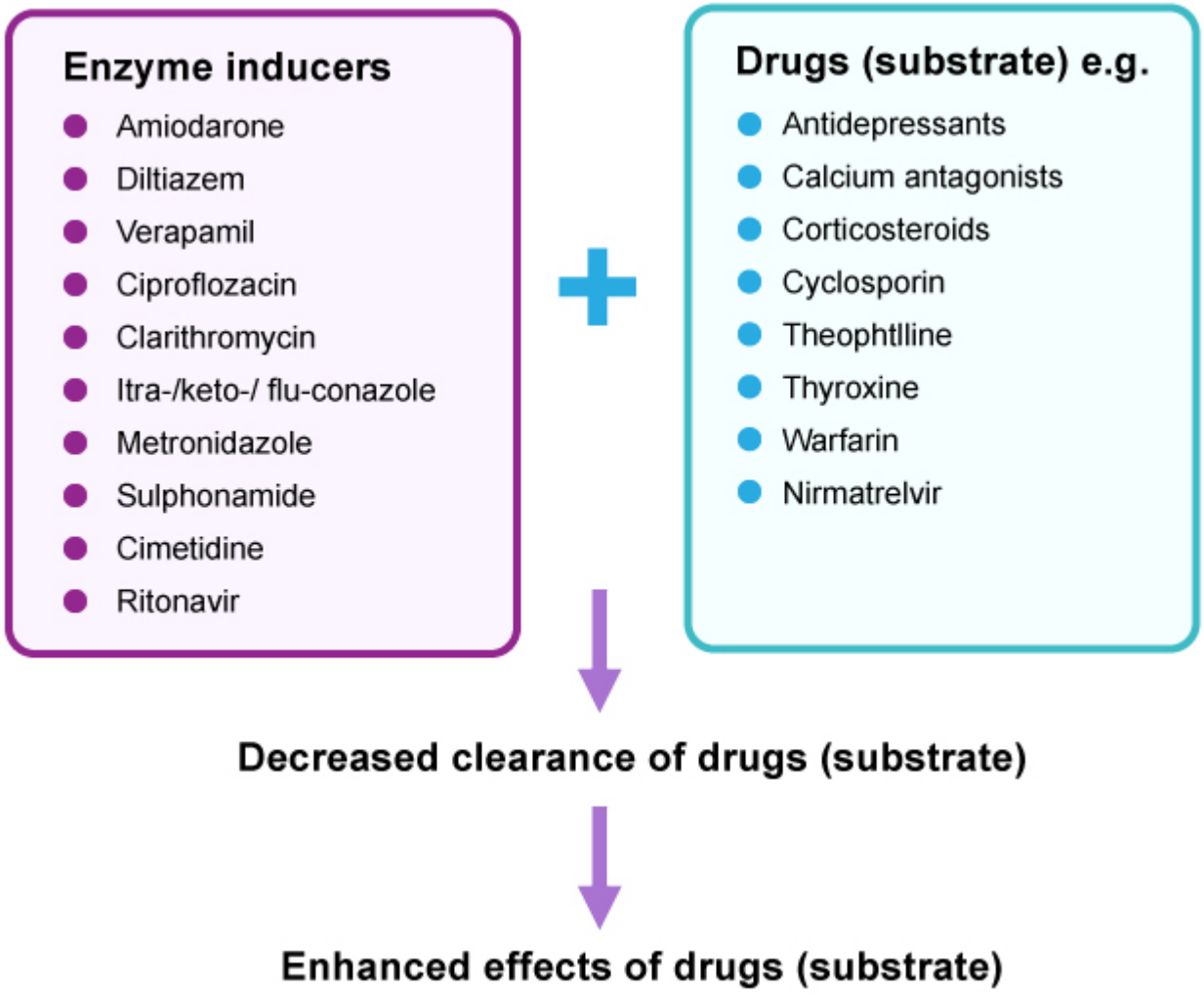
Drugs which decrease the activity of Cytochrome P450 isozymes:

- Amiodarone
- Diltiazem
- Verapamil
- Ciproflozacin
- Clarithromycin
- Itra-/keto-/ flu-conazole
- Metronidazole
- Sulphonamide
- Cimetidine
- Ritonavir

Induction of metabolism of one drug by another



Inhibition of metabolism on one drug by another



Case 1

- 60 years old lady.
- Past history: Double valve replacement, on warfarin for many years, aim INR 2.5 to 3 by cardiologist.
- Drug history: Lasix, Slow K, Diltiazem
- Developed sore throat for 2 days, with exudates over the tonsils, fever+.
- Seen by GP → Given Panadol, cough syrup, azithromycin – 5-day course.
- Noticed to have nose bleeding and bruising next morning.

Do you know why?

- Blood test:
  - INR >5
  - Platelet count normal
  - Hb 12 drop to 9 g/dl
- Diagnosis: Warfarin overdose due to **drug-drug interaction** by macrolides antibiotics.

Lesson to learn

Warfarin and Macrolides

- Examples of macrolides antibiotics are azithromycin, clarithromycin, erythromycin.
- Macrolides reduce the metabolism and clearance of warfarin → ↑ levels and effects of warfarin like bleeding.

Case 2

- 70 years old man.
- Known HT, IHD, DM & renal impairment (Creatinine around 100 baseline).
- Admitted to ward due to heart failure.
- Investigation:
    - BNP 5000
    - Echo – shows HFrEF (EF 35%)
- Treated with Lasix, Slow K, Acertil, Aldactone, Metaprolol Zok, Aspirin.
- Discharge from ward 3 days later, then follow up 3 weeks later in OPD.
- No complaint from the patient.
- Blood test repeated showing K 6.5, Creatinine 120 (The blood test was not hemolyzed).
- ECG SR with peak T waves.

- Diagnosis and treatment
    - Aldactone and ACEi interaction.
    - Slow K supplements → severe hyperkalaemia.
- Patient was admitted to hospital for urgently correcting hyperkalaemia.

Lesson to learn

ACEI and aldactone

- ACEI (Acertil, Lisinopril, Ramipril, Enalapril etc) interact with Spironolactone (Aldactone).
- Both have potassium increasing effects.
- So when adding together, a very high level K may occur.
- Close monitoring of K is needed.

Strategies for improving drug regime and adherence

Case 1

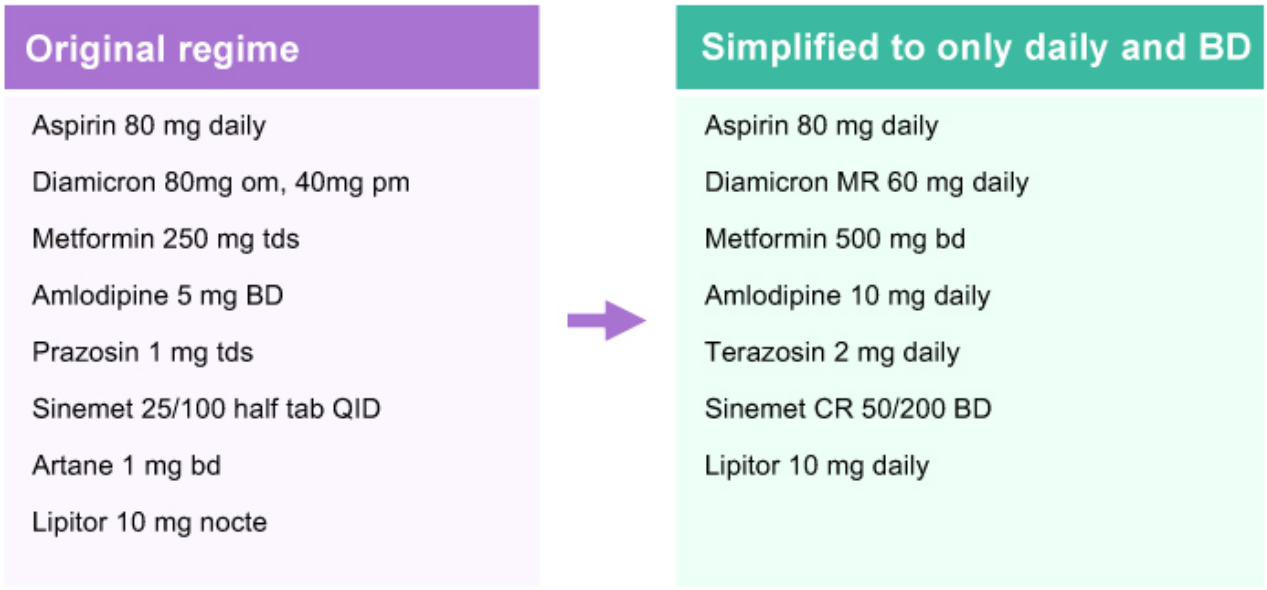
- 80 years old man, walk with stick, live alone.
- Past history: HT, Hyperlipidemia, dementia, DM, parkinsonism, BPH.
- Seeing different private doctors with drugs:
  - Aspirin 80 mg daily
  - Diamicron 80mg om, 40mg pm
  - Metformin 250 mg tds
  - Amlodipine 5 mg BD
  - Prazosin 1 mg tds
  - Sinemet 25/100 half tab QID
  - Artane 1 mg bd
  - Lipitor 10 mg nocte
- Patient admitted to hospital due to hyperglycaemia (hstix >20), malaise and polyuria.
- Blood test show HbA1c 9.5%, fasting blood sugar 12.
- Patient said he frequently forgot to take drugs especially those need to take more than 2 times per day.
- He has poor cognitive function with MoCA 5/30 (dementia range).
- No one alone to supervise him in taking medications.
- Geriatrician was consulted.

If you were the Geriatrician, what are your actions?

Let's consider drug review to simplify the drug regime, referral to community services and use medication tools!

- Drugs regimes were modified to limit to QD and BD.

  An example of how to modify drug regime to enhance adherence:



- Patient was referred to ICDS (Integrated Care and Discharge Support) program with case manager to do home visit to monitor his drug compliance.
- Drug box was given to patient by ICDS case manager to enhance adherence.

➔ Patient drug adherence improved & DM control became satisfactory.

Medication errors in institutional setting

Case 1

- 90 years old lady, bedbound, no relative, live in a small private RCHE without CGAT.
- Past history: CVA with vascular dementia, HT, renal impairment but no history of DM.
- Clinical Frailty Scale 8.
- Dysphagia, requiring puree as diet.
- Admitted to acute hospital due to hypoglycemia (Hstix 1.5 in ambulance).
- Immediately given D50 injection, put on dextrose infusion to maintain euglycaemia in ward for 3 days.
- Toxicology screening showed gliclazide (Diamicron) in blood.
- Review history again – patient had no DM and was NOT on any DM drugs.
- There were other residents in RCHE on DM drugs but they were not her roommates.
- The RCHE staff denied wrong medications given to index patient.

Can you guess what is happening?

- Results after thorough investigation:
    - Contamination of the mortar in RCHE which was used to grind the drug tablets

Mortar for grinding tablets

    - It was likely that there was Diamicron residue left on the mortar which belonged to other residents. When the staff grinded the tablets of the index resident, the drugs were contaminated by Diamicron residue of the previous residents.
    - Since the index resident had anorexia of ageing with poor intake, a small amount of Diamicron could lead to florid hypoglycaemia!

    - It often takes at least a few days for hypoglycaemia to improve as the half-life of Diamicron is prolonged in renal impaired older patients.
- The patient hypoglycaemia finally subsided after 3 days in hospital à discharge back to RCHE.
- RCHE staff practice was reviewed by CGAT nurses & advised to:
    - Buy more mortars so that each resident has its own mortar.
    - Use a paper to hold the drugs during grinding to minimize contamination of the mortar. Staff has to make sure no drug residues are left on the mortar before grinding tablets of other residents.
- Outcome
    - No more drug contamination incident in that RCHE.
    - Experience is shared with other RCHEs to avoid similar mistakes happening in other RCHEs.

Consideration in medication management in dementia person

Case 1

- A 90-year lady with advanced dementia, BPSD and delusional ideas. She always thought her daughter wanted to poison her, so she refused to take oral medications. She had Parkinson disease and Alzheimer's disease. She was on Sinemet 25/100 mg half tab BD and donepezil 5 mg daily.
- After discussion with Geriatrician about this problem,
    - oral Sinemet and donepezil were stopped.
    - PD drugs change to rotigotine transdermal patch once daily.
    - Donepezil changes to rivastigmine transdermal patch once daily.
- The patient accepted the use of transdermal patch without drug non-adherence. It also reduced carer stress as the daughter did not need to struggle to give oral medicine to patient.

Lesson to learn for dementia

- We need to understand the situation of each dementia patient.
- Personalized approach is needed to overcome the drug management problem in these patients.
- Make use of transdermal route (if available) if appropriate for selected patients.

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