

# Concerns about medicines with anticholinergic side effects

Dr David Branford

Chair

English Pharmacy Board

Royal Pharmaceutical Society

# Parasympathetic Nervous System

- ▶ A main part of the autonomic nervous system
- ▶ Responsible unconscious regulation internal organs & glands.
- ▶ Numerous effects in body and brain
- ▶ Bladder, vision, heart, bowels, blood pressure, memory

# Anti-cholinergic Effects

- ▶ Chemical - acetyl choline - common constituent of mushrooms
- ▶ Many drugs work against acetyl choline - anti-cholinergic effect
- ▶ Medicines that have anticholinergic activity include anti-depressants, cardiac meds, OTCs, anti-histamines
- ▶ In brain anti-cholinergic effect results in confusion
- ▶ Research - impact of “anti-cholinergic” polypharmacy on dementia

# MRC Study

- ▶ With colleagues developed scale to assess anti-cholinergic activity of medicines - called Anti-cholinergic Burden (ACB) (Boustani et al, 2008)
- ▶ Scale examine MRC database 13,004 older people in UK (Fox et al, 2011a)
- ▶ How many people taking anti-cholinergics
- ▶ Impact total ACB memory (cognitive impairment) and mortality

# MRC Study - Key Results

- ▶ 48% older people taking meds anti-cholinergic activity
- ▶ Worsen memory (as expected)
- ▶ Associated increased death rate (first signal)
- ▶ Didn't proof causality



# Drugs on the Anticholinergic Burden (ACB) scale

ACB Score 1 (mild)	ACB Score 2 (moderate)	ACB Score 3 (severe)
Alimemazine	Amantadine	Amitriptyline
Alprazolam	Belladonna alkaloids	Amoxapine
Alverine	Carbamazepine	Atropine
Atenolol	Cyclobenzaprine	Benztropine
Beclometasone dipropionate	Cyproheptadine	Chlorpheniramine
Bupropion hydrochloride	Loxapine	Chlorpromazine
Captopril	Meperidine	Clemastine
Chlorthalidone	Methotrimeprazine	Clomipramine
Cimetidine hydrochloride	Molindone	Clozapine
Clorazepate	Oxcarbazepine	Darifenacin
Codeine	Pethidine hydrochloride	Desipramine
Colchicine	Pimozide	Dicyclomine
Dextropropoxyphene		Diphenhydramine
Diazepam		Doxepin
Digoxin		Flavoxate
Dipyridamole		Hydroxyzine
Disopyramide phosphate		Hyoscyamine
Fentanyl		Imipramine
Fluvoxamine		Meclizine
Furosemide		Nortriptyline
Haloperidol		Orphenadrine
Hydralazine		Oxybutynin
Hydrocortisone		Paroxetine
Isosorbide preparations		Perphenazine
Loperamide		Procyclidine
Metoprolol		Promazine
Morphine		Promethazine
Nifedipine		Propentheline
Prednisone/Prednisolone		Pyrilamine
Quinidine		Scopolamine
Ranitidine		Thioridazine (withdrawn)
Theophylline		Tolterodine
Timolol maleate		Trifluoperazine
Trazodone		Trihexyphenidyl
Triamterene		Trimipramine
Warfarin		

# Recent research on anticholinergics

- ▶ Researchers studied participants in the Adult Changes in Thought (ACT) study conducted in the Seattle area (JAMA Internal Medicine, online, Jan. 26, 2015). These were older people enrolled in an integrated health care delivery system called Group Health. Over 3,000 individuals were included in the research, and none had dementia when they entered the study starting in 1994.
- ▶ Scientists tracked their drug use and cognitive function over the next two decades. The higher the dose of anticholinergic drugs and the longer such medications were taken, the greater the risk of dementia. In this study the most common anticholinergic drugs were antihistamines found in over-the-counter allergy drugs and night time pain relievers, antidepressants that are also prescribed for nerve pain and medications prescribed to treat incontinence or symptoms of overactive bladder. The authors conclude:
- ▶ “Higher cumulative anticholinergic use is associated with an increased risk for dementia. Efforts to increase awareness among health care professionals and older adults about this potential medication-related risk are important to minimise anticholinergic use over time.”

# Which of the following do you think DAA should advocate?

- a) All medicines with anticholinergic side effects should be banned
  - a) Yes or no
- b) There should be a warning in the product leaflets suggesting that people over 60 have an increased risk of memory problems
  - a) Yes or no
- c) Over the counter medicines with anticholinergic side effects should not be on general self selection and moved into the Pharmacy only category (P)
  - a) Yes or no
- d) Over the counter medicines with anticholinergic side effects should not be on general self selection and moved into the Prescription only category (POM)
  - a) Yes or no



# What did Professor Grey say ?

- ▶ Urges people not to stop their therapy based on the findings of this study - they should talk to their health care provider, and also tell them about all their over-the-counter drug use.
- ▶ "Health care providers should regularly review their older patients' drug regimens - including over-the-counter medications - to look for chances to use fewer anticholinergic medications at lower doses,"
- ▶ If providers need to prescribe anticholinergics to their patients because they offer the best treatment, then "they should use the lowest effective dose, monitor the therapy regularly to ensure it's working, and stop the therapy if it's ineffective,"
- ▶ Although the link between raised risk of dementia and anticholinergics has been found before, the new study uses more rigorous methods - including over 7 years of follow-up - to establish the strength of the link. By accessing pharmacy records, the researchers were also able to include non-prescription use of anticholinergics in their data.
- ▶ It is also the first study to show a dose-response effect, note the authors. That is, the higher the cumulative amount of drug taken, the higher the risk of developing dementia.
- ▶ And another first for the study, is that it also shows that dementia risk linked to anticholinergics may persist long after people stop taking the drugs.