

What is “Anticholinergic Burden”?



- * In the brain, acetylcholine is one of the key neurotransmitters involved in learning and memory
- * It is the main neurotransmitter implicated in Alzheimer's Disease

What is “Anticholinergic Burden”?

- * Anticholinergic (AC) drugs are used in many different conditions, such as Parkinson's disease, depression, nausea and vomiting, COPD and pain
- * “Anticholinergic Burden” is the consequence of taking multiple medications with anticholinergic potential:
 - * It is the cumulative effect of using multiple drugs with anticholinergic effects
 - * The adverse AC effects increase with increasing drug dose.
 - * Multiple low-level AC drugs can add up to the same burden as (or more than) a single high-level AC drug.

What is “Anticholinergic Burden”?

- * Individuals with cognitive impairment / early dementia are especially vulnerable to the effects of AC drugs, with research showing a high AC Burden can lead to an increase in confusion, falls and mortality.

Regenstrief Institute

SEARCHED 10/11/2019

First study to see if de-prescribing commonly used drug class prevents or delays dementia

Regenstrief researcher receives \$3.3 million NIA award for cause and effect study

Regenstrief Institute research scientist, Dr. Caroline R. Reynolds MD, has received a five-year \$3.3 million award from the National Institute on Aging (NIA) to conduct the first clinical trial designed to determine if anticholinergic (AC) drugs are a cause of dementia.

Anticholinergics:
A class of harmful drugs that includes some types

Two year longitudinal study by Fox et al (2011) looked at 13000 adults over 65yrs. At baseline, 47% of participants were taking medication with possible anticholinergic properties; 4%, definite properties.

Key findings:

- * **20% those taking drugs with total AC Burden score of 4+ had died by end of 2 year study**, compared with 7% of those taking no AC drugs
- * For every additional AC Burden point, **odds of dying increased by 26%**
- * Those taking drugs with combined **AC Burden of 5+ scored 4% lower in cognitive function test** than those taking no AC drugs
- * Increased risks of AC drugs shown to be cumulative – based on number of drugs and strength of each drug's effect.
- * Those who were older, lower social class, and greater number of health conditions tended to take the most AC drugs.

Measuring AC Burden

- * There is no single standard AC Burden scale to aid measurement of anticholinergic burden.
- * <http://www.acbcalc.com/>
 - * an online tool which calculates AC Burden quickly
 - * Uses drop-down lists for drugs – CAUTION!



Measuring AC Burden – Anticholinergic Risk Scale

- * (ARS; Rudolph et al, 2008)
 - * 500 most prescribed drugs reviewed
 - * Geriatrician and pharmacists
 - * “..estimating the extent to which an individual patient may be at risk of anticholinergic adverse events”
- * 49 drugs rated according to anticholinergic potential
- * Scale 0 (nil potential) to 3 (very strong potential)
- * High ARS scores = adverse anticholinergic effects

Measuring AC Burden

- * ARS modified – mARS (Sumukadas et al, 2014)
- * Inc. newer drugs available in UK
- * Exc. drugs not available in UK
- * Medications rated as “moderate-severe risk” on other scales included; those listed in BNF as having significant anticholinergic properties included

Measuring AC Burden – Anticholinergic Cognitive Burden scale

- * (ACB; Boustani et al, 2008)
- * Identifying severity of adverse reactions of AC drugs, particularly on cognition
- * Systematic review of medical literature looking at drugs with known AC effects
- * 88 drugs, ranked 0-3 based on severity of effect

Measuring AC Burden

- * ARS was found to be more specific than ACB in “capturing medication associated with a higher degree of cognitive and functional impairment” (Pasina et al, 2013)
- * Both scales supported the hypothesis that cumulative effects of AC drugs have a negative impact on the functioning of older adults.

Measuring AC Burden: Modified Anticholinergic Risk Scale (mARS)

- * Gives AC rating for a range of drugs in the following classes:
 - * Antidepressants
 - * Antipsychotics
 - * Nausea & vertigo
 - * Urinary antispasmodics
 - * Sedative
 - * Anti-allergics
 - * H2 blockers
 - * Anti-parkinson
 - * “Other”

Drugs to consider... Antidepressants

Drug	mARS score
Amitriptyline; Imipramine	3
Sertraline; Clomipramine, other TCAs	2
Trazadone; Mirtazapine; Paroxetine; Lofepramine	1
Venlafaxine; Duloxetine; Trazadone	Little or nil AC activity

Drugs to consider... Antipsychotics

Drug	mARS score
Chlorpromazine; Trifluoperazine; Thioridazine	3
Clozapine; Olanzapine	2
Quetiapine; Risperidone; Haloperidol	1
Aripiprazole	Least anticholinergic

Drugs to consider... Nausea

Drug	mARS score
-	3
Prochlorperazine	2
Metoclopramide	1
Domperidone	Alternative

Drugs to consider... Urinary anti-spasmodics

Drug	mARS score
Oxybutinin	3
Darifenacin; Dosulepine; Solifenacin; Tolteridone	2
-	1
Mirabegron	Alternative (different drug class); assess ongoing need for tx

Drugs to consider... Anti-allergics

Drug	mARS score
Chlorphenamine	3
Cetirizine; Loratidine	2
-	1
	Desloratadine may be an alternative.

Drugs to consider... H2 blockers

Drug	mARS score
-	3
Cimetidine	2
Ranitidine	1
PPIs	Alternative

Drugs to consider... Parkinson's medication

Drug	mARS score
Procyclidine	3
Amantadine	2
Levodopa; Carbidopa; Selegiline; Entacapone; Pramipexole	1
	No alternative suggested

Drugs to consider... Others

Drug	mARS score
Atropine; Dicyclomine; Orphenadrine; Tizanidine	3
Loperamide; Tiotropium Pseudoephedrine; Baclofen; Propiverine	2
Methocarbamol; Reboxetine	1

The Project – Expectations

“Patients with a high mARS score (3+) will have evidence of (increased) cognitive impairment and/or increased risk of falls”

A two-part scoping exercise:

- * A retrospective review of referrals to OPMH, where reason for referral was “cognitive impairment”
- * A review of 30 random drug charts from MOPRS
- * Both exercises were to explore whether there was correlation between mARS score, falls and cognitive impairment.

The Project – findings so far: retrospective referral review

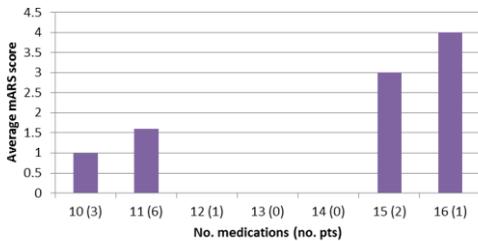
65 referrals for “cognitive impairment” in 3month period (Jan-Mar 2018); 27 referrals did not lead to assessment.

- * 45 F; 20 M
- * Average age = 83yrs

Of the 38 pts assessed:

- * 66% had cognitive impairment/dementia noted
- * 73% had hx of falls
- * Average no. medications prescribed = 7
- * Nearly half scored against mARS

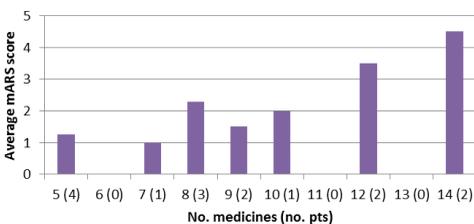
No. medications vs. mARS score



The Project – findings so far: drug chart review

- * 30 drugs charts reviewed; 15 F, 15 M
- * Average age = 87yrs
- * 43% had a diagnosis of cognitive impairment/dementia noted
- * 56% had hx falls
- * Average no. medications prescribed = 7
- * 50% scored against mARS

No. Medications vs. mARS Score



“Patients with a high mARS score (3+) will have evidence of (increased) cognitive impairment and/or increased risk of falls”

Referral review	score
68 patient histories reviewed:	2
11 individuals had:	2
- cognitive impairment identified plus high falls risk	3
- mARS score 2+	2
- no. medications ranging from 2-15	3
- from MH perspective, all were px at least one psychotropic drug	2
3 of the 11 individuals had:	2
- mARS score 3+	2
- no. medications ranging 7-15	6
	2

Case Review

78yr old lady

- * History of "recurrent depression"
- * Admitted with reduced mobility, "?drug-induced Parkinsonism" & polypharmacy
- * Physical health:
 - * Type 2 diabetes
 - * Peripheral vascular disease
 - * CKD 3a
 - * Hypothyroidism
 - * Ureteric stent
 - * Overactive bladder
 - * Constipation
 - * Recurrent UTIs
 - * Gastro-Oesophageal Reflux Disease

Current medication:

- * ATORVASTATIN 10mg nocte
- * PRIADEL (LITHIUM) MR 400mg nocte
- * AMITRIPTYLINE 30mg nocte
- * VENLAFAXINE MR 112.5mg od
- * FLUPENTIXOL 500mcg tds
- * LEVOTHYROXINE 150mcg mane
- * LANSOPRAZOLE 30mg mane
- * CHLORPROMAZINE 50mg nocte
- * BETAHISTINE 8mg tds
- * MOVICOL 2sachets bd
- * INSULIN as directed
- * SENNA 15mg nocte
- * LINAGLIPTIN 5mg od
- * ASPIRIN 75mg mane
- * SOLIFENECIN 10mg mane
- * GAVISCON ADVANCE 5-10mls tds
- * COLECALCIFEROL 3200units od
- * LOPERAMIDE 2mg prn, max bd

Case Review

"Offending" drugs (mARS score):

- * AMITRIPTYLINE (mARS=3)
 - * Tricyclic antidepressant
- * CHLORPROMAZINE (3)
 - * Antipsychotic
- * VENLAFAXINE (1)
 - * Antidepressant
- * SOLIFENECIN (3)
 - * Antimuscarinic for unstable bladder

OPMH Management plan:

- * Reduce and stop CHLORPROMAZINE
- * Reduce and stop AMITRIPTYLINE
- * Alternative to SOLIFENECIN can be used from different class of drug, e.g. MIRABEGRON

Recommendations (PrescQIPP, 2016)

B140 | July 2016 | 2.1

PrescQIPP
Community Interest Company

Anticholinergic drugs

This project reviews appropriate treatment with anticholinergic drugs. An increasing number of systematic reviews and meta-analyses report that drugs with anticholinergic effects are associated with

Recommendations (PrescQIPP, 2016)

- * Identify those taking anticholinergic drugs
- * Minimise their use where possible
 - * If on medication with mARS score of 2 or 3, or on a range of drugs that add up to a score of 3 or more, should be discontinued or switched to alternative
- * Review regularly for efficacy/tolerance
- * Review in older people who have had a fall/at high risk of falls (multifactorial risk assessment)

Recommendations cont.

- * In patients with dementia/cognitive impairment:
 - * Medication review – identify and minimise drugs which may exacerbate cognitive impairment
 - * If AC induced cognitive impairment suspected, conduct cognitive assessment (MMSE/MOCA) and consider switching/stopping treatment if confirmed/clinically appropriate
 - * Avoid prescribing anticholinergics with Acetylcholinesterase Inhibitors

What next?

- * Teaching session completed with junior pharmacists
- * To raise awareness with junior doctors
- * Trial project to embed measurement of ACB in the patient assessment pathway in PHT, and to assess its impact
- * To publish...



Shameless plug...

Prescribing for Mental Health (Closed Facebook group)

<https://www.facebook.com/groups/283868562285867/>

A forum for Non-Medical Prescribers to discuss practice in the diverse field of mental health. We have much experience and skill in our chosen specialties, and this is a great platform to share with fellow NMPs.

We have members from across the country, and this is an invitation for you to join us!

Engagement and discussion in the forum can be used toward CPD.



References

- Boustani, M. et al, 2008, Impact of anticholinergic drugs on the ageing brain: a review and practical application. *Ageing Health*; 4(3):11-20
- Fox, C., Livingstone, G., Maidment, I.D. et al, 2011, The impact of anticholinergic burden in Alzheimer's Dementia –the Laser-AD study. *Age Ageing*; 40: 730-5
- Pasina, L. et al, 2013, Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalised elderly: comparison of the Anticholinergic Cognitive Burden Scale and Anticholinergic Risk Scale. *Drugs Ageing*; 30: 103-112
- PrescQIPP, July 2016, "Anticholinergic Drugs", B140; 2.1 <https://www.prescqipp.info/media/1017/b140-anticholinergics-drugs-21.pdf>
- Rudolph, J. et al, 2008, The Anticholinergic Risk Scale and anticholinergic adverse effects in older persons. *Archives Intern Medicine*; 168 (5): 508-513
- SIGN, (2015), Polypharmacy Guidance http://www.sign.ac.uk/pdf/polypharmacy_guidance.pdf
- Sumukadas, D. et al, 2014, Temporal trends in anticholinergic medication prescription in older people: repeated cross-sectional analysis of population prescribing data. *Age & Ageing*; 42: 515-521