AntiCholinergic Burden score on medication prescribing in a psychiatric geriatric assessment unit

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BACKGROUND

Drugs with anticholinergic side effects are commonly used in many branches of medicine, sometimes unwittingly. It has recently been claimed that anticholinergic activity in the elderly may shorten life and lead to a worsening of cognitive function.⁽¹⁾ The anticholinergic burden (ACB) is a new tool from the work that allows the potential impact of medication to be estimated. We thought it fit to examine our own prescribing practice and calculate the ACB in the light of this claim (see appendix 1 for the ACB scoring system).

The aims of the audit were:

- to find out the ACB score of individual patients in Altham Meadows Assessment Unit
- to link the ACB score of each patient with their cognitive function (Mini-Mental State Examination (MMSE))

METHODOLOGY

Altham Meadows is an organic assessment unit for individuals over 65 years in age. All patients present on 15 July 2011 at Altham Meadows were included in the audit study audit approval.

A comprehensive table was devised in order to capture salient information, and scoring of each medication that each patient was taking was conducted using results presented by a 2008 study.⁽²⁾ Scoring was further divided into showing the ACB score from psychotropic medication and non-psychotropic medication; and the total ACB score was recorded.

RESULTS

When this study was carried out, ten patients were present on the ward at Altham Meadows, of whom 50% were male, 50% female. Ages ranged from 50-90 years (see figure 1 for age breakdown). In all patients, the higher ACB score came from non-psychotropic medication.

Within our study cohort, six patients had ACB scores greater than four. The ACB total score was then compared to that individual's MMSE score to illustrate a snapshot of cognitive function. Tables 1 and 2 show the relationship between cognitive impairment (low MMSE) and ACB.

ACB score from psychotropic medication	ACB score from other medication	Total ACB score	MMSE score
3	6	9	20
4	5	9	9
3	6	9	24
1	6	7	7
1	4	5	15
2	2	4	12
0	3	3	10
0	1	1	14
0	1	1	27
0	0	0	14

Table 1 ACB scores from the ten participants, sorted by 'Total Score'

ACB score from psychotropic medication	ACB score from other medication	Total ACB score	MMSE score
0	1	1	27
3	6	9	24
3	6	9	20
1	4	5	15
0	1	1	14
0	0	0	14
2	2	4	12
0	3	3	10
4	5	9	9
1	6	7	7

Table 2 ACB scores from the ten participants, sorted by 'MMSE Score'

DISCUSSION

Fox *et al* analysed data from a two-year longitudinal study of participants enrolled in the Medical Research Council's Cognitive Function and Ageing Study between 1991 and 1993.⁽¹⁾ The study looked at the prescribed drugs and drugs bought over the counter by more than 13,000 people aged 65 and over between 1991 and 1993 and found that over half of 65s were taking at least one drug with anticholinergic effect.

Fox emphasised the potential danger of ACB scores above four, so we have reflected on our own practice in this respect. Fox has stated that in patients with scores above or equal to four, mortality rate increases.

- 1 in 5 died within two years, whereas it was 1 in 14 of those who took no drugs with anticholinergic effects
- with every additional ACB point the risk of dying increases by 26%
- ACB scores above five were found to have lower cognitive function (impaired concentration and driving ability)
- in those already experiencing cognitive impairment, worsening of memory problems or depression occurred

Fox measured cognition using the MMSE, with each participant being administered the MMSE at baseline screening and at the follow-up assessment. Each participant's ACB was calculated using the anticholinergic cognitive burden scale.

Drugs were quantified as having anticholinergic properties using the following methods:

- serum radioreceptor anticholinergic activity assay (SAA)
- *in vitro* measurement of drug affinity to muscarinic receptors
- expert-based list of medications with anticholinergic activity
 - this is the most clinically useful way to measure cognitive or central anticholinergic effects of drug but the least standardised method

The scale was developed through a systematic review of the literature to identify drugs with documented anticholinergic activity. Content validity was tested by presenting the list to an expert interdisciplinary panel of geriatricians, pharmacists, geriatric psychiatrists, general physicians, specialist geriatric nurses, and aging-brain researchers.

Each drug was then given an ACB score on the basis of strength of anticholinergic activity (see appendix 2). The accumulative ACB score for each patient was then calculated.

Acetylcholine (ACh) has central and peripheral effects. Central actions are understood in terms of arousal and reward, association with memory, rapid eye movement (REM) sleep, enhanced sensory perception, and sustained attention. ACh peripheral effects include skeletal muscle contraction. It is a major neurotransmitter in the autonomic nervous system, and has an action on the muscarinic receptor to inhibit contraction of cardiac muscle (in particular, the M2 receptor to slow heart rate, reduce contractile forces of atrium and reduce conduction velocity of AV node).

There are three subtypes of muscarinic receptor, known as M1, M2, and M3. The actions of different drugs vary between receptor subtypes. The M1 receptor is a centrally acting receptor. Antagonism of the M1 receptor is most likely to be associated with changes in cognition. The presence of the blood-brain barrier shields the M1 receptor population from

certain types of drugs: molecular size and lipid solubility determine passage across the barrier.

The following anticholinergic effects on the body are listed:

- dry mouth
- dry eyes
- mydriasis, leading to:
 - blurred vision
 - exacerbation of glaucoma
- increased heart rate
- dry warm skin and/or flushing
- difficulty emptying bladder
- constipation
- headaches
- confusion

Elderly people have high exposure to anticholinergic drugs due to high medical co-morbidity and their use of multiple prescribing and over-the-counter medication use. They are very sensitive to developing anticholinergic-related cognitive impairment due to the ageing process. This is a consequence of age-related decline in hepatic and renal drug metabolism and an increase in blood-brain barrier permeability. The ageing process also causes a reduction in central cholinergic activity, and this process may underlay age-related changes in cognition.

It is important for the clinician to be aware how many drugs actually have anticholinergic properties as side effects. Drugs with such actions include: antihistamines, antidepressants, antihypertensives (eg atenolol, nifedipine), diuretics (eg furosemide), anti-emetics (eg hydroxyzine, scopolamine etc.), anticoagulants (eg warfarin), analgesics (eg codeine, dextropropoxyphene, pethidine), even medication for epilepsy (carbamazepine), antispasmodic (oxybutynin), eye drops (timolol) for glaucoma and bronchial dilator (beclomethasone) have anticholinergic properties.

In our audit, six patients had ACB scores of four and above, and in all patients a higher ACB score has come from non-psychotropic medication. In terms of showing correlation between total ACB score and effect of MMSE, no correlation was noted; this may be due to the fact that individuals residing in Altham Meadows already had some deterioration in cognitive function prior to being admitted. It would be useful to carry out the ACB assessment on individuals scoring high MMSE scores and conduct a longitudinal study to assess change in cognitive function on the initiation of prescribing an anticholinergic.

NEXT STEPS

As a result of conducting this audit, and in the spirit of implementing good practice, ACB scoring is now being implemented in Oakland Unit, which is a functional assessment unit for patients over 65 years, the aim of which is to minimise the ACB score to <4.

Action plan

1. ACB score chart⁽²⁾ should be available when medications are initiated or reviewed.
2. Review patients' psychotropic **and** non-psychotropic medication in inpatient/outpatient (community) and assess as per ACB score.

3. Review patients' health needs for the medication.
4. Liaise with the general practitioner or specialist if the non-psychotropic medication (especially high scoring) could be stopped or changed to drug with nil or low ACB score or any other non-pharmacological intervention.
5. Re-audit at Altham Meadows in one year's time.
6. As other researchers have pointed out that anticholinergic activities of several medications can impair cognitive functions this prompts the psychiatrist to scrutinise each patient's medication and using the ACB tool offers a good method to carry out this assessment.

REFERENCES

1. Fox C, Richardson K, Maidment I, et al. Anticholinergic Medication Use and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study. *J Am Geriatr Soc* 2011;59(8):1477-83
2. Boustani M, Campbell N, Munger S, Maidment I, Fox C. Impact of Anticholinergics on the Aging Brain: a review and practical application. *Aging Health* 2008;4(3):311-20

Commentary ...

Chris Coldwell is a consultant anaesthetist who has a special interest in pre-operative assessment. He has written material for the Royal College of Anaesthetists that teaches anaesthetists about the management of dementia.

The local work by Shukla examining the anticholinergic burden (ACB) of medications of patients in the Altham Meadows Unit emphasises the importance of considering the role of medications in patients with reduced cognitive functioning. Despite Shukla's small study numbers, the point is made that the ACB of these patients is not inconsiderable, with all but one of his patients taking a medication with anticholinergic effects.

The bottom line in Fox's work was that his study of 13,004 over-65s showed that the use of medications with anticholinergic actions was associated with increased mortality and a decline in Mini-Mental State Examination (MMSE) over a two-year period, even after adjusting for co-morbidities.

As an anaesthetist, there has always been an implicit understanding that anticholinergic side-effects are 'bad'. The routine use of premed anticholinergics as antisialogogues rapidly disappeared

when ether did. The general unpopularity of pethidine amongst anaesthetists (derided as an 'emetic with an incidental side-effect of mild analgesia') and such adages as 'a slow heart is a happy heart' show the disdain with which these drugs as a whole are held by the anaesthetic community. The insistence that atropine continues to be used in ALS protocols has long been a bug bear of many anaesthetists who have always been taught to use glycopyrrolate for bradycardia instead, as it does not cross the blood-brain barrier and hence causes less central effects such as postoperative confusion. It is interesting then that the group of doctors who have traditionally had most influence over the autonomic nervous system and acetylcholine on a day-to-day basis, namely anaesthetists, were not asked for their opinions on what constituted an anticholinergic drug in Fox's original work.

The list of medications which Fox *et al* considered to have anticholinergic effects is a long one and includes drugs from most specialities, some of which are more obvious than others. It would do most prescribing readers no harm to remind themselves of the drugs which have anticholinergic properties and bear in mind the messages from these articles!

APPENDICES

Appendix I – The ACB scoring system

Score		
0	No effect	Drugs with no anticholinergic effects
1	Mild effect	Drugs with possible effects (demonstrated by SAA or <i>in vitro</i> affinity to muscarinic receptor but with clinically relevant negative cognitive effects)
2	Moderate effect	Drugs with established and clinically relevant cognitive anticholinergic effects
3	Severe effect	Drugs with established and clinically relevant cognitive anticholinergic effects. In addition delirium (due to crossing blood-brain barrier)

Appendix 2 – Anticholinergic study drug list

Drugs on the Anticholinergic Burden (ACB) scale

(A total ACB scale score of three or more is considered clinically relevant)

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

Notes:

1. Certain medicines eg Risperidone (mild ACB), Quetiapine (severe ACB) and Olanzapine (severe ACB) were licensed after 1990 and therefore not prescribed to the original CFAS cohort.
2. Brand names may conceal generic drug names.
3. Some combination medicines contain anticholinergic drugs.
4. This list is indicative and some related medicines were taken by patients in the CFAS study; if appropriate these related medicines were given an ACB score based on the ACB of the related medicine in the Aging Health publication (see below).

References:

1. Boustani MA, Campbell NL, Munger S, Maidment I, Fox GC. Impact of anticholinergics on the aging brain: a review and practical application. *Aging Health*. 2008;4(3):311-20.
2. Campbell N, Boustani M, Limbil T, Ott C, et al. The cognitive impact of anticholinergics: a clinical review. *Clinical Interventions in Aging*. 2009;4(1):225-33

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GEORGE CUP RESULT 2011

This year's George Cup Golf Competition was held on Saturday, 9 July, at Morecambe Golf Club, in glorious conditions.

The competition results are as follows:

The George Cup

Dr Andrew Whitton 38 points
Dr Mike Bird 33 points
Dr Mel John 30 points

The John Wilkie Quaiche

Dr John Yarnall 17 points

The Phil Allen Plate

Ms Debbie Torr 21 points

The Freend's Silla

Mr David Lavelle 34 points

Hopefully, next year's competition will be held at Bentham Golf Club.

Andrew Whitton
Golf Secretary