

THE TABLET: PALLIATIVE CARE PHARMACY TIPS



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TODAY'S TOPIC: Anticholinergic Burden in Palliative Care

Background:

Anticholinergic medications competitively inhibit acetylcholine and have known side effects: drowsiness, urinary retention, constipation, dry mouth, confusion, flushing (not all-inclusive). The side effects can be cumulative when more than one anticholinergic medication is used. Articles below discuss this through screening tools such as drug burden index (DBI) or anticholinergic cognitive burden scale (ACB). These are two ways to assist with quantifying the risk with multiple anticholinergic medications. Increased anticholinergic burden is known to put patient's at higher risk for poor outcomes (falls, morbidity, adverse drug events). Palliative care patients are at higher risk for unintended side effects of anticholinergic use given their medical comorbidities and higher risk for polypharmacy.

Table 1. Anticholinergic cognitive burden scoring of drugs

Score 1	Score 2	Score 3
Alimemazine	Amantadine [†]	Amitriptyline ^{* †}
Alverine	Belladone alkaloids	Amoxapine
Alprazolam [†]	Carbamazepine [†]	Atropine ^{* †}
Atenolol	Cyclobenzaprine ^{* †}	Benztrapine ^{* †}
Brompheniramine maleate	Cyproheptadine [†]	Brompheniramine [†]
Bupropion hydrochloride	Empracet	Carbinoxamine [†]
Captopril [†]	Loxapine [†]	Chlorpheniramine [†]
Chlorthalidone [†]	Meperidine [†]	Chlorpromazine ^{* †}
Cimetidine hydrochloride	Methotrimeprazine [†]	Clemastine [†]
Ranitidine [†]	Molindone [†]	Clomipramine [†]
Clorazepate [†]	Oxcarbazepine [†]	Clozapine [†]
Codeine [†]	Pethidine hydrochloride	Darifenacin [†]
Colchicine	Pimozide [†]	Desipramine [†]
Coumadin		Dicyclomine ^{* †}
Diazepam [†]		Dimenhydrinate [†]
Digoxin [†]		Diphenhydramine ^{* †}
Dipyridamole [†]		Doxepin [†]
Disopyramide phosphate		Flavoxate [†]
Fentanyl [†]		Hydroxyzine ^{* †}
Furosemide [†]		Hyoscyamine ^{* †}
Fluvoxamine [†]		Imipramine ^{* †}
Haloperidol [†]		Meclizine ^{* †}
Hydralazine [†]		Nortriptyline [†]
Hydrocortisone [†]		Olanzapine
Isosorbide [†]		Orphenadrine [†]
Loperamide [†]		Oxybutynin ^{* †}
Metoprolol		Paroxetine
Morphine [†]		Perphenazine
Nifedipine [†]		Procyclidine [†]
Prednisone [†]		Promazine
Quinidine		Promethazine ^{* †}
Risperidone [*]		Propentholine [†]
Theophylline [†]		Pyrilamine [†]
Trazodone [*]		Quetiapine
Triamterene [†]		Scopolamine [†]
		Thioridazine ^{* †}
		Tolterodine [†]
		Trifluoperazine [†]
		Trihexyphenidyl ^{* †}
		Trimipramine [†]

A total Anticholinergic

* The same score given by Anticholinergic Risk Scale¹³; †The same score given by Anticholinergic Drug Scale¹².
Table with permission from Boustani M, Campbell N, Munger S, et al. Impact of anticholinergics on the aging brain: a review and practical application. Aging Health. 2008; 4:311-20.¹²

Importance:

It is important for palliative care clinicians to be aware of medications with anticholinergic properties to 1) assist with appropriate monitoring for cumulative effects and 2) identify potential candidates for deprescribing to minimize the risk for adverse drug events.

The Literature:

[Eur J Clin Pharmacol. 2020 Mar;76\(3\):319-335.](#)

Association between anticholinergic drug burden and mortality in older people: A systematic review

Results: N=27 studies (cross-sectional, nested case-control, 23 prospective or retrospective cohorts); most of "good" quality

- N=17 (63%) reported a positive correlation between anticholinergic burden and mortality
- 80% of studies had follow up period of 1 year or less
- Out of the 5 high-quality studies that met all domains of quality assessment criteria, 4 showed a positive association

[J Am Med Dir Assoc. 2021 Jan;22\(1\):56-64.](#)

Anticholinergic burden measures predict older people's physical function and quality of life: A systematic review

Results: N = 13 studies included, all rated moderate risk of bias

- 7/10 studies reported significant decline in physical function with increased anticholinergic burden
- 4/4 studies reporting on quality of life demonstrated decline in quality of life with increased anticholinergic burden

[Pharmacoepidemiol Drug Saf. 2021 Feb;30\(2\):144-156.](#)

Quantifying cumulative anticholinergic and sedative drug load among US Medicare Beneficiaries

Objective: Quantify drug burden index (DBI) drug exposure among older adults in the US
Methods: Retrospective cohort of Medicare beneficiaries (2013-2016) ≥ 66 years at the start of calendar year of interest

- Medications were categorized by geriatric, specialty-trained pharmacists
- DBI = daily dose / (daily dose + minimum recommended daily dose), ranging from 0-1
- Total drug burden is a sum of all DBI medications
- 0 < DBI ≤ 1 = low exposure, 1 < DBI ≤ 2 (medium exposure), DBI > 2 (high exposure)
- Factors associated with high DBI were younger age, female sex, high number of prescription fills, and white race.

CLINICAL PEARL: It is important to consider which medications may contribute to overall anticholinergic burden to avoid increased risk for medication-related adverse events when prescribing symptom medications for our palliative care population

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Results:

- Highest proportions of specific DBI medications were all sedatives: hydrocodone, gabapentin, tramadol

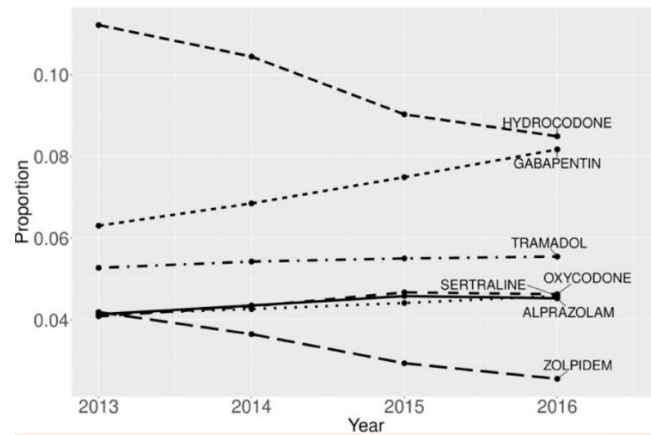


Figure: Temporal changes in the most commonly prescribed DBI medications

- Patient-level factors associated with high DBI exposure: high number of drug claims, white race, younger age, frailty, psychosis diagnosis code
- No changes in prevalence of any anticholinergic and/or sedative drug exposure were observed over the study period, although changes in types of medications in these classes

Conclusion: “Predictors of high DBI drug exposure can inform discussions between patients and providers about medication appropriateness and potential deprescribing”

[Palliat Med. 2009 Apr;23\(3\):257-65.](#)

Changes in anticholinergic load from regular prescribed medications in palliative care as death approaches

Objective: Quantify the anticholinergic burden of medications for comorbid disease, symptom control or medications that may be used for either indication in a palliative care population until death approaches

Methods: Secondary analysis of a previously presented RCT, utilized medications recorded at initial community-based reviews at initial referral, biweekly for 2 months and then at least monthly until death to calculate anticholinergic load (Clinician-Rated Anticholinergic Scale) as death approached

- As needed medications were excluded

Results: n = 461, average age 71(SD = 12), 91% cancer as life-limiting illness; known death date for N=304

- Dry mouth & difficulty concentrating were significantly associated with increasing anticholinergic load. Followed by hallucinations & confusion
- **Significant association of increasing anticholinergic load & decreasing functional status**

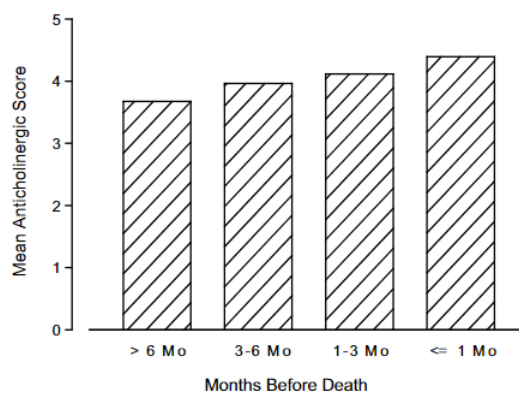


Figure 2 Mean total calculated anticholinergic score at time points (months) leading to death in 304 participants in a randomised controlled trial exploring improved models of service delivery in palliative care.

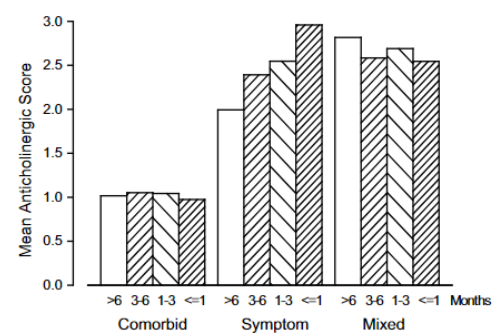


Figure 3 Mean total calculated anticholinergic score by three categories of prescribed medications at time points (months) leading to death in 304 participants in a randomised controlled trial exploring improved models of service delivery in palliative care.

Conclusion: “This study has documented in detail the longitudinal anticholinergic load associated with medications used in a palliative care population between referral and death, demonstrating the biggest contributor to anticholinergic load in a palliative care population is from symptom-specific medications, which increased as death approached.”

Bottom Line:

- Our patients are at high risk for higher anticholinergic burden given likelihood of polypharmacy (>5 medications) in our population
- Common effects of high anticholinergic burden are: confusion, hallucinations, dry mouth and constipation
- Anticholinergic burden is associated with increased morbidity and mortality
- Anticholinergic burden tends to increase as time to death shortens
- Most of the anticholinergic burden comes from symptom medications, many of which palliative care may be prescribing
- It is helpful to utilize references that quantify anticholinergic burden to identify potential candidates for deprescribing to reduce overall medication-related risks especially when prognosis is months to years as risks of anticholinergic use are seen in studies with follow up < 1 years

CLINICAL PEARL: It is important to consider which medications may contribute to overall anticholinergic burden to avoid increased risk for medication-related adverse events when prescribing symptom medications for our palliative care population