UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

New Literature: Prophylactic Scopolamine for Death Rattle

Background:

As part of the dying process, patients lose their ability to swallow and clear oral secretions. Noisy ventilations may be heard as air moves over the pooled secretions, otherwise known as death rattle, which can be distressing for patients' loved ones (more so than the patients themselves). We employ nonpharmacologic and pharmacologic treatment strategies to assist with the management of end-of-life secretions. Although evidence is questionable, we primarily utilize anticholinergic agents like hyoscyamine, glycopyrrolate, atropine, and scopolamine. Given that anticholinergics decrease the production of mucus, their use after the onset of death rattle may be less effective than prophylactic use. Anticholinergic medications also carry the risk of undesirable side effects such as delirium, constipation, urinary retention, palpitations, blurred vision, and sedation. Out of the agents listed above glycopyrrolate does not cross the blood brain barrier, therefore are less likely to cause sedation or delirium.

Importance:

Death rattle impacts our patients' families and caregivers perception of suffering at end of life. It is important for palliative care clinicians to be aware of the evidence for anticholinergics, such as scopolamine, use in our patient population for noisy respirations at end of life.

The Literature:

JAMA. 2021 Oct 5;326(13):1268-1276.

Effect of prophylactic subcutaneous scopolamine butylbromide on death rattle in patients at the end of life: The SILENCE randomized clinical trial

Objective: To determine if administration of prophylactic scopolamine butylbromide (SB) reduces death rattle

Methods: Multicenter (6 hospices), double bind, placebo-controlled trial; SB 20mg Subcutaneously (SUBQ) four times per day versus placebo once patient entered the 'dying phase'; adult patients with life expectancy of at least 3 days who were consentable, medication continued until death or if grade 2 death rattle occurred (treatment failure)

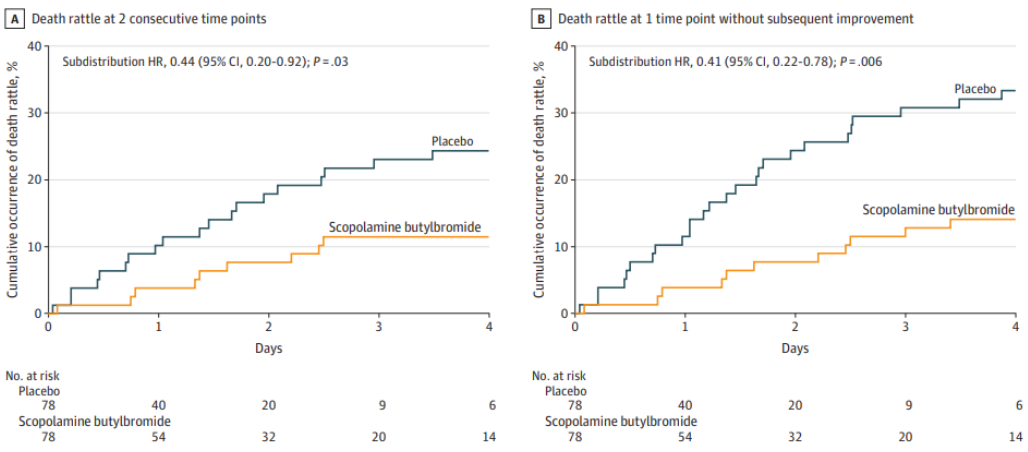
Outcomes:

- Primary: occurrence of Grade 2 (audible standing at end of bed) or higher death rattle, measured at 2 consecutive time points with a 4-hour interval
- Secondary: time between recognizing dying phase and onset of death rattle, anticholinergic side effects (Care Program for the During CPD assessment), Vancouver interaction and calmness scale for restlessness

Results: n = 157 patients, median age 76 years

- Grade 2 death rattle occurred in 10 patients (13%) in scopolamine group versus 21 patients (27%) in placebo group at two time points
- Median observed time to death rattle was longer for the SB group

Figure 2. Time Until the Death Rattle



A, The median observation time for the placebo group was 33.0 hours (IQR, 13.8-65.4 hours) and was 45.8 hours (IQR, 20.9-92.0 hours) for the scopolamine butylbromide group.

B, The median observation time for the placebo group was 41.0 hours (IQR, 13.8-72.0 hours) and was 43.5 hours (IQR, 20.9-94.6 hours) for the scopolamine butylbromide group.

HR indicates hazard ratio.

- Adverse effects were not significantly different between treatment and placebo groups

Conclusion:

- Prophylactic SUBQ scopolamine reduced occurrence of death rattle when compared to placebo

J Pain Symptom Manage. 2018 Dec;56(6):902-907.

Hyoscine butylbromide for the management of death rattle: sooner rather than later

Objective: Assess efficacy of hyoscine (scopolamine) butylbromide (HB) given prophylactically in the dying patient

Methods: Multicenter (2 hospices), prospective, and randomized trial; adult patients with reduced levels of consciousness (RASS ≤ 3) ; HB 20mg SUBQ or IV x1 then 60mg/24 hours either SUBQ Q8H, or continuous infusion ; group 1 = patients with defined death rattle score ≥ 1, group 2 = patients without death rattle

Outcomes:

- Primary: number of patients reporting DR and effectiveness of treatments, according to intensity in death rattle (0= not audible, 3=clearly audible at a distance of 9.5m) at 30 minutes, 1 hour, every 6 hours until death
- Efficacy defined as: intensity of 0 or 1 or with an improvement of at least one point in the score

Results: n = 132

- Death rattle occurred in only 3 patients (5.9%) in prophylactic group versus 49 patients (60.5%) in treatment group

Table 3

Number of Patients With DR, Intensity of Death Rattle (DRS), and RASS-PAL at the Various Intervals Examined

	T0	30'	One Hour	Six Hours	12 Hours	18 Hours	24 Hours	36 Hours	48 Hours	60 Hours	66 Hours
Overall											
No. of patients	132	132	129	126	107	92	85	73	61	45	45
DR, *n* (%)	0	4 (3.0)	7 (5.4)	24 (19.0)	24 (22.4)	20 (21.7)	21 (24.7)	26 (35.6)	16 (26.2)	13 (28.9)	12 (26.7)
DRS (mean)	0	1 (0)	1.28 (0.49)	1.37 (0.49)	1.25 (0.44)	1.20 (0.52)	1.19 (0.51)	1.04 (0.20)	1.25 (0.58)	1.31 (0.75)	1 (0)
RASS-PAL	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −5)	−4 (≤3, −5)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (−4, −5)	−4 (−4, −5)
Group 1											
No. of patients	81	81	78	76	65	56	52	45	37	25	25
DR, *n* (%)	0	4 (4.9)	7 (9.0)	24 (31.6)	24 (36.9)	20 (35.7)	21 (40.4)	23 (51.1)	15 (40.5)	13 (52.0)	12 (48.0)
DRS (mean)	0	1 (0)	1.29 (0.49)	1.35 (0.49)	1.25 (0.44)	1.2 (0.52)	1.19 (0.51)	1.04 (0.21)	1.2 (0.56)	1.3 (0.75)	1 (0)
RASS-PAL	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (≤3, −4)	−4 (−4, −4)	−4 (−4, −4)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −5)
Group 2											
No. of patients	51	51	51	50	42	42	33	28	24	20	20
DR, *n* (%)	0	0	0	0	0	0	0	3 (10.7)	1 (4.2)	0	0
DRS (mean)	0	0	0	0	0	0	0	1	1	0	0
RASS-PAL	−4 (≤3, −5)	−4 (≤3, −5)	−4 (≤3, −5)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −5)	−4 (−4, −4)	−4 (−4, −4)

DR = death rattle; DRS = death rattle score; RASS-PAL = Richmond Agitation-Sedation Scale—palliative version.

CLINICAL PEARL: Prophylactic management of secretions with anticholinergic medications may reduce overall presence or time to death rattle

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- Time to first occurrence of death rattle was 20.4 hours, median 12 hours for group 1 and 27.3 hours, median 36 hours for group 2 (p=0.0001)

Discussion:

- DR occurred in ~10% of prophylactic group compared to about 50% in treatment group
- Some patients may never have developed death rattle in group two so how sure are we that it was truly "prevented?"

Conclusion:

- Administration of HB prophylactically is an effective way to prevent formation of secretions

Of note, scopolamine was administered via SUBQ or IV route of administration in both studies. In the US, scopolamine is available only as transdermal patch

Bottom Line:

- Given mechanism of anticholinergics, it is unsurprising that prophylactic use of these medications for secretion management is more effective than their use to reduce secretions after death rattle is already present
- In US, we only have scopolamine as transdermal patch, which has an onset of action of ~12 hours and peak effect ~24 hours. This may not be the easiest agent to anticipate the "dying phase" timeline to utilize scopolamine patch in clinical practice
- We could apply the prophylactic management concept to use of other anticholinergics that we have available with quicker onset of action in the US (glycopyrrolate, atropine, hyoscyamine)
- What we don't know is if all the patients in the prophylactic group would have actually experienced noisy respirations… which is why the findings in the placebo-controlled trial is helpful!
- We sometimes worry about utilizing anticholinergic agents that cross the blood brain barrier in fear that they would precipitate delirium and therefore decrease quality time with family… It is reassuring that side effects between scopolamine group and placebo group did not differ in the JAMA article
- Would be interesting to study family members' perceptions of patient suffering as an outcome as we know death rattle is not particularly disturbing for patients…
- I will be eager to see if van Esch et al's secondary endpoints of quality of life outcomes and quality of dying according to relatives is published!

CLINICAL PEARL: Prophylactic management of secretions with anticholinergic medications may reduce overall presence or time to death rattle