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Grampians Regional Palliative Care Team

JOURNAL CLUB: HYOSCINE BUTYLBROMIDE FOR THE MANAGEMENT OF DEATH RATTLE: SOONER RATHER THAN LATER

Respiratory secretions in the terminal phase

Respiratory secretions in the terminal phase (often known as "death rattle") are potentially distressing noises produced by the inability of the dying person to swallow or cough saliva and respiratory tract secretions. This produces a noise that is considered distressing to families and carers, but evidence suggests that respiratory secretions are not associated with increased respiratory distress for the patient.[1]

Conventional wisdom in palliative medicine suggests that patients should be prescribed anti-cholinergic medication to minimise respiratory secretions in the dying patient. In Australia, the most commonly used medications are hyoscine butylbromide and glycopyrrolate, with hyoscine butylbromide the most readily accessible choice, especially in community settings. Hyoscine hydrobromide and atropine are known to cross the blood-brain barrier and can potentiate delirium and so should be avoided where possible.

What is known

Unfortunately, the use of anticholinergic medications for respiratory secretions in the dying person is not well supported by scientific evidence. A previous Cochrane review by Wee et al.[2] has suggested that no pharmacological or non-pharmacological intervention has been shown to be superior to placebo for treating this condition. This systematic review included only clinical trials and interrupted time series analyses in order to use the best quality evidence available to assess efficacy. More recently, Lokker et al.[3] conducted a systematic review with a broader inclusion criteria, including studies of lower quality, provided they contained original research. This was justified by considering the relative difficulty in conducting randomised control trials in a population of actively dying patients and yielded 11 studies for inclusion (compared with 4 in Wee's study). Although the quality of the included studies was variable, Lokker drew the same conclusion as Wee: that evidence does not support the standard use of antimuscarinics to treat noisy respiratory secretions in the dying. Given these findings attention should be given to the potential harms of administering anticholinergics in the face of a lack of evidence for benefit.

What is new

Previous studies have focused on the use of anticholinergic medication to treat established respiratory secretions. In their article published last year in the Journal of Pain and Symptom Management, Mercandante et al.[4] explored the use of prophylactic hyoscine butylbromide compared with administration if required (chosen as a proxy control due to concerns about administering a placebo in the study population).

In this open label, multicentre, prospective randomised trial, 132 actively dying cancer patients were randomised to receive hyoscine butylbromide either when they developed audible respiratory secretions, or prophylactically. Patients were given 20mg of hyoscine butylbromide parenterally, followed by a further 60mg over the following 24 hours. They were monitored for change in the noise intensity of the respiratory secretions at 30 and 60 minutes, then 6 hourly until death using an unvalidated 4-point scale. The primary outcomes of the study were the number of patients who developed audible respiratory secretions and the change in the intensity of the sound in response to treatment.

In this study, patients were excluded if they had taken antimuscarinic medications (which includes commonly used medications such as some antipsychotics and antidepressants) during the admission and those with other conditions (such as a respiratory tract infection or heart failure) which may mimic respiratory secretions. This reduces the generalisability of the results. Patient characteristics were notable for a greater percentage of male participants and some imbalances between the primary tumour site and oral morphine equivalent between the two groups. Only mean survival in hours and antiepileptic use was statistically significant however, with p-values of 0.05 and 0.01 respectively. Intention to treat analysis and follow-up rates are not specified. Medications other than the trial drug were allowed according to clinical need, with medication and dosages not recorded. This is a significant potential confounder. Intravenous hydration was reduced in both groups of patients to 10/mL hour of saline, in contrast to more typical Australian practice where intravenous hydration is generally ceased when a patient is actively dying.

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The findings of the study show a statistically significant difference in the rates of audible respiratory secretions between the two groups, with 60.5% and 5.9% respectively developing the issue between the start of the study and death (p=0.001). In addition, the amount of time without respiratory secretions was significantly greater in the prophylactically treated group compared with the group who commenced treatment after the problem developed.

This trial support the idea that antimuscarinics (which are unable to resolve existing secretions) are more effective when used early. It also supports previous work suggesting that there is little benefit in administering antimuscarinics once noisy respiratory secretions are already present. The findings of the study are somewhat problematic however. Firstly, the study methods contain significant flaws, which limit both the validity and generalisability of the results. Secondly, the implications for practice are challenging. Even if the findings of the study are believed, the results suggest that noisy respiratory secretions did not develop in 39.5% of studied patients who were not exposed to hyoscine butylbromide. If all dying patients are to be commenced on regular dosing of antimuscarinics, almost 40% of patients will be exposed to these drugs without ever developing an indication for their use. This study did not include any monitoring for adverse effects, but these must, at a minimum, involve increased burden associated with the administration of medication and financial cost. It is likely that some patients would also experience unnecessary drug toxicities, all to treat a symptom that is only causing distress to the people surrounding the patient during the terminal phase and not the patient themselves. These concerns are echoed by a number of other practitioners, including in Australia.[5-8]

Implications for practice

In conclusion, this study is unlikely to be practice changing, but does add to the existing body of literature which questions the use of antimuscarinics as they are commonly used. There may be a role for prophylactic antimuscarinics for selected patients and families, for whom noisy respiratory secretions are a cause of significant distress. For the majority of patients however, education and reassurance may be far more successful interventions.

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