Poster Number 136

A review of the use of mucolytic agents in Motor Neurone Disease (MND). Is there benefit to using multiple agents over mono-therapy?

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Introduction

In MND, progressive bulbar and diaphragmatic weakness cause weak cough and difficulty expectorating. This can cause difficulty in managing the amount of saliva produced, which can lead to sore skin, wet clothes, embarrassment and precipitation of choking episodes. Thicker sputum can compound this issue.

Mucolytics can be useful here, however guidelines for their use tend to be based around anecdotal experience rather than using higher level evidence. This particularly applies to the use of multiple mucolytics.

We performed a Medline literature search to examine for evidence surrounding mucolytic use in MND. This revealed a survey of UK-based Neurologists with a special interest in MND showing that clinicians preferred medications for sialorrhoea management included Hyoscine patches, Amitriptyline, Carbocisteine and Botulinum Toxin[1]. There were no studies identified which specifically examined mucolytics for tenacious phlegm in MND.

Ambroxol, Bromhexine, Carbocisteine, N-acetylcysteine, Erdosteine and Sobrerol have been found to have comparable efficacy in the symptomatic treatment of productive cough in a variety of respiratory conditions[2]. We know that Carbocisteine and Acetylcysteine have similar pharmacological characteristics, whilst Erdosteine has been reported to have local anti-inflammatory properties[3].

We aimed to learn more about the benefits and harms of multiple mucolytic therapy versus single mucolytic therapy in the management of tenacious phlegm MND. We hoped to develop a guideline outlining when each, or multiple, agents are appropriate in MND.

Methods

We retrospectively audited the notes of all patients with MND under the care of a Shropshire Palliative Care Team over a one year period and identified those on multiple mucolytic therapy. We noted outcomes of symptom improvement and side effects reported following initiation of multiple mucolytic therapy.

We also performed an email survey of practice amongst Palliative Medicine clinicians with an interest in neurological conditions to establish an understanding of current practice in the management of secretions in MND beyond our own team.

On Mucolytic Therapy?	Number of Patients	Median age (Range)
Yes	32	72.5 (51-85)
No	32	70 (41-93)
Total	64	71 (41-93)

Table 1. Number and age of patients identified under the care of a Shropshire Palliative Care team who were and were not on mucolytic therapy

Results

The email survey we sent out yielded 5 responses from a total of 68 clinicians to whom this was sent. This revealed that most clinicians favoured Carbocisteine for management of secretions in MND and titrate this based on response. Other medications used included acetylcysteine, hypertonic saline and propranolol.

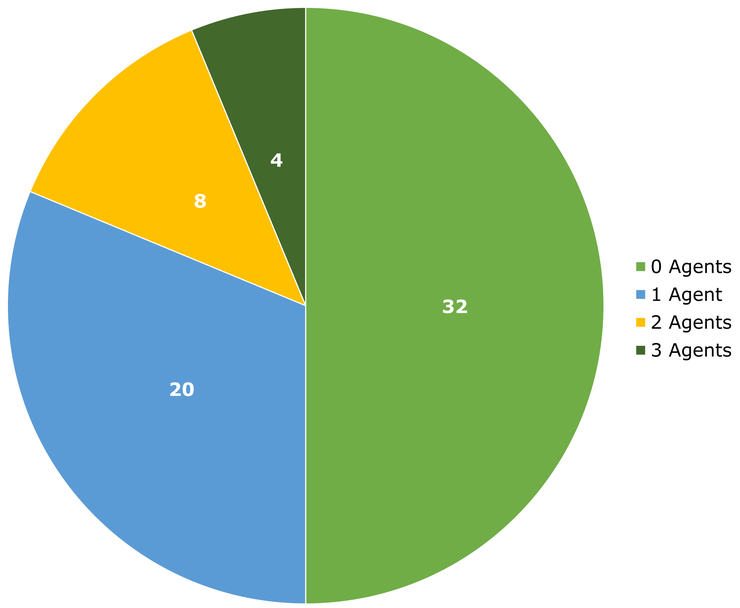
We identified 64 patients with MND under the care of the Shropshire Palliative Care Team over the year (Table 1). Half (32/64) of these required mucolytic therapy, with 31/32 being started on Carbocisteine initially.

Multiple mucolytic therapy was prescribed to 12/32(37.5%) patients – all those who required multiple mucolytics were started on Carbocisteine initially. Two thirds of patients on multiple mucolytics were on dual therapy and the remaining third were on three agents (Fig. 1). Additional mucolytics included Erdosteine, Acetylcysteine and Hypertonic saline.

Symptom improvement was reported in 2/12(16.67%) patients receiving multiple mucolytic therapy. In one of these patients the benefit followed the addition of Erdosteine as a second agent. The other patient also reported benefit after receiving Erdosteine as a third agent. This patient was also on hypertonic saline and there was also benefit seen from this.

Worsening of symptoms was reported in 1/12(8.33%) patients receiving more than one mucolytic. In 9/12(75%) patients, there was either no symptom improvement or no data describing outcomes.

Fig. 1. Total Number of patients by final number of mucolytic agents prescribed at one time



Conclusions

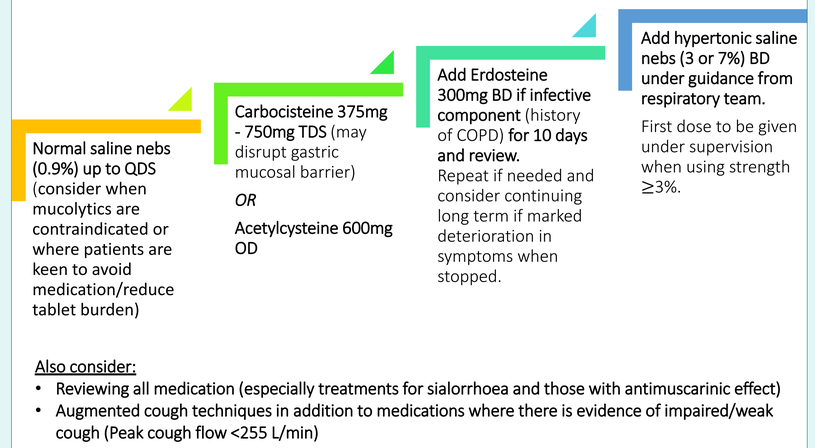
In most patients receiving multiple mucolytic therapy, there was either no symptom improvement or no recorded evidence of outcome on effect on tenacious phlegm.

Where multiple mucolytic therapy is used, Erdosteine may be the most effective second line agent, however larger numbers are needed to draw statistically significant conclusions.

Where patients were prescribed more than two mucolytics, these were added in cumulatively rather than switched. In most cases we identified this did not lead to documented symptom improvement.

Bearing in mind the similar pharmacology of Carbocisteine and Acetylcysteine and also given the variation in practice around second-line agent, we have produced a stepwise pathway for the management of tenacious phlegm in patients with MND, prioritising Erdosteine as a second line mucolytic where there is an infective component or history of COPD, given its anti-inflammatory properties (Fig. 2). Through this we hope to create a more structured approach to the management of tenacious phlegm in MND for clinicians caring for patients who are struggling with this symptom.

Fig 2. Stepwise pathway for the management of tenacious phlegm in patients with MND



Impact

Moving forwards, we aim to prospectively audit the new pathway outlined in Fig. 2 in our patient population. Further research in a wider cohort of patients is required to draw more definitive conclusions surrounding the effectiveness of mucolytic therapy in MND.

More robust documentation should be encouraged amongst prescribers to enable better understanding about the effects of treatment for this important symptom.

References

1. Hobson EV *et al.* Management of sialorrhoea in motor neuron disease: a survey of current UK practice. Amyotrophic Lateral sclerosis & Frontotemporal Degeneration. 14(7-8):521-7, 2013 Dec
2. Scaglione F and Petrini O. Mucoactive Agents in the Therapy of Upper Respiratory Airways Infections: Fair to Describe Them Just as Mucoactive? Clin Med Insights Ear Nose Throat. 12:1-9, 2019 Jan
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Conflicts of Interest

None Declared