A Multicentre Evaluation of Oropharyngeal Secretion Management Practices in Amyotrophic Lateral Sclerosis:

Word count for main text: 2862  
Number of references: 29

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Disclosures: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Acknowledgements: We are thankful for the support provided by the network of the Motor Neuron Disease Association Care Centres, who made this study possible.

This is an EU Joint Programme - Neurodegenerative Disease Research (JPND) project. The project is supported through the following funding organisations under the aegis of JPND - www.jpnd.eu (United Kingdom, Medical Research Council and Economic and Social Research Council). AAC receives salary support from the National Institute for Health Research (NIHR) Dementia Biomedical Research Unit at South London and Maudsley NHS Foundation Trust and King’s College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The work leading up to this publication was funded by the European Community’s Health Seventh Framework Programme (FP7/2007–2013; grant agreement number 259867).
ABSTRACT

Objective: Oral secretions can be a debilitating symptom for patients with ALS, but the treatment of this symptom is poorly defined and opinions on best practice are diverse. The objective of this study was to identify the treatments that are commonly prescribed, and to describe how experienced clinicians approach a patient with symptoms resistant to treatment.

Methods: Twenty-three clinicians were approached - nineteen clinicians from 16 centres across the UK provided case report forms for a total of 119 ALS patients, who were identified as having treatment for a secretion problem.

Results: The use of 5 types of anticholinergics, salivary gland botulinum toxin injections, conservative management approaches and carbocisteine were reported. Of the cases reviewed, 61% had symptomatic improvement following the introduction of a first anticholinergic. Only 19% of patients achieved any symptomatic improvement with the use of an alternative anticholinergic when an initial anticholinergic achieved no symptomatic improvement. There was marked variation in the doses of the anticholinergics prescribed. Combinations of anticholinergic drugs were used in 16 patients. Botulinum toxin injections into the salivary glands were used in 17 patients, chosen particularly in those who had failed to achieve a good level of secretion control with the use of anticholinergic medication and reported to improve symptoms in 57% of patients.

Conclusion: There are a variety of treatment options in use for oral secretion problems in ALS patients but the variation in management approaches highlights the need for further research in this area.

Search terms: Secretion management, sialorrhea, anticholinergics, botulinum toxin
INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease affecting the motor nerves supplying the limbs, trunk, bulbar region and respiratory muscles.[1]

It has been estimated that 50% of ALS patients suffer from saliva problems and a recent survey of clinicians estimated that in 42% of patients with secretion problems, these problems are poorly controlled.[2]

Symptoms and consequences include drooling (sialorrhea), breakdown of the skin around the mouth, speech disturbance, disruption of sleep, coughing and a higher risk of aspiration. These problems can lead to psychosocial symptoms including distress, embarrassment and social withdrawal.[3, 4]

Treatment is usually determined by clinician experience and includes treatments include anticholinergics, botulinum toxin, radiotherapy and surgery. [3, 5 - 19]

However, the studies evaluating these therapies are to an extent limited by lack of blinding, few participants and the use of outcome measures not designed for patients with ALS.[7, 13, 20 - 22] It should also be noted that the treatment of sialorrhea by any of these medications is unlicensed in the UK.

Patients with ALS also often suffer from problems with the collection of thick secretions in their throat and respiratory tract. These thick secretions may develop or be exacerbated following the treatment of excessive runny saliva. [6]

In the absence evidence-based guidelines, sharing experience and practice amongst clinicians is an approach which can be used to develop a better understanding of the merits of available treatments. In this paper we explore treatment approaches that
have been devised by neurologists working at amyotrophic lateral sclerosis care centres across the UK.

The aims of this study were to identify:

- Which therapies were used to manage oropharyngeal secretion problems?
- How the different treatment options were used in combination.
- Treatment approaches in patients with symptoms resistant to initial management.
- The type and impact of adverse effects in patients being treated for secretion problems.

METHODS AND PATIENTS

We conducted a retrospective cohort study, involving a review of the notes of patients identified to have a secretion problem. A case report form (CRF) for recording individual secretion management regimens, was circulated to 23 ALS care centre physicians with a special interest in the care of ALS patients from across the UK. These clinicians were asked to complete a case report using information recorded in the clinical record, for each consecutive patient they saw in clinic with a current or previous secretion problem, during the period between 01/12/2012 and 01/04/2013. This approach reduced recall and selection bias.

A secretion problem was defined as:

- Excessive saliva in a patient’s mouth which may cause drooling.
- The sensation of thicker secretions in the patient’s throat which results in a choking like discomfort.

During the census period, data was collected from patients attending clinics with a new secretion problem, and from patients attending clinics where they were followed
up for an existing secretion problem. Descriptive statistics were used to present the data. The treatments prescribed to patients with a secretion problem were recorded. When the patient had attended for follow up of a secretion problem, the side effects and the perceived benefit on symptoms of any treatment reported to the clinician were recorded. If there was no record concerning the effect on symptoms, these cases have been omitted from the descriptive statistic of the effect of treatment on symptoms.

RESULTS

One-hundred and nineteen patients were identified as having a secretion problem during the study period. Patient demographics are shown in Table 1. The type of secretion problem that had been experienced by the patients were reported to be: a problem with only excessive saliva in 48 patients (40%); a problem only with thicker secretions in 27 (23%); and a combination of both types of secretion problem in 44 (37%).

Problems with excessive saliva were reported to have been managed with anticholinergic drugs and salivary gland botulinum toxin injections. We identified five different types of anticholinergic drug used to manage problems with excessive thin saliva in the 92 patients who were reported to have a problem with excessive saliva. These were hyoscine hydrobromide (transdermal patch or oral preparation), oral amitriptyline, atropine (sublingual drops, transdermal patch, or tablets), oral propantheline, and oral glycopyrronium.

The most common first line treatment reported to have been used to manage problems with excessive saliva was the prescription of an anticholinergic, used in all 92 patients. For 13/92 of the patients, the visit during the data collection period was
the first identification a problem with excessive saliva and consequent prescription of an anticholinergic, therefore no follow up data was available. In 72/92, patients had been prescribed the anticholinergic at a previous appointment and had an effect on symptoms recorded at a follow up appointment. In these patients 44/72 (61%) had an improvement in symptoms recorded and in 28/72 it was recorded that the initial anticholinergic had not improved symptoms. In total, 79 patients had been seen again since the prescription of the initial anticholinergic, but in seven the effect of this treatment on symptoms had not been recorded. In these 79 patients side effects were reported in 54%. (Figure 1)

The most frequently used first line anticholinergics were hyoscine patches (56), amitriptyline (15) and atropine drops (11). Symptoms were reported to have improved in some patients following treatment with each of the types of first line anticholinergic, with rates ranging from 50% to 89% [Figure 2].

Of the 28/72 patients (39%) whose symptoms were reported to not have improved following an initial anticholinergic, 22 tried another anticholinergic. 21 of these patients had been seen again and had the second anticholinergics effect on their excessive saliva symptoms recorded, only four of whom (19%) had symptomatic improvement documented in their notes.

Sixteen patients were given a combination of two anticholinergics after a first anticholinergic was reported to improve symptoms but not sufficiently to adequately control the problem over time. Of the 11 with an effect on symptoms recorded, five patients symptoms had improved (45%) and six (55%) had not. Seven of the 13 (54%) patients who had been seen again since starting combination anticholinergic therapy had adverse effects to this treatment documented in their notes. Three of
these patients had not yet been seen again since the addition of a second anticholinergic and two had returned to clinic but the treatments effect on symptoms was not reported. Two patients were then given three anticholinergics in combination.

Different anticholinergic medications were prescribed on 161 occasions as a first, second, third or 4th line treatment for excessive saliva. Overall, anticholinergic treatment was recorded to improve symptoms in a proportion of patients ranging from 43% to 63% [Figure 3]. As previously described, the information about the effect of treatment on symptoms was not available for all patients who had been prescribed each drug. Whilst atropine drops and the hyoscine patch were generally used first line, glycopyrronium was generally used as a second line treatment [Figure 4]. The doses of anticholinergics which were prescribed were highly variable [Table 4]. The commonly used hyoscine patch was usually prescribed as either a full (n=54) or a half (n=10) 1mg patch per 72 hours. Symptomatic improvement was recorded in all seven patients with an outcome recorded after starting a half path.

Side effects were commonly reported with the use of anticholinergic medications. Undesired anticholinergic effects were frequently reported including an excessively dry mouth, confusion, drowsiness and urinary retention [Table 2]. In addition, hyoscine patches were reported to cause with a skin reaction at the patch site in 22% of these patients [Table 2], causing treatment discontinuation in 18% of those using hyoscine patches. Only one patient was reported to have tried to control these skin reactions, they applied topical steroid to the site of the reaction between patch applications, enabling them to persist with the patch. Overall 33% of patients discontinued hyoscine patches due to intolerable adverse effects. Sublingual atropine drops and oral glycopyrronium had lower reported rates of adverse effects, 24% and 28% respectively compared to the 60% reported for hyoscine patches.
As previously described, the information about the effect of treatment on symptoms was not available for all patients who had been prescribed each drug. Botulinum toxin was used in 17/119 (14%) of patients with a secretion problem across 10 centres. In 14/17 patients (82%) botulinum toxin was used 3rd line or later. Two patients received these injections under ultrasound guidance, and the time between the decision to give botulinum toxin injections and its administration varied from same day administration to 12 weeks later. In total, three brands (Dysport, Neurobloc, and Botox A) and 12 different dosing regimens of botulinum toxin were used, including injection of both the parotid and submandibular glands and parotid gland only injections. The doses of botulinum toxin ranged from 60 units of Dysport to 3000 units of Neurobloc [Table 4]. Despite being used in situations where symptoms were uncontrolled by anticholinergics, symptomatic improvement was documented in 8 (57%) of the 14 patients who had an outcome on symptoms recorded, demonstrating the usefulness of this intervention in patients with difficult to control symptoms. Three patients had not been seen again since treatment with botulinum toxin.

Of the 17 patients who had received an initial treatment with botulinum toxin injections, seven had already opted to receive additional injections and five had chosen to discontinue the injections following just one treatment. The reason for discontinuation was unacceptable side effects in one patient, inadequate symptom control in two, a combination of inadequate symptom control and unacceptable side effects in one, and one patient being unable to attend clinic. Two patients continued to use anticholinergic medication alongside botulinum toxin injections for ‘top up’
symptom control in between their botulinum toxin injections. Three patients were using carbocisteine syrup in addition to botulinum toxin injections to combat thickened secretions.

Of the 14 patients who had been followed up since receiving salivary gland botulinum toxin injections, 50% had experienced adverse effects. This included two cases of deteriorating bulbar function which in the clinician’s opinion was not due to disease deterioration. One of these cases was following injections to the parotid and submandibular glands and one following injections only into the parotid glands.

Problems with thick secretions were also frequently reported to be a problem in this ALS population. In total, 71 patients had suffered with thick secretions, in the absence of excessive thin secretions (27 patients), or alongside this problem (44 patients), possibly as a consequence of treatment with anticholinergic drugs or botulinum toxin. Carbocisteine syrup was prescribed to 45 of these patients and symptomatic relief was reported in 27 of 31 patients (87%) with an outcome recorded. In total, seven patients (19%) reported adverse effects when using carbocisteine including constipation (6%), excessive dryness in the mouth (6%), vomiting (2%), and worsening of thin secretion problems (2%), and further deterioration of thick secretion problems (2%). Conservative measures were also commonly used to manage thick secretions [Table 3].

Forty-six (39%) received some conservative therapy, some directed at excessive saliva and some at thickened secretion. This included the use of suctioning, reported to be useful in 15 (68%) of the 22 patients it was used in, and maintaining adequate
hydration, which was reported to be useful for all 6 of the patients who had this intervention documented [Table 3].

DISCUSSION

In the absence of a cure for ALS, an important aspect of management is to control symptoms in order to maximise patients’ quality of life.[6, 23]

Hyoscine patches were the most frequently used therapy for excessive saliva, a choice which is often made because of the ease of use of patches.[2] However, hyoscine patches were frequently associated with adverse effects (60%), in particular, a skin reaction to the patch. Rate of hyoscine patch discontinuation due to adverse effects was 33% and often due to this skin reaction, considerably higher than the 13% discontinuation rate reported in a previous study of hyoscine patch use in children.[24] The suggestion that topically applied steroids could reduce this skin reaction may be a way in which the tolerability of this simple but effective treatment could be improved. As anticholinergics are so commonly associated with adverse effects and symptomatic improvement was reported at lower doses, it may be most appropriate to always start at a low dose and titrate up as necessary and tolerated. The use of glycopyrronium was generally preferred second line. Perhaps further consideration could be given to this treatment as a first line option, especially given its relatively low rates of adverse effects due in part to poor penetration across the blood brain barrier. [25]

Interestingly, of those patients whose symptoms did not improve when using a first anticholinergic, only 19% had a symptomatic improvement if they tried an alternative.
Further work is needed to determine which treatments are appropriate if an initial anticholinergic is ineffective. In comparison, 45% of patients had symptomatic improvement reported when they started a second anticholinergic alongside their initial anticholinergic, when the first was reported to have improved symptoms but not control them sufficiently. In these patients side effects were reported in 54%, rates similar to those seen with the overall use of anticholinergics. The switching and combination of anticholinergics was common place in this study but is not well discussed in the literature and deserves further exploration. [3, 6, 19]

In line with the limited recommendations for saliva management, clinicians primarily chose botulinum toxin to treat patients with symptoms inadequately controlled by anticholinergic treatment. [5, 19] The 57% rates of symptomatic improvement reported in this study support the use of this treatment in such patients. There was a vast range of practice in the dose and injection site of the botulinum toxin. The biological activity of Dysport is 50 times that of Neurobloc meaning that the most commonly prescribed dose of Dysport (100 Units) has twice the activity of the most commonly prescribed dose of Neurobloc (2500 units). [26] With such variety in dosing and injection sites it is difficult to compare the efficacy, side effects and safety of this treatment.

With the use of botulinum toxin, there is concern about consequential deterioration of bulbar function,[2] such deterioration was reported in 14% of patients in this study. Despite greater anatomical distance between the parotid glands and the bulbar muscles compared to the submandibular glands, deterioration in bulbar function was also reported following parotid gland only injections. Bulbar deterioration could be a result of disease progression, however, in these cases the clinicians had specifically documented that the post injection deterioration in function was in their opinion a
consequence of the injection. The safety and efficacy of botulinum toxin injections need to be further assessed to enable clinicians to judge the risks to the benefits for their patients.

Whilst there are studies suggesting that salivary gland irradiation may an effective treatment, its use was not reported in this study. [27] Additionally, no surgical options were used; this may reflect the invasive and irreversible nature of these interventions.

A high proportion of patients were suffering from both thick and thin secretion problems, and thickened secretions were one of the most commonly reported side effects of the treatments for excessive saliva. A fine balance must be struck between the management of the different types of secretion problem. It would be useful for future studies to identify optimal practice for patients with different oral secretion profiles.

Despite remaining relatively unaddressed in many review and guideline articles, [3, 6, 5, 19] the use of conservative measures was often reported as part of the management for both thick and thin secretions. These are largely simple interventions which can be considered from the early stages of a secretion problem. A review of sialorrhea management by Hockstein et al. in 2005 highlights a number of possible conservative measures. [21]

Carbocisteine was the preferred medication for managing problems with thickened secretions, with high reported rates of symptomatic relief and infrequent adverse effects. This was often supplemented with conservative therapies such as using saline nebulisers.
The major limitation when conducting this study was the retrospective nature of the data collection. In the absence of a standardised follow up or outcome measure being used to assess the patients with secretion problems, it was not possible to determine the extent of any symptomatic improvement or severity of any adverse effects. Moreover, it is possible that not all side effects were reported to the physician and so rates of these may be higher than reported. As a result, it was not possible to compare one treatment to another.

A previous study of UK secretion management estimated that the centres invited to participate in this study cared for 73% of the patients with a new diagnosis of ALS in 2012.[2] However, this study only represents clinicians managing secretion problems in UK and therefore neglects treatments such as radiotherapy and tracheostomy which are commonly used outside of the UK. [28, 29]

**Conclusion**

Future work is needed to determine which treatment options are most effective and best tolerated for managing oropharyngeal secretion problems in ALS. Simple data has been presented in this study to provide baseline information about the treatments in use in the UK, which we hope will facilitate effective design of further studies to answer these questions.
REFERENCES

Table Legend

**Table 1:** Summary of the demographics of the patients whose secretion problem management was recorded in this study.

**Table 2:** Rates of reported adverse effects in patients receiving treatment for excessive saliva.

**Table 3:** Summary of the relative merits of the various conservative measures for secretion management and the type of secretion problem they were used to treat.

**Table 4:** Summary of the dose variation of the treatments prescribed for the management of oral secretions.
Figure Legend

**Figure 1:** Availability of outcome data for when patients received a first anticholinergic: *Summarising why not all patients who were prescribed an anticholinergic had efficacy data recorded.*

**Figure 2:** Proportion of patients who had a documented symptomatic improvement when receiving a first line anticholinergic for excessive saliva: *Summarising the percentage of patients, out of the patients who had an outcome to treatment recorded in their notes (improvement or no improvement), whose symptoms were documented to have improved when using each anticholinergic.*

**Figure 3:** Proportion of patients who had a documented symptomatic improvement when receiving a treatment for excessive saliva: *Summarising the percentage of patients, out of the patients who had an outcome to treatment recorded in their notes (improvement or no improvement), whose symptoms were documented to have improved when using each anticholinergic.*

**Figure 4:** Frequency of the various anticholinergics prescribed for secretion management: *Summarising the number of times each anticholinergic was documented to have been prescribed to patients for the control of a secretion problem. Data is broken down to present the frequency each anticholinergic was prescribed as a 1\textsuperscript{st}, 2\textsuperscript{nd} or 3\textsuperscript{rd} line or later treatment.*
Tables:

**Table 1**: Patient demographics  
(n=119)

<table>
<thead>
<tr>
<th></th>
<th>Mean (Range)</th>
<th>64 years (40-86 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Male</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Median (Range)</td>
<td>2.2 years (0.1 – 15.9)</td>
</tr>
<tr>
<td><strong>Disease Duration</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bulbar onset disease</strong></td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td><strong>Gastrostomy</strong></td>
<td></td>
<td>44%</td>
</tr>
<tr>
<td><strong>NIV</strong></td>
<td></td>
<td>18%</td>
</tr>
<tr>
<td><strong>Cough Assist</strong></td>
<td></td>
<td>7%</td>
</tr>
<tr>
<td><strong>Last ALSFRS-r Score</strong></td>
<td></td>
<td>28/48 (3-45)</td>
</tr>
</tbody>
</table>

when available  
(n=88)
Table 2: Rates of reported adverse effects in patients receiving treatment for excessive saliva:

<table>
<thead>
<tr>
<th></th>
<th>Hyoscine Patches (n=57)</th>
<th>Amitriptyline (n=25)</th>
<th>Atropine drops (n=21)</th>
<th>Oral Glycopyrronium (n=17)</th>
<th>Botulinum toxin injections (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessively Dry Mouth</td>
<td>6 (11%)</td>
<td>5 (20%)</td>
<td>3 (14%)</td>
<td>2 (12%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Thickened Secretions</td>
<td>10 (18%)</td>
<td>3 (12%)</td>
<td>2 (10%)</td>
<td>2 (12%)</td>
<td>5 (36%)</td>
</tr>
<tr>
<td>Skin Reaction</td>
<td>12 (22%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Confusion</td>
<td>5 (9%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>6 (9%)</td>
<td>8 (32%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4 (5%)</td>
<td>2 (8%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Light headed</td>
<td>4 (5%)</td>
<td>2 (8%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (5%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urinary Retention</td>
<td>1 (2%)</td>
<td>1 (4%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bulbar dysfunction</td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Overall proportions</td>
<td>34 (60%)</td>
<td>12 (48%)</td>
<td>6 (29%)</td>
<td>4 (24%)</td>
<td>7 (50%)</td>
</tr>
<tr>
<td>Proportion who discontinued due to adverse effects</td>
<td>33%</td>
<td>12%</td>
<td>6%</td>
<td>5%</td>
<td>13%</td>
</tr>
</tbody>
</table>

* One patient (14%) using oral hyoscine reported an excessively dry mouth (n=7)

* Infrequently prescribed anticholinergic preparations (n<3) have been omitted from this table
<table>
<thead>
<tr>
<th>Therapies for thinning out secretions</th>
<th>Total Used</th>
<th>Useful</th>
<th>Maybe Useful</th>
<th>Not useful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steam nebulisers</td>
<td>19</td>
<td>11 (58%)</td>
<td>4 (21%)</td>
<td>4 (21%)</td>
</tr>
<tr>
<td>Fruit juice</td>
<td>16</td>
<td>7 (43%)</td>
<td>7 (43%)</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Papaya</td>
<td>9</td>
<td>5 (56%)</td>
<td>3 (33%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Hydration</td>
<td>6</td>
<td>6 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Swabs</td>
<td>5</td>
<td>3 (60%)</td>
<td>0</td>
<td>2 (40%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Therapies for managing excessive secretions</th>
<th>Total Used</th>
<th>Useful</th>
<th>Maybe Useful</th>
<th>Not useful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech therapy</td>
<td>22</td>
<td>12 (52%)</td>
<td>6 (26%)</td>
<td>5 (22%)</td>
</tr>
<tr>
<td>Suction</td>
<td>22</td>
<td>15 (68%)</td>
<td>3 (14%)</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>Swallow reminders</td>
<td>11</td>
<td>6 (55%)</td>
<td>4 (36%)</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Positioning collar</td>
<td>9</td>
<td>3 (33%)</td>
<td>3 (33%)</td>
<td>3 (33%)</td>
</tr>
</tbody>
</table>
Table 4: Summary of the dose variation of the treatments prescribed for the management of oral secretions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of different doses</th>
<th>Dose range</th>
<th>Most common dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticholinergic medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyoscine Patch (n=69)</td>
<td>8</td>
<td>¼ of 1mg patch per 72 hours – 1 ½ 1mg patch per 24 hours</td>
<td>1mg patch per 72 hours</td>
</tr>
<tr>
<td>Oral Hyoscine (n=8)</td>
<td>4</td>
<td>0.15mg TDS – 0.3mg TDS</td>
<td>0.3mg TDS</td>
</tr>
<tr>
<td>Amitriptyline (n=25)</td>
<td>13</td>
<td>10mg ON – 175mg</td>
<td>10mg ON</td>
</tr>
<tr>
<td>Sublingual Atropine Drops (n=24)</td>
<td>15</td>
<td>1% solution 2 drops ON – 1% solution 2 drops QDS</td>
<td>1-2 drops TDS</td>
</tr>
<tr>
<td>Glycopyrronium (n=19)</td>
<td>13</td>
<td>0.2mg BD – 3mg TDS</td>
<td>1mg TDS</td>
</tr>
<tr>
<td><strong>Botulinum Toxin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysport</td>
<td>12</td>
<td>60U – 400U</td>
<td>100U</td>
</tr>
<tr>
<td>Neurobloc</td>
<td>6</td>
<td>1000U – 3000U</td>
<td>2500U</td>
</tr>
<tr>
<td>BOTOX A</td>
<td>2</td>
<td>14U – 100U</td>
<td>Each used once</td>
</tr>
<tr>
<td><strong>Mucolytics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbocisteine</td>
<td>7</td>
<td>125mg TDS – 750mg TDS</td>
<td>375mg TDS</td>
</tr>
</tbody>
</table>

*U = Units; ON = Once nightly; BD = twice daily; TDS = 3 times daily; QDS = 4 times daily

*The 175mg dose of amitriptyline was prescribed by GP for emotional labiality.

* Infrequently prescribed anticholinergic preparations (n<3) have been omitted from this table
Figures

Figure 1

92 patients who were prescribed an initial anticholinergic drug

79 of these had had the anticholinergic prescribed at a previous clinic appointment and were attending for follow up at the clinic when the data was collected

72 patients had an outcome documented in the case report forms

For 7 patients no information about the effect of this anticholinergic was documented in the case report form

13 patients had this drug prescribed for the first time at the clinic appointment

No data on the effect of the anticholinergic was available for these patients
Figure 2

*Infrequently prescribed anticholinergic preparations (n<5) have been omitted from this table*
Figure 3

*Infrequently prescribed anticholinergic preparations (n<5) have been omitted from this table*
**Figure 4**

Anticholinergics reported to have been prescribed across the UK

*Infrequently prescribed anticholinergic preparations (n<5) have been omitted from this figure*
Appendix

Case report form sent to clinicians