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

Word count for main text: 3000
Number of references: 29

ALEXANDER J MCGEACHAN MBChB 1, ESTHER V. HOBSON BMBCh 1, AMMAR AL-CHALABI PhD 2, JODIE STEPHENSON MSc 1, SIDDHARTHAN CHANDRAN PhD 3, FRANCESCA CRAWLEY FRCP 4, DAVID DICK MD 5, COLETTE DONAGHY MD 6, CATHY M ELLIS PhD 7, GEORGE GORRIE PhD 8, C. OLIVER HANEMANN MD 9, TIMOTHY HARROWER FRCP 10, AGAM JUNG MD 11, ANDREA MALASPINA PhD 12, KAREN E. MORRISON DPhil 13, RICHARD W. ORRELL MD 14, KEVIN TALBOT DPhil 15, MARTIN R. TURNER PhD 15, TIMOTHY L. WILLIAMS PhD 16, CAROLYN A. YOUNG MD 17, PAMELA J. SHAW PhD 1 & CHRISTOPHER J. MCDERMOTT PhD 1

Corresponding author:
Dr Christopher McDermott PhD FRCP,
Reader in Neurology
Sheffield Institute for Translational Neuroscience
University of Sheffield
385a Glossop Road
Sheffield S10 2HQ
Telephone: +44(0)114 2222261
Fax: +44(0)1144222290
Email: c.j.mcdermott@sheffield.ac.uk

Co-author’s email addresses:
Alex McGeachan: amcgeachan1@sheffield.ac.uk
Esther V Hobson: esther.hobson@gmail.com
Ammar Al-Chalabi: ammar.al-chalabi@kcl.ac.uk
Jodie Stevenson: jstephenson2@sheffield.ac.uk
Siddharthan Chandran: siddharthan.chandran@ed.ac.uk
Francesca Crawley: francesca.crawley@wsh.nhs.uk
David Dick: david.dick@nnuh.nhs.uk
Colette Donaghy: donaghy1a@hotmail.com
Cathy Ellis: cathyellis@nhs.net
George Gorrie: George.gorrie@nhs.net
Oliver Hanemann: oliver.hanemann@pms.ac.uk
Timothy Harrower: timothy.harrower@nhs.net
Agam Jung: agam.jung@leedsth.nhs.uk
Andrea Malaspina: a.malaspina@qmul.ac.uk
Karen Morrison: k.morrison@bham.ac.uk
Richard Orrell: r.orrell@ucl.ac.uk
Kevin Talbot: kevin.talbot@ndcn.ox.ac.uk
Martin Turner: martin.turner@ndcn.ox.ac.uk
Tim Williams: Tim.Williams@nuth.nhs.uk
Carolyn Young: carolyn.young@thewaltoncentre.nhs.uk
Pamela J Shaw: pamela.shaw@sheffield.ac.uk
1 Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, &
Academic Directorate of Neurosciences, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
2 King’s College London, Institute of Psychiatry, Department of Clinical Neuroscience, London, UK
3 Department of Neurology, Royal Infirmary of Edinburgh, Edinburgh, UK
4 Department of Neurology, West Suffolk NHS Foundation Trust, Bury St. Edmunds, UK
5 Department of Neurology, Norfolk and Norwich University Hospital, Norwich, UK
6 Department of Neurology, Royal Victoria Hospital, Belfast, UK
7 Motor Neuron Disease Care and Research Centre, Kings College Hospital, London, UK
8 Institute of Neurological Sciences, Southern General Hospital, Glasgow, United Kingdom
9 Institute of Translational and Stratified Medicine, Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth, UK
10 Department of Neurology, Royal Devon and Exeter Foundation Trust Hospital, UK
11 Department of Neurology, Leeds General Infirmary, Leeds, UK
12 Centre for Neuroscience and Trauma, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, & Department of Neurology, Basildon University Hospital, Basildon, UK
1 Institute of Clinical Sciences, College of Medical and Dental Sciences, University of Birmingham, and Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK,
14 Department of Clinical Neuroscience, University College London Institute of Neurology, London, & MND Care and Research Centre, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK
15 Oxford University Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital,
Authors contributions: AJM, EVH, PJS and CJM conceived the case report series together with the Dementias and Neurodegenerative Diseases Research Network (DeNDRoN) secretions working group (CAY, CE, RWO, AAC, AM, CJM) and AAC, SC, FC, DD, CD, CE, GG, OH, TH, AM, KM, RWO, KT, MT, TW, CAY, PJS and CJM completed the case report series. AJM and JS acquired and analysed the data and AJM, EVH, AAC, JS, SC, FC, DD, CD, CE, GG, OH, TH, AM, KM, RWO, KT, MT, TW, CAY, PJS and CJM prepared and reviewed the paper.

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: Failure to clear oral secretions can be debilitating for patients with amyotrophic lateral sclerosis, ALS, but the treatment of this symptom is poorly defined and there is no consensus on best practice. The objective of this study was to identify the treatments that are commonly prescribed, and to describe how experienced clinicians manage a patient with treatment resistant symptoms.

Methods: Twenty-three clinicians were approached, of which 19 from 16 centres across the UK provided case report forms for a total of 119 ALS patients identified as having problematic oral secretions.

Results: The use of five anticholinergics, salivary gland botulinum toxin injections, conservative management approaches and carbocisteine were reported. Of the 72 patients who were evaluated following the initiation of a first anticholinergic, 61% had symptomatic improvement. Only 19% of patients achieved symptomatic improvement with the use of an alternative anticholinergic when an initial anticholinergic achieved no symptomatic improvement. Problems with thick and thin secretions often co-existed with 37% of patients receiving treatment for both types of problem.

Conclusion: A variety of treatment options are employed by expert clinicians for problematic oral secretions in ALS patients. The variation in management highlights the need for further prospective 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 problematic oral secretions 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 the use of anticholinergic medications, botulinum toxin injection, radiotherapy and surgery [2, 3, 5 - 19]. However, studies evaluating these therapies are 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 treatments for excessive thin saliva [6].

In the absence of 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 build on work from a previous survey of clinician opinion about secretion management by
detailing the treatment approaches that are actually being used by neurologists working at ALS care centres across the UK [2].

The aims of this descriptive 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) [Appendix 1] for recording individual secretion management regimens was circulated to 23 ALS care centre physicians with 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.

Data was collected from the clinical notes of 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 reported in the notes were recorded. When the notes contained details of patient attendance for follow up of a secretion problem, at any point during their illness, the side effects and the perceived benefit on symptoms of any treatment reported to the clinician were recorded in the case report form. In some cases 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

During the census period 119 patients, who had at some point during their illness experienced a secretion problem, attended clinics. A case report form was completed following a notes review of all 119 patients. The time period covered ranged from 01/12/2012 to 01/04/2013. Nineteen of the 23 approached clinicians returned case report forms. Patient demographics are shown in Table 1. The types of secretion problems experienced by patients were reported as: a problem solely with excessive saliva in 48 patients (40%); a problem solely 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 in the 92 patients who were reported to have an excessive saliva problem. These were hyoscine hydrobromide/ scopolamine (transdermal patch or oral preparation), oral amitriptyline, atropine (sublingual drops, transdermal patch, or tablets), oral propantheline, and oral glycopyrronium bromide/ glycopyrrolate. The doses of these anticholinergics was commonly adjusted, either because an initial dose
was not providing sufficient symptomatic improvement, or in an attempt to reduce side effects.

The most common first line treatment used to manage problems with excessive saliva was the prescription of an anticholinergic, used in all 92 patients. 72 of the 92 patients had been prescribed an anticholinergic at a previous appointment and had an effect on symptoms recorded at a follow up appointment. An improvement in symptoms was recorded in 44 (61%) of these 72 patients, while in 28 (39%) it was recorded that the initial anticholinergic had not improved symptoms. In addition to these 72 patients, a further seven patients had been seen again since the prescription of an initial anticholinergic, but the effect of this treatment on symptoms had not been recorded. Side effects were reported in 43 (54%) of the 79 patients seen again. For 13 of the 92 patients no follow up data was available owing to the fact that their excessive saliva problem was first identified at the clinic visit during the data collection period. Figure 1 describes why not all patients who were prescribed an anticholinergic had outcome data recorded.

The most frequently used first line anticholinergics were hyoscine patches (56), amitriptyline (15) and atropine drops (11). Symptoms were reported to have improved in patients following treatment with each of these of first line anticholinergics, with rates ranging from 54% to 89% [Figure 2].

Of the 28/72 patients (39%) whose symptoms were reported to not have improved following an initial anticholinergic, 22 tried treatment with another anticholinergic. 21 of the 22 had an outcome on symptoms recorded, only 4 (19%) of whom had any symptomatic improvement documented in their notes following instigation of the second anticholinergic. 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 of 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 went on to be prescribed three anticholinergics in combination.

Different anticholinergic medications were prescribed on 161 occasions as a first, second, third or fourth line treatment for excessive saliva. Overall, anticholinergic treatment was recorded as improving symptoms in a proportion of patients ranging from 43% to 63% [Figure 3]. Whilst atropine drops and hyoscine patches 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 2]. 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 half a patch.

Undesired anticholinergic side effects reported included drying of the oral cavity, confusion, drowsiness and urinary retention [Table 3]. In addition, hyoscine patches were reported to cause a skin reaction at the patch site in 22% of patients [Table 3], leading to treatment discontinuation in 18% of those using hyoscine patches. One patient was reported to have tried to control patch related skin reactions by applying topical steroid to the site of the reaction, 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 29% respectively, compared to the 60% reported for hyoscine patches [Table 3].

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 as a third line or later agent. 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 parotid and submandibular glands and parotid gland injections alone. 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 a symptom outcome recorded. Three patients had not been seen again since treatment with botulinum toxin.

Of the 17 patients who received initial treatment with botulinum toxin injections, seven had already opted to receive additional injections and five had chosen to discontinue 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 unable to attend clinic. Two patients continued to use anticholinergic medication alongside botulinum toxin injections for ‘top up’ symptom
control in between botulinum toxin injections. Three patients used carbocisteine syrup alongside botulinum toxin injections to combat thickened secretions.

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

Problems with thick secretions were also frequently reported to be a problem in this study population. In total 71 (60%) patients had reported thick secretions, in the absence of excessive thin secretions in 27 (23%) patients, or alongside this problem in 44 (37%) patients, possibly as a consequence of treatment with anticholinergic drugs or botulinum toxin. Carbocisteine syrup was prescribed to 45 of these patients, 19 of whom only ever used carbocisteine, 9 of whom started carbocisteine first and then were also given anticholinergics for a subsequent thin secretion problem, and 17 of whom started an anticholinergic drug first and had carbocisteine added at a later date. In total symptomatic relief with carbocisteine was reported in 27 of 31 patients (87%) with a documented outcome. 12 of these 31 patients only had a problem with thick secretions, all 12 (100%) had a documented improvement. 15 (79%) of the 19 patients with both thick and thin secretion problems reported symptomatic improvement. In total, seven patients (19%) reported adverse effects when using carbocisteine including constipation (6%), excessive dryness of the mouth (6%), vomiting (2%), 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 4].
Forty-six (39%) received conservative therapies, directed either at excessive saliva or thickened secretions. This included the use of suctioning, reported as useful in 15 (68%) of 22 patients where it was used, and maintaining adequate hydration, which was reported to be useful for all 6 of the patients in whom this intervention was documented [Table 4].

**DISCUSSION**

In the absence of a cure for ALS, an important aspect of management is to control symptoms in order to maximise quality of life [6, 23]. The objective of this study was to explore the current management of saliva related problems by experienced clinicians at ALS centres in the UK.

*In general, the approach with anticholinergic medication sensibly appeared to be to adjust the dose to maximise benefits whilst minimising side effects.*

Hyoscine patches were overall the most frequently used therapy for excessive saliva, a choice which is often made because of the ease of use [2]. However hyoscine patches were frequently associated with adverse effects (60%), in particular, a skin reaction to the patch. The rate of hyoscine patch discontinuation due to adverse effects was 33%, 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 simple method to improve tolerability. As anticholinergics are so commonly associated with adverse effects and symptomatic improvement was reported at lower doses, it is most appropriate to consider their introduction at a low dose and to
titrate up as necessary against tolerance and effect. The use of glycopyrronium was generally preferred as second line. Further consideration could be given to this treatment as a first line option, especially given its relatively low rates of adverse effects, in part due to its poor penetration of the blood brain barrier [25].

Interestingly, of those patients whose symptoms did not improve with the first anticholinergic, only 19% had a symptomatic improvement if an alternative was tried subsequently. Further work is needed to determine which treatments are appropriate if an initial anticholinergic is ineffective. In comparison, 45% of patients reported symptomatic improvement when they started a second anticholinergic alongside their initial anticholinergic, when the first was reported to have provided significant but insufficient symptomatic control. Side effects were reported in 54% of such patients, a rate similar to that seen overall with 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]. It would also be useful to identify the common factors in patients who do not respond well or are intolerant to anticholinergics.

In line with the limited available 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. 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 was not possible to consider differences in efficacy, side effects and safety profiles of this treatment.

With the use of botulinum toxin, there is concern regarding a consequential deterioration in bulbar function [2], such a 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 isolated parotid gland injections. Bulbar deterioration could be a result of disease progression. However, in these cases the clinician had specifically documented that the post injection deterioration in function was, in their opinion, a consequence of botulinum toxin. The safety and long term efficacy of botulinum toxin injections in this setting needs to be further assessed to enable clinicians to judge the risks and benefits for their patients.

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

37% of patients were suffering from both thick and thin secretion problems. Furthermore, thickened secretions were one of the most commonly reported side effects of the treatments for excessive saliva. Carbocisteine was the preferred medication for managing thickened secretions often supplemented with conservative therapies, such as the use of saline nebulisers. A balance must be struck between the management of the different types of secretion difficulties. It would be useful for future studies to identify optimal practice for patients with different oral secretion profiles.
Despite remaining relatively unaddressed in many reviews 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 at the early stages of a secretion problem. A review of sialorrhoea management by Hockstein et al. in 2005 highlights a number of possible conservative measures [21].

This was a retrospective study. In the absence of a standardised follow up or outcome measure for patients with secretion problems, it was not possible to determine the extent of any symptomatic improvement or severity of any adverse effect. Moreover, it is possible that not all side effects were reported to the physician and so rates may have been higher than reported. As a result, it is not possible to compare different treatments.

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 the UK and therefore neglects treatments such as radiotherapy and tracheostomy which are commonly used outside of the UK [28, 29].

**Conclusion**

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


15. Neppelberg E, Haugen DF, Thorsen L, Tysnes OB. Radiotherapy reduces sialorrhea in amyotrophic lateral sclerosis. European journal of neurology : the


Table Legend

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

**Table 2:** Summary of the dose variation of the treatments prescribed for the management of oral secretions.

**Table 3:** Rates of reported adverse effects in patients receiving treatment for excessive saliva.

**Table 4:** Summary of the relative merits of the various conservative measures for secretion management and the type of secretion problem they were used to treat.
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 1st, 2nd or 3rd line or later treatment.*
Tables:

<table>
<thead>
<tr>
<th>Table 1: Patient demographics (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td><strong>Disease Duration</strong></td>
</tr>
<tr>
<td><strong>Bulbar onset disease</strong></td>
</tr>
<tr>
<td><strong>Gastrostomy</strong></td>
</tr>
<tr>
<td><strong>NIV</strong></td>
</tr>
<tr>
<td><strong>Cough Assist</strong></td>
</tr>
<tr>
<td><strong>Last ALSFRS-R Score when available (n=88)</strong></td>
</tr>
<tr>
<td><strong>Last ALSFRS-R bulbar subscore when available (n=88)</strong></td>
</tr>
</tbody>
</table>
Table 2: Summary of the dose variation of the treatments prescribed for the management of oral secretions

<table>
<thead>
<tr>
<th>Anticholinergic medications</th>
<th>Number of different doses</th>
<th>Dose range</th>
<th>Most common dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hyoscine Patch (n=69)</strong></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><strong>Oral Hyoscine (n=8)</strong></td>
<td>4</td>
<td>0.15mg TDS – 0.3mg TDS</td>
<td>0.3mg TDS</td>
</tr>
<tr>
<td><strong>Amitriptyline (n=25)</strong></td>
<td>13</td>
<td>10mg ON – 175mg</td>
<td>10mg ON</td>
</tr>
<tr>
<td><strong>Sublingual Atropine Drops (n=24)</strong></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><strong>Glycopyrronium (n=19)</strong></td>
<td>13</td>
<td>02.mg BD – 3mg TDS</td>
<td>1mg TDS</td>
</tr>
</tbody>
</table>

**Botulinum Toxin**

<table>
<thead>
<tr>
<th>Total dose given i.e. split between glands</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dysport</strong></td>
</tr>
<tr>
<td><strong>Neurobloc</strong></td>
</tr>
<tr>
<td><strong>BOTOX A</strong></td>
</tr>
</tbody>
</table>

**Mucolytics**

| **Carbocisteine** | 7 | 125mg TDS – 750mg TDS | 375mg TDS |

*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 lability.*

*Infrequently prescribed anticholinergic preparations (n<3) have been omitted from this table*
Table 3: 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>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Total Number (%)</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 4: 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>
<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>
<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>