Sialorrhoea management in Parkinson's disease

Parkinson's disease is a debilitating illness, primarily causing motor impairment. The non-motor complications of Parkinson's disease also have a significant impact on patients' lives. One such complication is sialorrhoea, or drooling. **Drs Jason Raw, Sarita Bhat** and **Nicholas Roberts** assess its impact on the patient and review therapies with proven evidence, including some novel therapies that may prove beneficial.

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Sialorrhoea is the term for excessive drooling or hypersalivation, and is associated with advancing Parkinson's disease (PD) in adults. It is defined as saliva beyond the margin of the lip[1]. It is known to occur in a variety of other medical conditions for differing reasons, such as cerebral palsy, motor neurone disease, oral cancer and drug-induced sialorrhoea (*Table 1*). The salivary glands have parasympathetic innervations originating in the pons and medulla. There is also sympathetic innervation to the muscles surrounding the salivary glands and ducts, which induce contraction and promote salivary flow. Psychologically, patients with sialorrhoea will find the constant drooling symptoms very distressing, often having to carry around a towel or tissues to mop themselves. This can lead to lowering of self-esteem and social isolation. Sialorrhoea is also associated with physical symptoms such as peri-oral chapping, irritation, maceration and bleeding[1].

Sialorrhoea is known to affect 75–80 per cent of patients with PD[2,3]. It has long been thought this was due to hyper secretion of saliva as a result of autonomic dysfunction. However, more recent research has suggested that, far from producing excess saliva, patients with PD actually tends to produce less saliva than matched controls[4,5,6]. These studies suggest that, due to delayed swallowing disorders also common in PD, patients are unable to swallow all their saliva as it is being produced; this then leads to the apparent drooling symptoms. It is thought the average human can produce 1.5 litres of saliva a day[7] which, if you have a delayed swallow, is hard to keep up with.

Table 1. Aetiology of sialorrhoea

- Hyper secretion
  - > Inflammation (teething, dental caries, oral-cavity infection, rabies)
  - > Medication (antiepileptics, antipsychotics, tranquilisers)
  - > Gastroeosophageal reflux
  - > Toxin exposure (mercury vapour)
- Neuromuscular/sensory dysfunction
  - > Mental retardation*
  - > Cerebral palsy*
  - > Stroke***
  - > Parkinson's disease**
  - > Bulbar palsy***
- Anatomic
  - > Macroglossia
  - > Dental malocclusion

* *Most common causes in children and adolescents*
** *Most common cause in adults*
*** *Less common causes in adults*

Assessment

Beyond the obvious drooling on the affected patients' chin and clothes, it is possible to objectively assess sialorrhoea to aid diagnosis or

Table 2. System for assessment of frequency and severity of drooling†

Severity	
Dry (never drools)	1
Mild (wet lips only)	2
Moderate (wet lips and chin)	3
Severe (clothing becomes damp)	4
Profuse (Clothing and objects become wet)	5
Frequency	
Never drools	1
Occasionally drools	2
Frequently drools	3
Constantly drools	4

Total score of >5 indicates need to consider treatment

Regular checks allow objective assessment of treatment response

evaluate therapy. There have been several measures developed, and these often involve unusual or inconvenient measuring techniques, such as wearing measuring cups attached to the chin or weighing saliva soaked cotton placed inside the mouth for a given time. Outside of the research arena, there are rating scales that are easy to use and helpful (*Table 2*). These rating scales allow objective measure of sialorrhoea and response to treatment and are practical in the GP's surgery.

Treatment

There has been much research into sialorrhoea treatments, though the majority concerns children and adolescents with mental retardation or cerebral palsy. Research has also been extended to the treatment of drug-induced sialorrhoea due to antipsychotic medication. Treatment of sialorrhoea is difficult, but can bring enormous relief. The main therapies tested with PD include: simple methods of measurement, anticholinergic medications and botulinum toxin injected directly into the salivary glands. There are very few simple measures that can be employed; even fewer have been assessed scientifically, other than in children. In the main it is helpful to try to improve patients' swallowing ability through speech and language therapy, which may also employ the use of cues or prompts to aid the deliberate swallowing of the patients' saliva[8]. Anticholinergic medication has been tried for all causes of sialorrhoea with diverse effect. Due to their effect on the parasympathetic innervations of the salivary glands, a side effect of anticholinergic medication will be dry mouth. There are numerous other side effects of anticholinergic medication that are well

documented and to which the elderly are particularly vulnerable. These include; constipation, blurred vision, drowsiness, hallucinations, difficulty with micturition and urinary retention. In particular, anticholinergic medications have been shown to cause mild cognitive impairment and lead to patients being wrongly diagnosed with dementia[9]. For these reasons, while anticholinergic drugs may well be effective, the dose needs to be the smallest possible to achieve therapeutic benefit and the most active salivary gland targeted as specifically as possible to avoid side effects.

The only anticholinergic drug with evidence of benefit tested in patients with PD is sublingual atropine[10]. It was a small study of only seven patients, six with PD and one with progressive supranucleur palsy. It was an open-label pilot study and each patient was given sublingual atropine drops for one week. There was significant reduction, both subjectively and objectively, in saliva production after three hours and after one week of therapy. There were no other reported anticholinergic side effects in any of the patients.

Alternative treatments

The only other anticholinergic medication tested includes transdermal scopolamine patches and ipratropium inhaler, in patients with terminal cancer and clozapine therapy as the respective causes of their sialorrhoea[11, 12]. In both those studies there was significant benefit gained from the medication; however, it is unclear if the same benefit would occur in PD patients. The mechanism of drooling is neurological dysphagia in PD, compared with upper digestive tract obstruction caused by tumour in cancer or drug-induced effects on the salivary glands with clozapine. This may expose PD patients to a greater risk of side effects such as dry mouth.

Clonidine is a centrally acting alpha 2 agonist,

normally used for hypertension management. It has been shown to be of benefit in the treatment of sialorrhoea due to PD[13]. The main side effects of this drug are dry mouth and fatigue. This study was a randomised, double-blind and placebo controlled, and had 32 patients with PD enrolled, with an average age of 71 years. Each patient randomised to receive clonidine was given 0.15mg/day, and the results showed clinically significant improvement in sialorrhoea symptoms after one month and three months of treatment (P = <0.00001). The investigators claim there were no extra side effects noted with the clonidine group.

Newer treatments

The treatment gaining evidence for benefit is botulinum toxin, injected directly into the salivary glands. Botulinum neurotoxin is a product of the bacteria Clostridium botulinum. There are several serotypes A-G, with A and B being the types evaluated most in PD patients. It binds irreversibly to the neuromuscular junction and inhibits the release of acetylcholine neurotransmitter. Depending on the site of administration it can cause muscle relaxation or inhibit parasympathetic and cholinergic postganglionic sympathetic neurones[14]. Although the toxin binds irreversibly, after two to three months new receptors develop to compensate. It has proven benefit in many conditions including muscle spasticity in stroke, multiple sclerosis and hyperhydrosis in sweat glands. There have been at least five randomised trials of botulinum toxin injected into the salivary glands[15,16,17,18,19], four of these were with botulinum toxin type A and one was type B (thought to have higher rates of dry mouth). The toxin is injected either blindly using anatomical landmarks, or by ultrasound guidance, into the parotid gland and sometimes the submandibular gland, and saliva production is measured objectively and subjectively following this. In each study, the results show significant reduction in saliva production with little in the way of side effects.

Key points

- Sialorrhoea affects 75–80 per cent of patients with Parkinson's disease.
- The condition is due to impaired swallowing rather than excessive saliva production.
- Speech and language therapy can help.
- Anticholinergic drugs, such as sublingual atropine drops, have been shown to be of benefit; however, side effects may be intolerable.
- Botulinum toxin administered locally to the parotid glands with ultrasound guidance is a safe and effective treatment.

In one study, a comparison of ultrasound guided injections versus blind injections suggested the ultrasound method produced more efficacious results with less adverse effects, though both methods were effective[16]. The difficulties with botulinum toxin injections are that it should only be administered by health professionals experienced with injection of the toxin, and can require a significant resource increase if ultrasound guidance is needed. As the toxin diffuses through the tissues after injection it can affect other areas, such as the oropharynx, and result in worsening dysphagia or voice effects. There is one report of recurrent jaw dislocation after botulinum toxin injections were used to treat spasticity in a patient with motor neurone disease[20]. Due to the rejuvenation of the synaptic function two to three months after injection, patients can expect a recurrence of the sialorrhoea and need further injections.

Conclusion

It would seem that despite the unpleasant and aesthetically distressing symptom of drooling with PD, the proven treatment options are disappointingly few. The use of anticholinergic medications and botulinum toxin injections are the mainstay of tried therapies. Both are effective. The decision in either of their use is dependent upon accepting the possibly significant side effects with the anticholinergic drugs and their lack of evidence in patients with PD as opposed to the botulinum toxin injections, which have much greater trial evidence albeit mostly with small participant numbers, but require skilled willing hands and improved resources. If we can at least show patients affected by this condition that we know its origins – and acknowledge and understand the distress it causes – we can then begin to discuss possible therapeutic options they may wish to try or that may become available in the future. In the meantime, some possible help can be provided through speech and language therapy involvement.

Conflict of interest: none declared.

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