Management of drooling in disabled patients with scopolamine patches

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Drooling is a common problem in disabled individuals and has significant physical, psychosocial and aesthetic repercussions. Scopolamine has been used to treat drooling in a number of medical specialties, including otorhinolaryngology, neurology and palliative care. This study evaluates the efficacy of this treatment in severely disabled patients.

WHAT THIS STUDY ADDS

- Transdermal scopolamine can be a therapeutic option to control drooling in unco-operative patients. It is an effective and safe method, although it requires appropriate patient selection and is not free from adverse effects.

AIM

To evaluate the efficacy of scopolamine administered transdermally for the treatment of drooling in severely disabled patients.

METHODS

A prospective, randomized, double-blind, crossover, placebo-controlled clinical trial was designed. The study group consisted of 30 handicapped patients with persistent drooling. The exclusion criteria were the specific contra-indications of scopolamine. Severity of drooling was quantified using a modified Thomas-Stonell and Greenberg visual scale simplified into three grades: 1 = dry; 2 = mild/moderate; 3 = severe/fulsome. The frequency of drooling was estimated using the number of bibs used each day. The baseline observational phase was followed by the application of a 1.5 mg scopolamine (Scopoderm TTS; Novartis Consumer Healthcare, UK) or placebo patch every 72 h for a fortnight. This was followed by a 1 week washout period and then crossover of assignments for 2 weeks.

RESULTS

At baseline, 77% of patients showed grade 3 of drooling. The placebo administration showed no significant reduction in drooling. We found a significant drooling reduction ($P < 0.005$) in the scopolamine group in the 1 and 2 week controls (69% and 80% respectively $\leq$ grade 3). The mean number of bibs/day decreased during the scopolamine phase from 6/day at baseline to 3/day at the 2 week control. Four patients (13.3%) dropped out because of scopolamine side effects and minor adverse reactions were observed in three other patients. No blood alterations were found during the study period.

CONCLUSION

Scopolamine can be useful to control drooling in severely disabled patients although it requires appropriate patient selection and is not free from adverse effects.

Introduction

Sialorrhea, or drooling, consists of an overflow of saliva from the mouth, usually associated with oral motor dysfunction, insufficient swallowing ability, a deficit of the oral sphincter or, less frequently, with an increase in saliva flow [1]. Drooling is considered normal up to 15–18 months of age due to the physiological immaturity of orofacial motor development; however, it is considered pathological after 4 years of age [2].

Sialorrhea is a common problem among children with neuromuscular disorders such as cerebral palsy, although it is also associated with severe mental retardation [2–4]. Drooling is also a common problem in Down's syndrome [5] and learning disability [6, 7]. In adults, drooling is frequent among patients diagnosed with other neurological conditions such as amyotrophic lateral sclerosis, Parkinson's disease (about 45% of parkinsonian patients complain about drooling) or stroke [8, 9]. It may also be seen in patients with oropharyngeal tumours, congenital or acquired deformities of the tongue, or partial loss of the mandible and/or lips due to injury [10, 11].

Drooling can have physical, psychosocial and aesthetic repercussions that affect the patients and their social and physical environment. In the most severe cases, drooling can soil clothing, the floor, and furniture, leading to a need for continual changes of clothes or bibs throughout the day. It can also inhibit manifestations of affection towards these patients, further increasing their isolation. Apart from the aesthetic component, drooling can impede masticatory function, provoke peri-oral infections and, in the most severe cases, even lead to states of dehydration [2, 9, 12].

A wide variety of treatments aimed at alleviating the problem of drooling have been proposed, varying from non-invasive techniques such as motor re-education or the administration of antisialagogues, to radical surgical procedures or radiotherapy [2, 6, 12, 13].

Scopolamine is an anticholinergic agent with anti-emetic and hypnotic-sedative properties. After oral or parenteral administration, its effects persist for 5–6 h, but this may be extended to up to 24–72 h if the drug is administered transdermally via skin patches. As scopolamine blocks parasympathetic innervation of the salivary glands, one of its indications is to reduce saliva secretion [14, 15].

The objective of this study was to evaluate the efficacy of scopolamine administered transdermally for the treatment of drooling in severe disabled patients.

Methods

A prospective, randomized, double-blind, crossover, placebo-controlled clinical trial was designed. After explaining all possible adverse effects and risks related to the study, written informed consent was obtained from the

parents or legal guardians. The University of Santiago de Compostela (Spain) Ethics in Human Research Committee approved the study.

The study group consisted of 30 disabled patients (16 male, 14 female) with a mean $\pm$ SD age of 30 ± 14 years (range 12–58 years) and with persistent drooling. The medical conditions of the selected patients were: 11 cerebral palsy, five epilepsy, four autism, three Down's syndrome and three cases of rare disorders. Moderate or severe mental retardation was present in 80% of patients. A thorough medical and dental history, and head and neck examination were performed. Some diagnostic tests (i.e. 3-Oz test, image tests, radiosialography, etc.) were not applied because of lack of collaboration. Most of the patients showed neurological disturbances or oral motor dysfunction but no-one had a previous history of congested breathing, or aspiration. Therefore it was assumed that the pharyngeal and oesophageal phases of swallowing were not severely altered (posterior drooling), and the main problem being in all cases the oral phase of swallowing (anterior drooling). Only 12% ($n = 3$) of patients were not receiving medical treatment. Twenty-seven of them received at least one of these drugs: 44% anti-epileptics, 23% anxiolytics plus anti-epileptics, 12% antipsychotics, 11% anxiolytics plus anti-parkinson drugs, 10% anxiolytics (mean two drugs per patient). Patients were not taking any medical treatment known to induce sialorrhea (i.e. clozapine, olanzapine, risperidone, nitrazepan, bethanecol, etc.). The exclusion criteria were posterior drooling suspicion, specific contra-indications to scopolamine, including heart disease, glaucoma, prostatic hypertrophy, pyloric obstruction, liver or renal dysfunction, and hypersensitivity to the drug.

The severity of drooling was determined subjectively by means of interviews with the carers and medical staff and by direct observation. Drooling was quantified using the Thomas-Stonell and Greenberg scale [16] which differentiates five degrees of drooling: 1 = dry (no drooling); 2 = mild (moist lips); 3 = moderate (wet lips and chin); 4 = severe (damp clothing); and 5 = fulsome (wet clothing, hands and objects). The frequency of drooling was estimated using the number of bibs used each day.

Patients from the study population were randomly distributed into two subgroups: one group formed of 15 patients who were initially treated with scopolamine skin patches (Scopoderm TTS, Novartis Consumer Healthcare, UK) and the other formed of 15 patients who initially received placebo skin patches. Both skin patches were circular, with a diameter of 1.8 cm and thickness of 0.2 mm, with an impermeable protection and an adhesive that was in contact with the skin. The skin patch was placed behind the ear, at the level of the mastoid process (Figure 1). The scopolamine skin patch included a reservoir of the drug containing 1.5 mg of scopolamine that was released slowly, achieving a maximum serum concentration at 12–24 h. Its effect was maintained for 72 h. After this time,

Figure 1

Application of the scopolamine skin patch on the mastoid process

the skin patch was replaced by a new one, positioned behind the other ear.

Before starting the study, baseline quantification of the degree of drooling was performed on two occasions separated by 1 week, and the mean of these two estimates was considered. After this, a scopolamine or a placebo skin patch was applied; the skin patches were changed every 72 h for a period of 2 weeks. After a 1-week washout period, the skin patches were applied in a crossover manner for a further 2 weeks. During the 5 week study period, weekly quantifications were made of the intensity of drooling in order to determine the efficacy of treatment; blood tests (full blood cell counts, biochemistry and electrolytes) were also performed at baseline and at the end of the second and fifth weeks of the study in order to exclude the presence of subclinical drug adverse effects.

Statistical analysis

The results of the Thomas-Stonell and Greeberg scale, used to determine the effect of the scopolamine and placebo skin patches on the severity of drooling, were analyzed by means of the Wilcoxon and Friedman tests. In order to improve the statistic analysis, the five clinical categories relating to the severity scale of drooling were grouped into three grades: grade 1 = dry; grade 2 = mild/moderate drooling and grade 3 = severe/fulsome drooling. The effect of scopolamine and placebo on the number of bibs used per day was analyzed using a paired-sample ANOVA test.

Results

Four patients (13.3%) dropped out because of moderate scopolamine side-effects: one case of irritability, one case of agitation and two cases of skin reaction. In consequence only 26 patients completed the study period.

At baseline, no significant differences in the severity of drooling were found between the placebo and scopolamine groups (Friedman test, $P > 0.05$). The 77% of patients ($n = 20$) presented drooling graded 3, and 23% ($n = 6$) showed a grade 2 of drooling (Figure 2).

Figure 2 shows the distribution of patients according to the severity of drooling (based on the modified Thomas-Stonell and Greeberg's 3 grades scale) at baseline and at the end of the first and second weeks of treatment with the placebo skin patches. The severity of drooling during the period of treatment with placebo was similar to the baseline measurement (Friedman test, $P > 0.05$).

The distribution of patients according to the severity of drooling at baseline and after the first and second weeks of treatment with the scopolamine skin patches is shown in Figure 2. Both measurements performed during the period of treatment with scopolamine showed a statistically significant reduction in drooling compared with baseline (Friedman test, $P < 0.001$). The highest reduction was detected after 1 week of treatment (7.7% = grade 1 and 69.2% < grade 3; Wilcoxon test, $P < 0.001$) and it persisted in the 2 weeks control (19.3% = grade 1 and 80.8% < grade 3) (Figure 2). Differences between the first and the second week were not statistically significant (Wilcoxon test, $P = 0.206$).

The frequency of drooling, an evaluation based on the number of bibs used each day, was found to decrease progressively during treatment with scopolamine from 6 bibs/day at baseline to 4 bibs/day after the first week of treatment ($P < 0.005$) and to 3 bibs/day after the second week of treatment ($P < 0.005$). During the period of treatment with placebo, the number of bibs used per day was similar to the number at baseline.

Minor adverse effects related to the use of the scopolamine skin patch were observed in three patients (11%): one case of skin reaction, one case of urinary retention and one case of mydriasis. With the placebo skin patch, there was only one case of agitation. After a medical examination, it was considered unnecessary that any of these patients discontinued treatment. No changes were detected in the blood tests during the course of the study.

Discussion

It has been suggested that anticholinergic drugs such as benztropine, glycopyrrolate and scopolamine could be useful in the treatment of drooling. However, to date it has not been shown that any one anticholinergic is more effective than another [17]. Scopolamine skin patches for trans-

Figure 2

Evolution of drooling after placebo and scopolamine administration during the follow-up period (n = 26). Grade 1 (□); Grade 2 (▨); Grade 3 (■)

dermal administration could be a useful alternative in the treatment of these patients, and a number of studies have detected a reduction in saliva secretion with this treatment, although efficacy varies between patients [15, 18–20].

The results of the present study coincide with those published by other authors such as Brodtkorb *et al.* [21]; in that study of 15 patients with mental retardation, treatment with scopolamine led to a significant reduction in drooling at 24, 48, and 72 h after application of the skin patch, compared with placebo. Lewis *et al.* [15] also found that drooling completely resolved in one third of cases in a group of 11 children with mental retardation and moderate-severe drooling. The difficulty for quantifying drooling in disabled patients explains the variability of results, with efficacies between 19% and 67% being reported in the literature [14, 15, 19, 20]. The volumetric quantification of drooling (e.g. external collection devices, intraoral suction hook, etc.) provides an objective evaluation of the quantity of saliva produced and can help guide treatment and assess outcomes [1, 19, 20]. However the limited collaboration in disabled patients requires the use of alternative methods of quantification. In these cases, it is frequently the use of semi-quantitative clinical scales that limits the objectivity of the results obtained [15, 21].

In addition, we have found no prospective studies in the literature that have evaluated the effects of scopolamine beyond 3–5 months [15, 19], although, anecdotally, our group recently published a case report in which treatment had been continued for 3 years [22].

Pupillary dilatation and urinary retention are the more common adverse effects of scopolamine skin patches [14, 15, 20]. Lewis *et al.* [15] observed pupillary dilatation in 66% of patients during treatment with scopolamine skin

patches. Talmi *et al.* [20], in a study of 12 patients treated with transdermal scopolamine for a short period (1–6 days), reported four cases of blurred vision and one of urinary retention for which treatment had to be interrupted. The prevalence of blurred vision and accommodation problems was lower in the present series, but it could be underestimated as most of the patients had no speech and were unco-operative. Due to these adverse effects some authors recommend the use of appropriate spectacles when anticholinergic patches are used [23]. These and other studies suggest that the majority of adverse effects developed during the initial hours or days of treatment [15, 20, 23]. In the present study, the changes in behaviour were observed within the first 48 h of treatment with scopolamine and so, treatment was interrupted. However, behaviour went back to normal after 12–24 h once the patch was removed. All in all, it could be concluded that adverse reactions were of minor importance. Nevertheless we cannot rule out the appearance of further side-effects if the treatment were prolonged. Other, less common adverse effects have been reported, including tachycardia, anxiety, disorientation, hallucinations and psychosis [9, 12, 15].

In conclusion, transdermal scopolamine can be a therapeutic option to control drooling in severely disabled patients. It is an effective and safe method, although it requires appropriate patient selection and is not free from adverse effects. Its long-term efficacy remains unknown.

Competing interests

There are no competing interests to declare.

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