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Nasal polyps treated by beclomethasone nasal aerosol

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SUMMARY

A double-blind cross-over study of the effect of insufflation of beclomethasone dipropionate 400 μg per day for four weeks showed favourable results, as verified statistically, concerning nasal blockage at the end of the treatment period. Rhinomanometry also showed that the nasal patency was significantly improved during the beclomethasone period. There was also a tendency, though not statistically significant, for nasal secretion to react favourable. The polyps did not disappear during the active treatment period and short-term treatment with beclomethasone aerosol can thus only be used as an adjuvant to other modes of therapy, whether medical or surgical, in nasal polyps. No clinical side-effects of any importance were observed during the study.

INTRODUCTION

The traditional treatment for nasal polyps comprises oral administration of antihistamines and ephedrine derivatives and various kinds of operation from polypectomy to more radical procedures. Since the principal aetiology of nasal polyps is believed to be infection and/or allergy, surgery can only be expected to give temporary relief. It is also well known that the polyps very often recur and further operations have to be performed, sometimes annually. It is therefore natural that new forms of treatment have been tried in order to find a more causal and more effective treatment regimen for this condition. Short-term therapy with ACTH has been reported to have a good effect on nasal polyps (Tayler, 1973) and oral treatment with corticosteroids has also proved beneficial (Wentges, 1967). Our own experience with corticosteroids was that they had a good initial effect, but the polyps recurred as soon as the treatment was withdrawn. The general complications caused by corticosteroids, like Cushingoid habitus and adrenal suppression, also constitute a contraindication to such treatment when the indication is not more serious than nasal polyps.

The introduction of beclomethasone dipropionate for inhalation therapy in asthma represented an important advance, with remarkable relief of symptoms and no systemic side effects (Brown et al., 1972; Clark, 1972; Lal et al., 1972). It has been possible to keep the dose of beclomethasone at a low level (400 μg) and still achieve favourable results. It is a common finding that patients treated

with steroid orally can often withdraw or reduce this treatment gradually after initiation of beclomethasone inhalation therapy (Bruun and Hansen, 1973; Graff-Lonnevig and Kraepelien, 1974; Nou and Rosenhall, 1976). It has been noted that this withdrawal is sometimes accompanied by increasing symptoms (Godfrey and König, 1973; Nou and Rosenhall, 1976). Studies of the plasma cortisol level have shown no changes during inhalation therapy with beclomethasone in doses up to 1 gram/day (Harris et al., 1973; Graff-Lonnevig and Kraepelien, 1974), but Mygind and Hansen (1973) found a suppression of 17-ketogenic steroids in urine at doses of 800 μg/day and doses of 400 μg also appeared to give slight suppression. No atrophy of the bronchial mucosa has been observed in man after treatment with beclomethasone for 4-6 months (Andersson, 1975; Thiringer et al., 1975). Growth of monilia in the mouth and throat has been reported, however (Graff-Lonnevig and Kraepelien, 1974).

Beclomethasone has also been used in patients with allergic or vasomotor rhinitis. Favourable clinical results have been reported in hay fever (Mygind, 1973; Vilsvik, 1974; Prahl et al., 1976; Löfkvist and Svensson, 1975) and perennial rhinitis (Gibson et al., 1974; Hansen and Mygind, 1974; Löfkvist and Svensson, 1976) and these studies have mostly been performed as double-blind cross-over trials. Studies of adrenal function during nasal insufflation therapy with beclomethasone showed no or insignificant changes of 17-ketosteroids with 400 μg/day (Mygind, 1973; Prahl et al., 1976).

It seems logical to study the effect of beclomethasone in patients with nasal polyps also. Since the completion of the clinical study presented below, results from a similar study have become available. Mygind et al. (1975) performed a double-blind investigation of beclomethasone in 35 patients with moderate to severe polyps and 19 of them received beclomethasone and 16 placebo. Patients who complained only of nasal obstruction were excluded from the investigation and operated upon immediately. On average, the patients had been operated upon eight times for nasal polyps before taking part in the investigation. The dose was 400 μg/day, but of this 30 per cent was considered to be retained in the canister and therefore only 250-300 μg was applied to the nasal cavities. The duration of treatment was three weeks. Sneezing, nasal secretion and blockage were reduced according to the patient's recording of symptoms. When corrected for the placebo effect the symptoms were reduced to 68 per cent of the initial level, which was much less than in the treatment of seasonal or perennial rhinitis with beclomethasone.

The purpose of the present investigation was to perform a double-blind cross-over study of beclomethasone aerosol on nasal polyps in patients who have been operated upon for nasal polyps only a few times, and to analyse the results not only by evaluation of the patient's symptoms but also by rhinomanometry.

PATIENTS AND METHODS

Twenty-three consecutive patients who were outpatients at the Department of Otolaryngology and had nasal polyps giving symptoms and who had not been

operated upon more than four times previously for nasal polyps were included in the study. The study was carried out during the autumn and winter. Those who had asthma or were receiving steroid treatment were exluded, as also were patients with nasal operations within the preceding six months. Three of the patients in the series were later excluded: one had a coronary heart attack, one was found to have a nasal fibroma instead of polyps and one received placebo by mistake during both periods of the investigation. The study thus comprised 20 patients aged from 18 to 88 years (mean age 52 years). Treatment was given in two consecutive four-week periods, with beclomethasone during one period and placebo during the other. The insufflators were identical and it was not possible to detect which of them contained active material and which placebo. The daily dose was one puff in each nostril four times a day, which for beclomethasone means 50 μg per puff or 400 μg per day. In analogy with the discussion above, some of this drug was probably retained in the canister, however. The patients were allowed to continue with antihistamines or other drugs as before.

The evaluation included rhinoscopy with estimation of the size of the nasal polyps in four cathegories: no visible polyps (0); small polyps with good patency on respiration and inspection (1); moderate polyps with some patency (2); and large, obstructing polyps (3). Rhinomanometry was performed at the beginning of each treatment period and after the last period. In addition, the patients rated their nasal blockage and nasal secretion during each of the eight weeks of the study. The rating scale was: reduced, unchanged or increased for each of these two symptoms. The general impression of the patient concerning nasal symptoms during each treatment period was also recorded.

The rhinomanometry was done as posterior rhino-rheomanometry and the results were expressed in accordance with the principles laid down by Drettner (1961). This means that the patency of the two nasal cavities was expressed as the expiratory air flow (in litres/min) at a pressure difference of 10 mm H_2O between the nasopharynx and the nostrils.

Side effects during the treatment were also recorded. No laboratory investigation was done concerning systemic effects of steroids.

Statistical evaluation was performed by measuring the difference in scores or other numerical values between period I and II for each individual. These differences for those given beclomethasone in period I were compared with those for patients given placebo in period I by using Fischer's permutation test (Odén and Wedel, 1975). This method is more rigorous than merely comparing scores from the active treatment period and the placebo period for each individual. Systematic differences between the two periods, e.g. concerning climate, pollen in the air etc are avoided in this way.

RESULTS

When the code was broken it was found that nine of the patients had started with beclomethasone and eleven with placebo. The number of earlier polypecto-

mies did not differ between these two groups and the mean was 1.0 in each group.

The rhinoscopic estimation of the size of the nasal polyps showed that the initial score, which was on average 1.5 on both sides, decreased to 1.1 on both sides during the active treatment period while it was 1.5 and 1.2, respectively, on the right and left side during the placebo period. A score of 1 means small polyps with good patency and a score of 2 moderate polyps with some patency. The difference in size of the polyps was not statistically significant, however.

The rhinomanometry showed that the initial mean value of 15.1 litres/min increased to 19.7 litres/min during the active treatment period while it was 13.5 during the placebo period. This difference was statistically significant ($p < 0.05$) and means that the nasal patency was better during the beclomethasone period than during the placebo period.

The nasal symptoms as assessed by the patients were analysed in four different ways: by comparing the mean for all weeks in the active period and the placebo period with the situation before the investigation, by comparing the last week in each period, by comparing the first week in period II with the preceding week, and finally by comparing period I with period II. The first method showed no significant difference, but the symptoms were on average less pronounced during the active treatment period, both for nasal blockage and for nasal secretion. During the last week in each period nasal blockage was less severe during the active treatment period than during the placebo period ($p < 0.05$) and a similar, though not significant, tendency was found for nasal secretion. When the preference for active drug or placebo was studied for the first week in period II in relation to the preceding week, it was found that nine patients preferred the active drug and four preferred placebo for relief of nasal blockage while the remainder showed no preference. For relief of nasal secretion eight preferred active drug and three placebo, while the remainder showed no preference. When the subjective evaluation in period I was compared with that in period II there was a similar tendency: less nasal symptoms during the active treatment period, but no significant difference.

The general impression of improvement or no improvement of nasal symptoms during each of the two periods showed that seven patients improved during the active treatment period and four during the placebo period, while the remainder were unimproved. This difference was not significant.

Side effects were reported for two patients: one had headache during the placebo period and one had small ulcers in the nostrils during the active treatment period. The remaining patients had no side effects.

DISCUSSION

The present investigation is the first study of beclomethasone aerosol treatment of nasal polyps in which each patient served as his own control, which provides a more certain means of assessment than a simple double-blind study. The present study also included rhinomanometry, which is com-

pletely objective. It is therefore of interest to note that rhinomanometry revealed significant better results with beclomethasone than with placebo. The evaluation made by the patients showed that nasal blockage was significantly less severe during beclomethasone treatment than during placebo treatment during the last week of the two periods, i.e. when the patient had been receiving the treatment for three weeks. There was also a tendency, though not significant, for beclomethasone to have a beneficial effect on nasal secretion.

Whether the improvement of nasal patency was caused by reduction of the size of the polyps or by general shrinkage of the nasal mucosa is uncertain. Rhinoscopy showed a decrease in the size of the polyps during the active treatment period, but this difference was not significant. It thus seems that the improvement of the nasal patency was at least partly an effect of reduction of the size of the nasal polyps. This effect, however, was never of such magnitude that the polyps disappeared completely.

Beclomethasone is thus a useful adjuvant in the treatment of nasal polyps, but it cannot replace other forms of medical or surgical treatment. As the effectiveness of the methods of treatment available so far is unreliable and usually temporary, it is an advantage to have access to another mode of therapy in this disease. Beclomethasone insufflation may therefore be used either as the sole treatment in small polyps or as a complement to other medical treatment in small or moderate polyps. Also, it may be used after polypectomy in patients with moderate or large polyps. In the latter case, it seems logical to remove the polyps before beclomethasone treatment is started since the insufflation will otherwise probably not be able to reach sufficiently large areas. The fact that statistically significant results were not obtained until the fourth week of therapy indicates that the treatment must be continued for some time before its effect is judged. It is obvious that beclomethasone may be used early as well as late in the course of nasal polyps since the present study comprised patients operated upon only once on average, while Mygind et al. (1975) studied patients operated upon eight times on average before the investigation, and both studies gave favourable results.

Only short-term treatment has been tested in the present study and in that reported by Mygind et al. (1975). Several of the patients in this series have, however, continued the therapy after the investigation, mostly with good subjective results, but no controlled study has been done. We wish to stress that several of the patients in this study also underwent polypectomy after the investigation. Some of the other patients had only slight nasal symptoms after the investigation and could therefore at least temporarily abstain from any kind of treatment.

No clinical side-effects of any importance were observed during the study. However, neither the systemic effect of steroids nor possible growth of bacteria or fungi in the nose or throat were investigated. Other studies have shown that nasal insufflation of 400 μg beclomethasone per day does not cause any systemic steroid effect (Mygind, 1973; Prahl et al., 1974). Since higher doses may have a systemic effect, at least when given by inhalation for asthma, it seems wise not to increase the dose above 400 μg. No investigation has been done in which

dose-response effects have been studied in beclomethasone treatment of nasal polyps and it is therefore impossible to judge whether an increase in the dose will also give an increased effect.

ZUSAMMENFASSUNG

Eine doppelblinde Cross-over-Untersuchung der Wirkung von insuffliertem Bechlomethasondipropionat, 400 μg täglich während vier Wochen, zeigte gute Ergebnisse, die am Ende der Behandlungsperiode in Bezug auf nasale Blockierung statistisch belegt wurden. Rhinomanometrie zeigte ebenfalls, dass die Nasenverstopfung während der Bechlomethason-Periode signifikant abnahm. Es wurde ausserdem eine Neigung, die zwar nicht statistisch signifikant war, zu einer günstigen Reaktion der nasalen Sekretion festgestellt. Die Polypen verschwanden nicht im Laufe der aktiven Behandlung, und derartige, kurzfristige Therapie mit Bechlomethason-Aerosol kann folglich nur eine Ergänzung anderer Behandlung, medikamentöser oder chirurgischer, von nasalen Polypen sein. Es wurden in der Untersuchung keine klinischen Nebenwirkungen von Bedeutung festgestellt.

RÉSUMÉ

Un double examen dit "aveugle" de l'effet de l'insufflation quotidienne de 400 μg de dipropionate de béclométhasone pendant quatre semaines a donné des résultats favorables, vérifiés statistiquement, concernant l'obstruction nasale à la fin de la période thérapeutique. La rhinomanométrie a aussi démontré que les voies nasales restaient moins obstruées durant la période de traitement au béclométhasone. On a aussi pu constater que la sécrétion nasale avait tendence à réagir d'une manière favorable, mais cette tendence n'était pas statistiquement significative. Les polypes n'ont pas disparu au cours du traitement actif, et le béclométhasone, utilisé en aérosol pour ce traitement de courte durée, ne peut donc être considéré que comme un adjuvant à d'autres types de traitements, médicaux ou chirurgicaux, des polypes nasaux. Aucun effet clinique secondaire d'importance appréciable n'a été observé au cours de cette étude.

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