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Dose-related efficacy and tolerability of fluticasone propionate nasal drops 400 μg once daily and twice daily in the treatment of bilateral nasal polyposis: a placebo-controlled randomized study in adult patients

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Summary

Background Topical corticosteroids are the accepted medical adjunct to surgery in patients suffering from nasal polyposis. Fluticasone propionate (FP) is a potent, topically active corticosteroid which has been formulated as nasal drops specifically for the treatment of polyposis.

Objectives To evaluate dose-related efficacy and tolerability of FP nasal drops (FPND) in the treatment of mild to moderate bilateral polyposis; in a double-blind, placebo-controlled, multicentre international study.

Methods Adult patients ($n = 142$) with bilateral nasal polyps were randomized to receive either FPND 400 μg once daily (o.d.), FPND 400 μg twice daily (b.i.d.) or placebo for 12 weeks. The majority then entered a further 12 week open period during which all patients received FPND 400 μg o.d. The primary efficacy endpoint was the physicians' visual assessment of polyp size. Secondary clinical endpoints were nasal blockage and overall rhinitis (0–3 scores), peak nasal inspiratory flow (PNIF), olfactory function tests, and requirement for polypectomy. The patients also kept twice daily records of symptom scores, peak nasal inspiratory flow (PNIF) and use of rescue medication.

Results At the end of the 12 week randomized treatment period, polyp size was reduced significantly by FPND 400 μg b.i.d. as compared with placebo ($P = 0.006$). Clinical assessments of nasal blockage and overall rhinitis showed significant improvements at several stages of treatment with both doses of FPND. Clinic PNIF was also improved significantly by both doses of FPND in comparison with placebo, and FPND 400 μg b.i.d. was significantly more effective than 400 μg o.d. ($P = 0.045$). Patient diary card scores supported the clinical assessments. Two patients on placebo required polypectomy and all treatments were well tolerated with a similar incidence of adverse events.

Conclusion FPND 400 μg once or twice daily is an effective and well-tolerated treatment for bilateral nasal polyposis.

Keywords: fluticasone propionate, nasal corticosteroid, nasal drops, nasal polyposis

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Introduction

Nasal polyposis is a condition which affects some 1–2% of the adult population in Europe [1]. The aetiology is largely unknown but certain conditions are associated with increased frequency of nasal polyps, including cystic fibrosis, bacterial

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infection, asthma, aspirin intolerance and allergy [2]. The connection between nasal polyps and allergy is somewhat controversial [3,4], however, symptoms of sneezing, rhinorrhoea and itching often accompany nasal blockage due to polyposis and the extracellular polyp fluid contains increased levels of histamine and immunoglobulin (Ig) E [5]. There is also degranulation of mast cells and increased numbers of eosinophils in polyp tissue [6,7]. This characteristic eosinophilia appears to define nasal polyposis as an aspect of chronic eosinophilic rhinosinusitis, since the presence and severity of polyps were found to correlate with eosinophil infiltration in a consecutive series of patients undergoing endoscopic sinus surgery [8].

The current treatment of nasal polyps involves a combination of pharmacological intervention and surgery [9]. A recent position statement published by an international panel of experts recommended that mild or moderate polyposis should be treated with topical corticosteroids, whilst more severe polyps should be treated with short-term systemic corticosteroids followed by topical steroids; patients failing to respond to treatment should then be considered for surgery [10]. Surgery alone has no effect on the underlying inflammatory condition, however, and recurrent polyposis is common, with topical corticosteroids again commonly prescribed to prevent post-surgical polyp regrowth [8]. Topical corticosteroids, presented as aqueous nasal spray, aerosol, dry powder or nasal drop formulations for the medical treatment of polyposis effectively reduce both polyp size and rhinitis symptoms [9,11–16] although none is widely registered with a polyp indication. Fluticasone propionate (FP) is a potent topically active corticosteroid, with minimal systemic absorption following application of the aqueous nasal spray (FPANS) [17]. FPANS is effective in the treatment of seasonal and perennial rhinitis in adults and children [18–21] and has also demonstrated efficacy in the treatment of nasal polyps [9,11,12]. Nasal drop formulations have been shown to allow greater exposure than sprays to the paranasal sinus mucosa, the site where nasal polyps most commonly arise [22–24]. FP nasal drops (FPND) have therefore been developed specifically for the treatment of nasal polyps and is presented as an unpreserved, 400 μg unit dose, from which the systemic bioavailability of FP is 0.06%, compared with 0.51% from FPANS [25]. This apparent discrepancy between improved distribution yet lower systemic bioavailability of FPND is thought to arise as a result of the increased ciliary clearance that occurs in the posterior nasal cavity. Low systemic bioavailability is an important consideration in patients requiring long-term topical treatment with corticosteroids and unit dose FPND has advantages over betamethasone sodium phosphate, the only alternative steroid nasal drops currently available, which has shown systemic side-effects and can be over-dosed [26,27]. FPND is therefore indicated for the regular treatment of nasal polyps. The recommended dose in adults is the contents of one unpreserved unit dose containing 400 μg FP, divided equally between the nostrils, given once or twice daily. The purpose of this study was to compare the efficacy and tolerability of these once daily and twice daily FPND with placebo in patients with bilateral nasal polyposis over a 12-week randomized treatment period. This was followed by a 12-week open period of treatment with FPND 400 μg o.d. to obtain additional safety data.

Materials and methods

Study design

This was an international, multicentre, randomized parallel group placebo-controlled study conducted in 12 centres in Denmark (three centres), Finland (one centre) and Sweden (eight centres). Before entering the treatment phase, patients underwent a 2-week run-in period during which they ceased all medication for polyposis except for loratadine tablets which were provided as rescue therapy for the relief of troublesome symptoms. Following the run-in period, patients were randomized to receive FPND 400 μg o.d., FPND 400 μg b.i.d., or placebo for 12 weeks (see Fig. 1). With the exception of the Danish centres, all patients completing the randomized treatment phase received FPND 400 μg o.d. for a further 12 weeks. Patients attended the clinic at the beginning and end of the run-in period and after 4, 8, 12 and 24 weeks treatment. A follow-up visit was made 2 weeks after the end of the open phase. At the initial visit (visit 1) patients underwent physical and oropharyngeal examinations and details of clinical history were recorded. Blood and urine samples for biochemistry and haematology screens and urinalysis were taken at visit 1 and

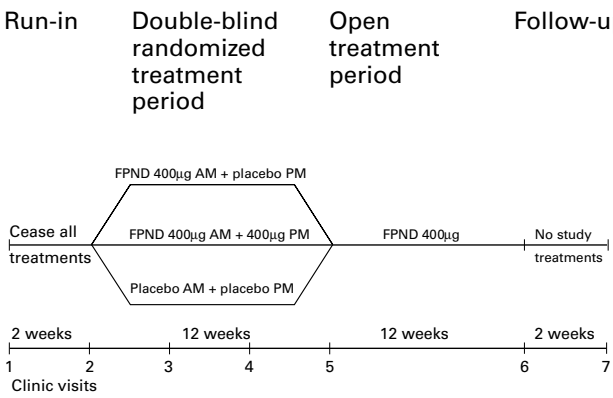

Fig. 1. Schematic representation of the study design. Loratadine tablets were permitted as rescue medication throughout the duration of the study. FPND = fluticasone propionate nasal drops.

at the end of both treatment periods. Efficacy and safety parameters were assessed after 4, 8 and 12 weeks of randomized treatment, after the 12 week open phase and at follow-up.

Patients

Patients were required to be at least 16 years of age and suffering from bilateral nasal polyposis diagnosed as mild (small polyps not reaching the upper edge of the inferior turbinate, causing only slight obstruction) or moderate (medium-sized polyps reaching between the upper and lower edge of the inferior turbinate and causing troublesome obstruction). Patients were excluded from the study if they had severe polyposis (large polyps reaching below the lower edge of the inferior turbinate, causing total obstruction), had a concurrent purulent nasal infection, or were unable to cease treatment with intranasal steroids or sodium cromoglycate during the 2 week run-in period. Also excluded were patients who were currently receiving inhaled corticosteroids or who had received depot or oral steroids within the previous 3 months, and patients who had received astemizole in the 6 weeks prior to visit 1, or other antihistamines in the 48 h prior to visit 1. Patients who had undergone surgery to treat their nasal polyps in the previous 3 months, had hypersensitivity or contraindication to steroids, or had allergic rhinitis or any other disease likely to interfere with the outcome of the study were excluded, as were females who were pregnant, lactating, or likely to become pregnant during the study period.

Prior to starting the study, approvals were obtained from the local ethics committees, and written informed consent was obtained from each patient. The study was conducted in accordance with the Declaration of Helsinki (1989, 1996) and in accordance with good clinical practice.

Treatments

The treatments were given as described in Fig. 1. Active and placebo nasal drops were provided in identical single-dose containers and the contents of each were divided between both nostrils (200 μL per nostril), in the head down and forward position [28]. The Danish patients did not receive FPND 400 μg o.d. in the 12 week open treatment period phase. Patients were supplied with rescue loratadine tablets for the relief of troublesome symptoms as required, subject to a maximum dose of 10 mg daily. No other medication for polyposis was allowed.

Clinical assessments

Polyp size, degree of nasal blockage and overall rhinitis were assessed and peak nasal inspiratory flow (PNIF) was measured at each clinic visit. Polyp size and nasal blockage were assessed using predefined scales (Table 1). Overall rhinitis symptoms (sneezing, rhinorrhoea and nasal itching) were also assessed on a scale of 0 = no symptoms to 3 = severe symptoms. Olfactory function was assessed at the end of baseline and at the end of the double-blind phase using two tests: the Butanol Threshold Test [29] and a modified (International) version: University of Pennsylvania Smell Identification Test (UPSIT) [30].

Diary card assessments

During the run-in and throughout the randomized treatment period, patients kept daily diary cards on which they recorded overall rhinitis symptoms (sneezing, rhinorrhoea, nasal itching) morning and evening on a 4 point scale (0 = none to 3 = severe). They also recorded their degree of nasal blockage (Table 1) and sense of smell (0 = normal, 1 = slight difficulty in differentiating odours, 2 = moderate

Table 1. Scoring system for clinical assessments of polyp size and nasal blockage

Polyp size

0 = No polyps
1 = Mild polyposis − small polyps not reaching the upper edge of the inferior turbinate, causing only slight obstruction
2 = Moderate polyposis − medium sized polyps reaching between the upper and lower edge of the inferior turbinate and causing troublesome obstruction
3 = Severe polyposis − large polyps reaching below the lower edge of the inferior turbinate and causing total or almost total obstruction

Nasal blockage

0 = Breathing through nose freely and easily
1 = Slight difficulty breathing through nose
2 = Moderate difficulty breathing through nose
3 = Breathing through nose was very difficult/impossible

difficulty in differentiating odours, 3 = sense of smell absent), rescue medication usage and any adverse events. PNIF was measured each morning and evening by the patients, using a Youlten PNIF Meter [31], prior to taking the study medication. The best of three maximal inspiratory efforts was recorded on the diary card.

Safety evaluation

Patients were asked to record adverse events on the daily record card, and these were assessed by the investigator at each visit, in terms of severity and possible relationship to the study treatment. Physical examinations including measurements of blood pressure and heart rate were carried out at visit 1, at the end of randomized treatment, and at the end of the open treatment phase of the study, with a further follow-up examination in case of any abnormality. Oropharyngeal examinations were conducted at each clinic visit, and a swab test taken to confirm the presence of *Candida albicans* if clinically indicated. Any abnormalities were followed up to resolution. Urine and venous blood samples were taken at visit 1, at the end of randomized treatment and at the end of the open treatment phase of the study, with a follow-up examination in case of any abnormality. Standard haematological and biochemical analyses including serum cortisol were conducted at a central laboratory (Covance, Geneva).

Statistical methods

The primary population for the analysis of efficacy and safety was the Intent-to-Treat Population which included all randomized patients who took at least one dose of study medication.

The physicians' assessments of nasal polyps, nasal blockage, overall rhinitis symptoms, olfactory function and diary card data (score frequencies expressed as percentage of days and nights) were analysed using the Van Elteren extension to the Wilcoxon Rank Sum test, with country as the stratifying variable. Confidence intervals for the median difference between treatment groups were based on the unstratified Wilcoxon Rank Sum Test. Clinic and diary card PNIF data were analysed using an analysis of covariance and pairwise between-treatment comparisons made using linear contrasts to calculate 95% confidence intervals for the differences between treatment groups.

Laboratory parameters were recorded but not formally analysed. The treatment groups were also compared in terms of the incidence of the most common adverse events (6% or more patients experiencing an adverse event from any treatment group) using Fisher's Exact Test (twice the one-sided test).

Analyses were performed using the SAS system, Version 6.12 (SAS Institute Inc., Cary, NC, USA) and treatment differences were analysed using two-sided tests at the 5% level of significance.

Results

Patients

A total of 142 patients were randomized to treatment, of whom 47 received FPND 400 μg b.i.d., 48 received FP 400 μg o.d. and 47 received placebo. Basic patient demographic data are shown in Table 2: the demographic characteristics were similar for all three groups.

Sixteen patients were withdrawn during the randomized treatment phase, the majority due to lack of efficacy (five placebo, one FP 400 μg o.d., two FP 800 μg b.i.d.) or adverse events (five placebo, one FP 400 μg o.d., two FP 400 μg b.i.d.). One patient in the placebo group withdrew due to requirement for polypectomy. Two patients withdrew during the open phase, one requiring a polypectomy, the other for unspecified reasons.

Efficacy

Clinical assessments after 4, 8 and 12 weeks treatment are summarized in Table 3. At the end of the 12 week treatment period, the percentage of patients showing a reduction in polyp size was significantly greater in the FPND 400 μg b.i.d. group (41%) compared with the placebo group (15%). The reduction in polyp size at 12 weeks with FPND 400 μg o.d. (24%) was better than with placebo but without statistical significance. Similar group trends in polyp size were seen after 4 and 8 weeks, with FPND 400 μg b.i.d. always significantly better than placebo, and significantly more effective than FPND 400 μg o.d. at week 8. Clinical assessments of nasal blockage and overall rhinitis showed significant improvements with both b.i.d. and o.d. 400 μg doses of FPND compared with placebo after 4 weeks. The effects of FPND treatment were sustained and, except for rhinitis in the 400 μg b.i.d. group, remained statistically significant vs placebo at week 12. Dose-related increases in PNIF were measured at clinic visits after 4, 8 and 12 weeks of treatment. FPND 400 μg o.d. (increases of 28, 33 and 32 L/min, respectively) was consistently better than placebo (1, 8, 8 L/min) and the difference was statistically significant ($P < 0.05$) at week 4. The effect of FPND 400 μg b.i.d. on clinic PNIF (51, 53, 51 L/min) was significantly better than both placebo ($P < 0.001$) and FPND 400 μg o.d. ($P < 0.05$) at each visit.

Analysis of olfactory function by UPSIT showed the median number of identifiable smells to be generally similar after treatment, with 8.0 in the placebo group and 9.5 in each of the active treatment groups: one statistically significant difference ($P = 0.024$) was detected in favour of FPND 400 μg b.i.d. compared with placebo. When the test was

Table 2. Patient demographic characteristics —— Intent-to-Treat Population

		FPND		
	Placebo	400 μg o.d.	400 μg b.i.d.	Total
Number of patients				
Male	33	36	38	107
Female	14	12	9	35
Age (years)				
Mean	50	49	53	51
Range	26–79	22–83	27–75	22–83
Height (cm)				
Mean	176	176	176	176
Range	155–192	162–191	155–189	155–192
Weight (kg)				
Mean	80.3	79.6	77.2	79.0
Range	58–116	55–104	56–112	55–116
History of polyposis (years) n (%)				
< 2	8 (17)	4 (8)	10 (21)	22 (15)
2–5	7 (15)	9 (19)	8 (17)	24 (17)
5–10	5 (11)	10 (21)	6 (13)	21 (15)
> 10	27 (57)	25 (52)	23 (49)	75 (53)
Previous polypectomy n (%)				
Yes	37 (79)	35 (73)	30 (64)	102 (72)
No	10 (21)	13 (27)	17 (36)	40 (28)

stratified by baseline value (baseline median number of identifiable smells for placebo, FPND 400 μg o.d. and FPND 400 μg b.i.d. were 8.0, 4.0 and 7.0, respectively), statistically significant differences were observed in favour of each FPND treatment in comparison with placebo ($P = 0.004$ and 0.001 for FPND 400 μg o.d. and FPND 400 μg b.i.d., respectively). No significant differences between treatment groups were detected in the butanol smell threshold test.

Diary card data (Fig. 2) for patients receiving FPND 400 μg b.i.d., FPND 400 μg o.d. and placebo showed median nasal blockage scores < 2 (none or mild) on waking on 87, 76 and 54% of nights, and median daytime scores < 2 on 88, 85 and 68% of days, respectively. The only significant differences (night and day) were between FPND 400 μg b.i.d. and placebo. Median occurrences of overall rhinitis scores < 2 were found on 99, 94 and 77% of nights and 98, 97 and 81% of days, respectively, both doses of FPND being significantly better than placebo. Considerable improvements in sense of smell also occurred but with no significant treatment differences. Mean daily PNIF measurements are summarized in Fig. 3, demonstrating

Table 3. Clinical assessments of polyp size, nasal blockage, and overall rhinitis during 12 weeks of treatment with FPND 400 μg o.d., FPND 400 μg b.i.d. or placebo (percentage of patients showing improvements after 4, 8 and 12 weeks)

	Week	Placebo	FP 400 μg o.d.	FP 400 μg b.i.d.
Polyp size	4	9	15	33*
	8	21	20	39*†
	12	15	24	41**
Nasal blockage	4	20	49**	39*
	8	36	46	41
	12	23	52**	41*
Overall rhinitis	4	23	43**	57**
	8	36	48	59*
	12	33	52*	50

FPND vs placebo: *$P < 0.05$, **$P < 0.01$; FPND 400 μg b.i.d. Vs FPND 400 μg o.d.: †$P < 0.05$.

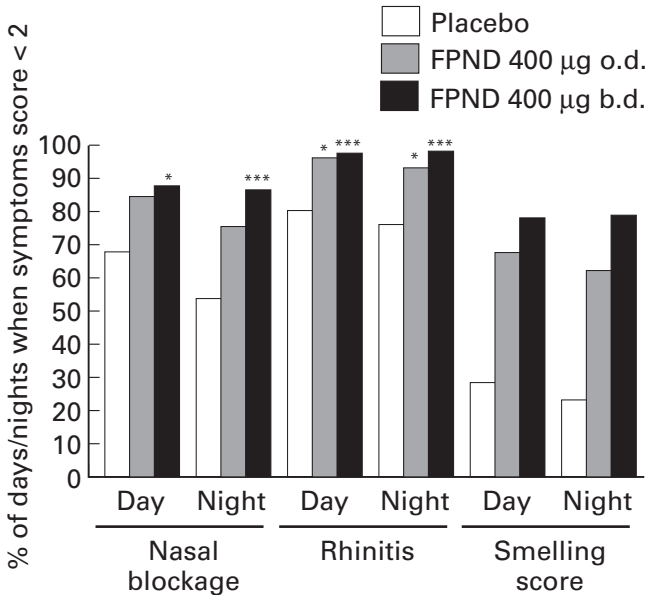

Fig. 2. Diary card symptom severity assessed by patients with nasal polyposis over 12 weeks of randomized treatment with FPND 400 μg b.i.d., FPND 400 μg o.d. or placebo. Statistical significance: FPND vs placebo: $*P<0.05$, $***P<0.001$

significant improvements from baseline with both doses of FPND in comparison with placebo. FPND 400 μg b.i.d. had a more marked effect than FPND 400 μg o.d., although there was no statistically significant difference between the two active treatments. Use of loratadine rescue medication remained low throughout the study, but was statistically higher in the placebo group than the FPND 400 μg b.i.d. treatment group ($P=0.021$).

Safety

During the randomized treatment phase 27 (57%) patients in the placebo group, 16 (33%) patients in the FPND 400 μg o.d. group and 21 (45%) patients in the FPND 400 μg b.i.d. group experienced adverse events. The most commonly reported event was upper respiratory tract infection (15, 8 and 15% of patients in the placebo, FPND 400 μg o.d. and FPND 400 μg b.i.d. groups, respectively). Other events commonly reported included epistaxis (2, 8 and 9% of patients, respectively), nasal congestion/blockage, sinusitis and cough. During the randomized treatment phase, there was no statistically significant difference between placebo and the active treatment groups in the incidence of these events and there were no serious treatment-related adverse events.

Nine patients were withdrawn due to adverse events during the randomized treatment phase: six from placebo,

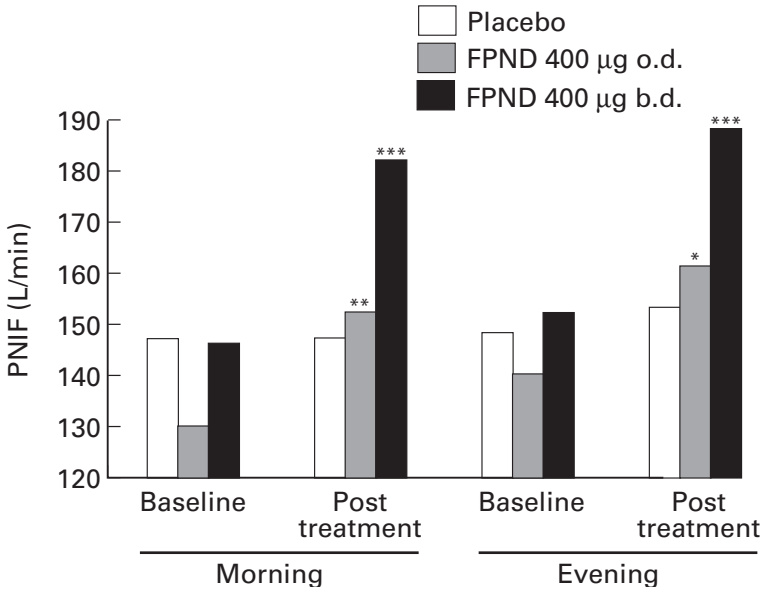

Fig. 3. Mean changes in diary card peak nasal inspiratory flow (PNIF) over 12 weeks of randomized treatment with FPND 400 μg b.i.d., FPND 400 μg o.d. or placebo. Statistical significance: FPND vs placebo: $*P<0.05$, $**P<0.01$, $***P<0.001$

one from FPND 400 μg o.d. and two from FPND 400 μg b.i.d. In the placebo group four patients were withdrawn due to ear, nose and throat conditions, one due to nausea and vomiting and one due to asthma. None of these events was serious but all except asthma were assessed as possibly treatment related. The patient on FPND 400 μg o.d. was withdrawn due to asthma (not serious or treatment related). In the FPND 400 μg b.i.d. group, one patient was withdrawn due to epistaxis and one due to abdominal distension and nausea. Neither event was considered serious but both were assessed as possibly treatment related.

During the open phase, when all patients received FPND 400 μg o.d., adverse events were reported by 24 (22%) of the 107 patients, 10 of whom had previously received placebo and seven each the two active treatments. Five of these events were considered to be treatment related: two epistaxis, one nasal irritation, one throat irritation and one gastrointestinal disorder; however, none was serious or led to withdrawal. One patient reported a serious adverse event at follow-up (candidiasis of the oesophagus) which was assessed as 'probably related' to the study medication. This patient had received placebo during the double-blind phase, prior to FPND 400 μg o.d. during the open phase.

There were no clinically relevant treatment effects on any routine parameters of haematology, blood biochemistry or urinalysis and no differences between either dose of FPND or placebo.

Discussion

The primary objectives in treating nasal polyposis are to eliminate or considerably reduce the size of the polyps, re-establish nasal breathing, eliminate the symptoms of rhinitis, restore the sense of smell and prevent the recurrence of polyps after surgery [32]. Topical corticosteroids are widely recognized as the fundamental medical treatment for nasal polyps [8–10] although the available systems for intranasal drug delivery are not ideally suited to the long-term corticosteroid usage required to control polyposis. Accurate drug delivery and low systemic bioavailability are of particular importance in these chronic conditions, and the FPND unit dose formulation has been developed specifically to address the problem of safe and effective treatment of nasal polyps [22–27]. Previous studies have demonstrated significant reductions in polyp size using the aqueous nasal spray formulation (FPANS) at a dose of 200 μg b.i.d. [9,11] and the activity of FPANS in patients with severe polyposis compared favourably with beclomethasone dipropionate nasal spray at the same dose [12]. It was therefore unexpected to find that whereas FPND 400 μg b.i.d. reduced polyp size significantly compared with placebo, but that the effect of 400 μg o.d. on polyp size was not statistically significant. However, the FPANS studies were relatively small and employed a different scoring system for assessing polyp size: wholly subjective assessments were made using a five-point scale running from zero (no polyps) to 4 (complete obstruction), with scores of 1, 2 or 3 representing small, medium or large polyps, respectively. In the present study a semiquantitative four-point scoring system was used; this was intended to reduce subjectivity but in fact had the disadvantage that a 'medium' polyp which had undergone substantial reduction in size during treatment might be given the same score both pre- and post-treatment. This could explain why 60% of patients in this study remained unchanged with regard to polyp size despite the occurrence of statistically significant and dose-related improvements in the objective measurements of PNIF in the FPND-treated groups. In addition, the investigators and patients reported significant improvements in the major symptom of nasal blockage as well as overall rhinitis with both doses of FPND. The improvement in nasal blockage recorded by the patients on the diary card was not statistically significant. It has been established previously that PNIF is more sensitive to the effects of treatment than symptom scores [11,12].

The patients' daily assessments showed a better overall effect vs placebo with the higher dose of FPND, although the difference between b.i.d. and o.d. doses was not often statistically significant. A similar daily trend occurred in ability to smell, and it is of interest that patients receiving FPND 400 μg b.i.d. had significantly improved olfactory function, as measured by UPSIT [30]. Clinical experience indicates that the effect of topical corticosteroids on smell is poor compared with systemic steroids [32] but few controlled studies have been carried out. The effects of FPND 400 μg b.i.d. on sense of smell in this study may have been due to the higher dose, combined with the nasal drop formulation, which maximizes exposure of the nasal and paranasal sinus mucosa and may therefore allow the drug to penetrate further into the nasal cavity and closer to the olfactory receptors. This is suggested by the work of Hardy *et al*. [22] who investigated patterns of deposition in the nose following administration of spray and drops. They found that the spray was deposited mainly in the anterior part of the nose with little reaching the turbinates, whereas drops were extensively dispersed from the atrium to the nasopharynx. Whilst FPANS 200 μg b.i.d. is the highest dose required for treatment of rhinitis in adult patients [18], the need for increased dosage of intranasal corticosteroids in treating polyposis is supported by studies demonstrating the active inflammatory nature of polyp tissues. Thus, Mullol *et al*. [33] found that epithelial cell cultures from polyps released significantly more cytokines than normal nasal epithelium, whilst eosinophils primed by the polyp cell supernatants were abnormally steroid-resistant.

Prolonged administration of high doses of topical

corticosteroids has been associated with increased local and potentially serious systemic side-effects, including suppression of the hypothalamo-pituitary-adrenal (HPA)-axis, although this risk must be considered in the context of the therapeutic benefit afforded by the drug [28]. In this study, both doses of FPND were well tolerated by the patients, with no significant differences from placebo in the incidence of adverse events. The low mean absolute bioavailability from FPND, estimated at 0.06% in comparison with 0.51% for FPANS [25], would be expected to minimize any steroid-related side-effects attributable to treatment with FPND. A further safety advantage of FPND is that each dose is contained in a single (unpreserved) unit, so there is no risk of the patient inadvertently taking more than the prescribed dose. The only other corticosteroid currently available in a drop formulation is betamethasone, which is supplied in a standard dropper device. In a recent study with betamethasone nasal drops, 10 volunteer doctors took between 41 and 338% (average 132%) of the prescribed dose, due to difficulties in applying the correct number of drops from a standard dropper [27]. In addition, unlike FP, betamethasone is completely systemically absorbed, and because of potential systemic steroid effects the long-term use of betamethasone nasal drops is not recommended [26,34]. Thus, the minimal systemic absorption of intranasal FPND [25] is particularly relevant for the safety of patients requiring long-term corticosteroid treatment, whilst the effectiveness of topical FP therapy in the management of nasal polyposis may be exemplified by the faster action of FPANS compared with BDP in reducing nasal polyp symptoms [11].

Conclusion

This study showed that both FPND 400 μg o.d. and 400 μg b.i.d. are effective and well-tolerated treatments for adult patients with mild to moderate bilateral nasal polyposis. Dosage with FPND 400 μg o.d. significantly improved nasal breathing and reduced nasal blockage, whilst FPND 400 μg b.i.d. had a stronger beneficial effect and statistically significantly reduced polyp size over a 12 week period.

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