

Efficacy and tolerability of fluticasone propionate nasal drops 400 µg once daily compared with placebo for the treatment of bilateral polyposis in adults

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Summary

Background Chronic eosinophilic rhinosinusitis underlies a range of respiratory disorders including nasal polyposis. Surgical and medical methods are used to control polyps, with topical steroids commonly being used for their anti-inflammatory properties. Fluticasone propionate nasal drops (FPND) is a formulation developed specifically for an effective and well tolerated corticosteroid treatment of nasal polyposis.

Objectives To assess efficacy and tolerability of FPND in the treatment of bilateral nasal polyposis in adults.

Methods This multicentre, randomized, parallel-group study compared FPND 400 µg once daily (o.d.) with placebo for 12 weeks in adult patients with mild to moderate bilateral polyposis. The primary efficacy endpoint was visual assessment of polyp size by the physician at monthly clinic visits. Nasal blockage, rhinitis, peak nasal inspiratory flow (PNIF), olfactory function and requirement for polypectomy were also assessed at visits. The patients kept diary card records of symptoms, PNIF, and use of rescue antihistamine. Additional safety data were provided by a 12-week open extension, when all patients received FPND 400 µg o.d.

Results After 12 weeks double-blind treatment with FPND ($n = 52$) or placebo ($n = 52$), polyp size was reduced in 27% and 16% of patients, respectively; clinical reduction of nasal blockage significantly favoured FPND over placebo (55% vs 22%; $P = 0.002$), and clinic PNIF had increased significantly with FPND (by 52 L/min vs -3 L/min for placebo; $P < 0.001$). Diary card measurements showed significant benefits of FPND vs placebo for daily PNIF, nasal blockage, rhinitis and use of loratadine rescue medication. Both treatments were well tolerated and no serious adverse events occurred during randomized treatment. Epistaxis was more frequent with FPND than placebo but was generally mild and did not result in withdrawals. Mean serum cortisol levels did not change significantly with either treatment.

Conclusion This study showed FPND 400 µg o.d. to be an effective and well tolerated treatment for bilateral nasal polyposis in adults.

Keywords: fluticasone propionate, intranasal corticosteroid, nasal drops, nasal polyps

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Introduction

Simple nasal polyps are commonly formed in about 2% of adults as benign bilateral prolapses of the mucous lining of the ethmoid sinuses, which become visible as pale bodies

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within the nasal cavity. Nasal polyposis is associated with a range of respiratory disorders, including cystic fibrosis as well as late-onset asthma and aspirin hypersensitivity, and no definite link with allergic diseases has been established [1]. Mucosal inflammation characterized by localized mast cell degranulation and eosinophilia, is associated with persistent submucosal oedema, high levels of IgE and histamine. The resultant nasal obstruction is often accompanied by typical rhinitis symptoms of sneezing, itching and rhinorrhoea [2–4]. A recent review that there are multiple causes of the range of conditions involving chronic eosinophilic rhinosinusitis [5]. Consistent with this is evidence of a correlation between submucosal eosinophil infiltration and polyp severity as graded by visual assessment [6].

Traditionally, the preferred treatment for bilateral nasal polyposis may be surgical, but the problem often recurs after polypectomy and many patients will benefit from anti-inflammatory treatment with corticosteroids—especially intranasal treatments, which largely avoid the risk of systemic side-effects [7–12]. An international position statement has recently recommended that corticosteroid treatment of polyposis should be introduced prior to any surgical intervention [7]. Fluticasone propionate is a potent, topically active corticosteroid which has proved highly effective in treating seasonal and perennial rhinitis when administered in the form of an aqueous nasal spray (FPANS) [13–15] and has been found to have a faster onset of action than beclomethasone dipropionate aqueous nasal spray in reducing the symptoms of nasal polyposis [10,11]. It has been shown, however, that nasal drops allow greater exposure than nasal sprays to the affected sinus mucosa [16] and a unit dose nasal drop formulation of fluticasone propionate (FPND) has been developed specifically for the treatment of nasal polyps. FPND has safety advantages over betamethasone sodium phosphate, currently the only other steroid available as nasal drops, since the systemic bioavailability of fluticasone propionate from FPND is remarkably low (0.06%) and the unit dose presentation guards against any possibility of over-dosage and systemic corticosteroid effects, as encountered with betamethasone nasal drops [17–19]. The recommended daily dose for adults is the contents of one unpreserved unit dose containing 400 µg of fluticasone propionate, divided equally between the nostrils, given once or twice daily [20]. The present study was designed to examine efficacy and tolerability of FPND 400 µg o.d. in the treatment of bilateral nasal polyposis in adult patients.

Materials and methods

Study design

This was an international multicentre, double-blind, randomized, parallel group study which was conducted at 11

centres in Canada and Finland, with local ethics committee approval, in accordance with the Declaration of Helsinki (1989 and 1996) and Good Clinical Practice. Patients who met the screening criteria were entered into a 2-week run-in period where they kept a daily record of symptoms. They were then randomized to receive either FPND 400 µg o.d. or placebo nasal drops each morning for 12 weeks, continuing to record symptoms on diary cards. The 12-week double-blind period was followed by a further 12-week open treatment period, during which all patients received FPND 400 µg o.d. Clinic assessments were made at monthly intervals during double-blind treatment, and at the beginning and end of the open treatment period, with a final follow-up visit made 2 weeks after completion of treatment.

Patients

Male and female outpatients aged 16 years and over who had a diagnosis of bilateral nasal polyposis were screened. Polyps were graded by clinical assessment during rhinoscopic examination, severity scores of 1 (small) or 2 (medium) being required for entry into the study. Patients were not entered who had large (grade 3) polyps, indicating severe nasal obstruction, or had undergone surgical treatment for nasal polyps during the last 3 months. Patients who were suffering from cystic fibrosis were excluded from entry to the study. Patients were also excluded if they had a purulent nasal infection, allergic rhinitis, or any other disease likely to interfere with the study parameters, or gave evidence of any serious or unstable concurrent disease or psychological disorder. Patients with hypersensitivity or contraindication to steroids were not admitted to the study; neither were those currently receiving inhaled corticosteroids, those who had received depot or oral steroids during the previous 3 months, and those who were unable to cease treatment with intranasal steroids, or inhaled or intranasal sodium cromoglycate, at the screening visit. In addition, eligible patients must not have taken astemizole during the last 6 weeks or other antihistamines within the last 48 h, or received any other research medication during the previous month. All patients entering the study were able to comply with the protocol instructions and gave written, informed consent. Women of child-bearing age were included if they were neither pregnant nor lactating and, in the investigator's opinion, were taking adequate contraceptive measures to avoid becoming pregnant during the study. Patients randomized to treatment had correctly completed the daily diary card during the run-in period.

Treatments

During the double-blind study, patients were randomized to receive either FPND 400 µg o.d. or placebo nasal drops,

each morning for 12 weeks. For each dose, the contents of one nasal drop container were divided between both nostrils by the patient, using the head down and forwards position [21]. The correct technique for administration of the nasal drops was emphasized to the patients by the investigator, and was specifically detailed in the patient information leaflet. FPND (400 µg unit dose preservative-free suspension) and placebo solution were supplied in identical opaque nasal drop containers, in a foil pack. Each investigator was given a block of treatments, precoded with computer-randomized numbers, which were assigned in ascending numerical order as patients presented. At the end of 12 weeks' treatment, all patients received FPND 400 µg o.d. for a further 12 weeks. Loratadine tablets were provided as rescue medication for relief of troublesome symptoms of rhinitis, to be used as needed, at a maximum dose of 10 mg o.d. No other medication was allowed for polyposis or rhinitis.

Efficacy measurements

The primary endpoint criterion was the physician's assessment of polyp size after 12 weeks of treatment. At all clinic visits, the investigator assessed the size of the bilateral polyps and nasal symptoms by rhinoscopic examination, using 4-point scoring systems. If polypectomy was required, the patient was withdrawn from the study. Polyp size was scored as 0 (no polyps), 1 (mild polyposis) – small polyps not reaching the upper edge of the inferior turbinate and causing only slight obstruction, 2 (moderate polyposis) – medium 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 almost/total obstruction. Nasal blockage scores of 0–3 reflected the physician's assessment of obstruction (none, mild, moderate, severe). Rhinitis symptoms (sneezing/rhinorrhoea/nasal itching) and nasal discomfort were scored 0 (none), 1 (mild) – symptoms present but not troublesome, 2 (moderate) – symptoms frequently troublesome but not interfering with daily activity or night-time sleep, or 3 (severe) – symptoms troublesome and interfering with daily activity and/or night-time sleep. Peak nasal inspiratory flow (PNIF) was measured at each clinic visit [22]. Two tests of olfactory function were also conducted during clinic visits at the start and end of double-blind treatment: a modified (international) University of Pennsylvania Smell Identification Test (UPSIT) [23] and the Butanol Threshold Test [24].

Patients were supplied with daily record cards and were asked to measure PNIF and assess their symptoms of polyposis and rhinitis each morning (before dosage) and evening. Nasal blockage, nasal discomfort and rhinitis symptoms were each scored using the 0–3 severity ratings

described. Sense of smell was rated as normal (0), slightly (1) or moderately impaired (2) or absent (3). Daily use of loratadine tablets was also recorded.

Safety evaluation

Patients were asked to note adverse events on the daily record card, and these were reviewed by the investigator and any problems discussed with the patient at each clinic visit. All adverse events were then recorded by the investigator, who also assessed the relationship of the event to the study treatment.

Physical examinations including measurements of blood pressure and heart rate were carried out at screening, at the end of the double-blind 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 screening, at the end of the double-blind treatment and at the end of the open treatment phase of the study, with a follow-up examination in case of any abnormality. Standard biochemical and haematological analyses were conducted at a central laboratory (Covance, Geneva, Switzerland) and included serum cortisol. Wherever possible, blood samples were collected between 08.00 and 10.00 am. The sensitivity of serum cortisol measurements is acknowledged as being not ideal, however, other methods of determining HPA axis status were deemed to be impractical in this multinational, multicentre study.

Statistical methods

Treatment differences were assessed using 2-sided tests, which were performed at the 5% significance level. Analyses were performed using the SAS system, Version 6.12. The primary population for the analysis of efficacy and safety was the intent to treat population, including all randomized patients who took at least one dose of study medication. Withdrawals requiring polypectomy were included by carrying forward the last observation.

Between treatment comparisons of changes in clinicians' assessments of nasal polyps and symptoms and olfactory function tests, were performed using the Van Elteren extension to the Wilcoxon Rank Sum Test, with country as the stratifying variable. Effects of treatment on changes in either PNIF or serum cortisol were investigated using analysis of covariance, with country and sex as factors in the model, and with age and baseline (end of run-in) values as covariates. Where significant, between-treatment

comparisons were performed using linear contrasts to calculate 95% confidence intervals. Treatment comparisons of diary card data (symptom scores and use of rescue medication being calculated as percentage of days affected during specific periods) were carried out as for clinical assessments. The numbers of patients failing to complete the study were compared using Fisher's Exact Test (twice the one-sided test) and including all withdrawals. This test was also used to compare the incidence of adverse events between treatments.

Results

Study population

One hundred and four patients were randomized to treatment with either FPND 400 µg o.d. (52) or placebo (52). Six patients were withdrawn during the double-blind phase of the study: one from the FPND group (due to lack of efficacy) and five from the placebo group (three due to an adverse event and two requiring a polypectomy). The 98 patients who completed double-blind treatment then entered into the open treatment phase and all received FPND 400 µg o.d. for a further 12 weeks; none were withdrawn from this phase of the study.

In the intent-to-treat population, 70% of the patients were male and 98% were Caucasian. Approximately half fell into the 45–64 years age-group, 74% had had polyps for more than 5 years, and 69% had undergone a previous polypectomy. Approximately 22% of the patients were atopic

and allergic to one or more allergens. Patients were, however, not allowed to enter the study if they were allergic to any relevant allergen. Aspirin sensitivity was not an exclusion criterion and two patients were included who were reportedly aspirin sensitive. On entry to the study, the two treatment groups were well matched demographically (Table 1), and for concurrent illnesses and physical abnormalities.

Efficacy

After 12 weeks of treatment, 14 patients (27%) in the FPND group showed an improvement in polyp size, compared with eight (16%) in the placebo group; this treatment difference was not statistically significant. The investigator's assessment of nasal blockage at week 12 demonstrated a significantly higher rate of improvement with FPND (55% of patients) than placebo (22%; $P = 0.002$) (Table 2). Clinical assessments of rhinitis and nasal discomfort showed improvements after 12 weeks with both FPND (43% and 29%, respectively) and placebo (39% and 24%, respectively) and no significant treatment differences occurred. Clinic PNIF measurements showed significantly greater improvements in the FPND group than the placebo group after 4, 8 and 12 weeks (mean changes of 38 vs –1, 47 vs 1, and 52 vs –3 L/min, respectively; $P < 0.001$ throughout). Daily PNIF also improved steadily during treatment with FPND and the mean increase over weeks 1–12 was highly significant compared with placebo, which had no effect (Fig. 1). Patient diary card symptom assessments showed

Table 1. Patient demography at study entry: intent-to-treat population

		Number (%) of patients	
		FPND 400 µg o.d.	Placebo o.d.
Number of patients		52	52
Sex	Male	38 (73)	35 (67)
	Female	14 (27)	17 (33)
Age (years)	Mean ± sd	49 ± 12	47 ± 13
	Range	29–80	25–75
Height (cm)	Mean ± sd	174 ± 9	173 ± 9
	Range	155–192	151–191
Weight (kg)	Mean ± sd	81.8 ± 16.1	80.8 ± 17.3
	Range	52.0–133.2	54.0–159.6
Smoking history	Never smoked	24 (46)	22 (42)
	Former smoker	17 (33)	18 (35)
	Current smoker	11 (21)	12 (23)
Polyposis history	< 2 years	4 (8)	5 (10)
	2–5 years	8 (15)	10 (19)
	> 5–10 years	13 (25)	14 (27)
	> 10 years	27 (52)	23 (44)
Previous polypectomy	Yes	38 (73)	34 (65)
	No	14 (27)	18 (35)

Table 2. Clinical assessment of nasal blockage during 12 weeks of double-blind treatment with fluticasone propionate nasal drops (FPND) 400 µg o.d. or placebo drops o.d., followed by 12 weeks of open treatment with FPND 400 µg o.d. (all patients). Severity score: 0 = none, 1 = mild, 2 = moderate, 3 = severe.

Study phase	Week	Treatment group (n)	Blockage score		Number (%) of patients improved	P-value
			Median	Range		
Double-blind	0	FPND (52)	2.0	0–3		
		placebo (52)	2.0	0–3		
	4	FPND (52)	1.0	0–3	23 (44)	0.066
		placebo (51)	2.0	0–3	16 (31)	
	8	FPND (52)	1.0	0–3	24 (46)	0.073
		placebo (50)	2.0	0–3	13 (26)	
Open (FPND)	12	FPND (51)	1.0	0–3	28 (55)	0.002**
		placebo (49)	2.0	0–3	11 (22)	
	24	FPND (51)	1.0	0–3		
		placebo (47)	1.0	0–3		
Follow-up	26	FPND (51)	1.0	0–3		
		placebo (50)	1.0	0–3		

** $P < 0.01$

differences favouring FPND over placebo, significant for nasal blockage and overall rhinitis (Fig. 2). In addition, the percentage of days without use of rescue medication was significantly greater ($P = 0.024$) in the FPND treated patients, of whom 46% used no loratadine at any time during randomised treatment, compared with 32% of the placebo group. Results of the olfactory function tests showed no significant differences between FPND- and placebo-treated patients.

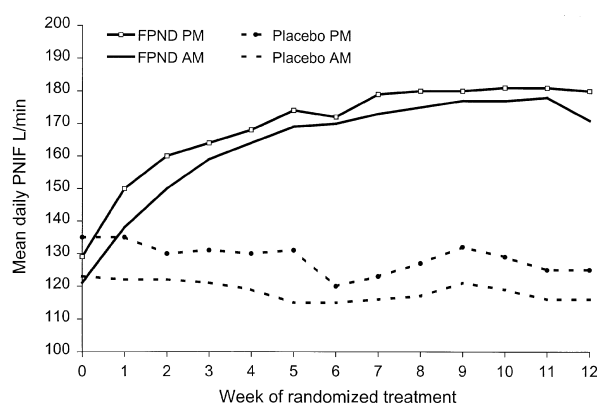


Fig. 1. Time course of daily mean peak nasal inspiratory flow (PNIF) recorded each morning (AM) and evening (PM) by patients receiving either FPND 400 µg o.d. or placebo nasal drops o.d. for 12 weeks. Overall changes in PNIF during weeks 1–12 were (AM) 45 L/min and –2 L/min, respectively ($P < 0.001$); (PM) 41 L/min and –4 L/min, respectively ($P < 0.001$).

Safety

No serious adverse events occurred during the double-blind phase of the study and the overall incidence of events (61%) was similar for both treatments. The most commonly reported events are summarized in Table 3. Significantly more patients reported epistaxis in the FPND group (19%) than in the placebo group (4%), but none were evaluated as severe. Three patients, all in the placebo group, were with-

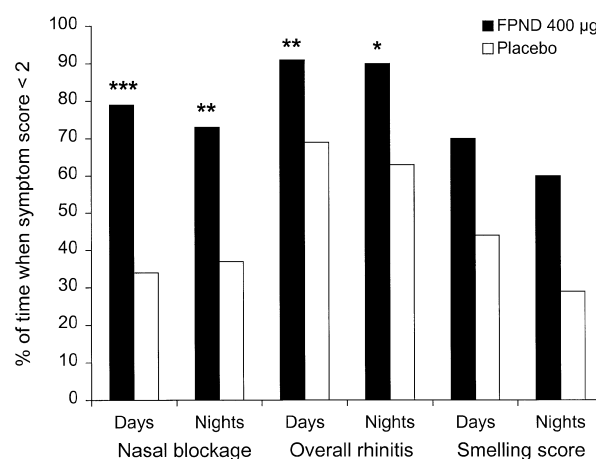


Fig. 2. Diary card symptom severity assessed by patients with nasal polyposis over 12 weeks of double-blind treatment with FPND 400 µg o.d. or placebo nasal drops o.d. Symptom severity score: 0 = none, 1 = mild, 2 = moderate, 3 = severe. Statistical significance: FPND vs placebo: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

	FPND 400 µg	Placebo	Total	P-value
<i>Double-blind phase</i>				
Number of patients	52	52	104	
Number (%) with adverse events	31 (60)	32 (62)	63 (61)	
Number (%) drug-related events	12 (23)	9 (17)	21 (20)	
Headache	4 (8)	10 (19)	14 (13)	0.149
Upper respiratory tract infection	7 (13)	5 (10)	12 (12)	0.760
Epistaxis	10 (19)	2 (4)	12 (12)	0.028*
Viral respiratory infections	2 (4)	4 (8)	6 (6)	0.678
<i>Open phase</i>				
Number of patients			98	
Number (%) with adverse events			36 (37)	
Number (%) drug-related events			9 (9)	
Upper respiratory tract infection			11 (11)	
Epistaxis			4 (4)	

* $P < 0.05$ (FPND vs placebo).

drawn because of adverse events, two owing to sinusitis and one owing to asthma.

There were no major differences between the treatment groups for parameters of clinical chemistry, hepatic or renal function, haematology or urinalysis. Two patients receiving FPND had a serum cortisol level that was above the upper threshold limit of the normal range but no individual's cortisol fell below the lower threshold limit. The geometric mean serum cortisol levels increased slightly with both treatments and at the end of treatment there was no significant difference between the two groups (Table 4). During the open phase of FPND treatment, one patient with a history of depression, developed psychosis; the investigator considered this unlikely to be related to the study medication. The incidence of epistaxis was lower

during the open phase of treatment with FPND, being 4%. No patients were withdrawn during this phase and there were no reports of oral candidiasis at any stage of study treatment.

Discussion

This placebo-controlled study examined the efficacy and tolerability of a new intranasal formulation of the topical corticosteroid, fluticasone propionate, in the treatment of bilateral nasal polyposis. The unpreserved 400 µg unit dose nasal drop presentation (FPND) has been developed specifically for optimal administration of the recommended adult dose of fluticasone propionate to the inflamed surface of the polypoid sinus mucosa, using the head down and forward position [16,21]. Previous studies have shown treatment with FPANS 400 µg o.d. to be highly effective in controlling seasonal and perennial rhinitis, and to compare well with beclomethasone dipropionate aqueous nasal spray (BDPANS) [13–15]. FPANS, administered as 200 µg b.d., has also been shown to compare favourably with BDPANS in the treatment of both moderate and severe nasal polyposis, having a more rapid onset of action and resulting in significantly reduced polyp severity scores [10,11]. In view of the improved delivery using drops rather than sprays [16], the lack of a significant decrease in polyp size in this study was unexpected. It is possible that a more sensitive scale or a longer duration of treatment may have found a difference, or that twice daily dosage may be necessary in some patients. A recently completed safety and biopsy study in which patients with perennial allergic rhinitis received FPANS 100 µg b.d. or placebo for a period of 12 months [25] showed an initial reduction in rhinitis symptoms at

Table 4. Levels of serum cortisol (geometric means of all samples collected, with percentage coefficient of variation) measured before and after 12 weeks of double-blind treatment with FPND 400 µg o.d. or placebo drops o.d.

	Placebo	FPND
Number of patients	47	50
Baseline geometric mean, nmol/L (cv)	375 (46%)	373 (47%)
Week 12 geometric mean, nmol/L (cv)	377 (44%)	402 (41%)
Adjusted geometric mean, nmol/L (cv)	385	412

FPND-placebo comparison: ratio, 1.07; 95% CL, 0.93, 1.23. P -value 0.326 (analysis of covariance). FPND, intranasal fluticasone propionate 400 µg once daily; cv = coefficient of variation; CL, confidence limits.

4 weeks, with a further reduction after 8 months of FPANS treatment, suggesting that long-term treatment is needed to elicit the maximum effectiveness of intranasal corticosteroids in chronic inflammatory conditions. Previous FPANS polyposis studies [10,11] differed in employing completely subjective scales for clinical assessment of polyp size, whereas the present study used an objective, but limited scale for visual assessment of polyp size which may have reduced the ability to detect a reduction in polyp size. Thus, size 2 (medium) polyps might reach any point between the upper and lower edge of the inferior turbinate, allowing for a considerable reduction in size without altering the score. The most troublesome symptom of polyposis is nasal blockage, which increases with polyp size, whilst about one-half of patients suffer associated rhinitis symptoms [1]. Our clinical assessments of nasal blockage, in line with the patients' own nasal blockage scores, demonstrated significant improvements during treatment with FPND 400 µg o.d., whilst clinic and diary PNIF, the only objective measurements in this study, also showed steady and significant improvements. These results imply that important reductions in polyp size did in fact occur, in addition to antirhinitic effects of treatment on the nasal turbinate.

The defined objectives of treatment are to eliminate or considerably reduce the size of polyps, to re-establish nasal breathing, eliminate symptoms of rhinitis and restore the sense of smell, and to prevent postsurgical recurrence [26]. Topical corticosteroids, the basis of nonsurgical intervention, are currently recommended for treatment of mild or moderate symptoms and, following short-term systemic corticosteroids, for severe polyposis. It is recommended that patients failing to respond in one month should then be considered for surgery [7]. Studies have demonstrated the effectiveness of various intranasal corticosteroid preparations in reducing the size of nasal polyps and the symptoms of rhinitis [8–11,27–29] and in delaying recurrence after polypectomy [30,31]. In our study, treatment with FPND 400 µg o.d. resulted in significantly more patients recording improved subjective diary card scores for nasal blockage, overall rhinitis symptoms and use of rescue antihistamine medication compared with placebo. This accords with the effects of FPANS seen in patients with seasonal and perennial allergic rhinitis [32] and lends support to the evidence for a relationship between nasal polyposis and allergy [33]. The present study excluded patients with a proven diagnosis of allergic rhinitis; however, polyp histopathology suggests the involvement of an allergic inflammatory response in polyposis, with degranulated mast cells and eosinophils present in the tissue and increased IgE and histamine in the polyp oedema [2–4,34]. The probability that steroids may reduce polyp size by affecting eosinophilic mucosal inflammation is supported by cellular studies in allergic rhinitis and by the evidence of dose-related effects

of corticosteroids on *in vitro* survival of eosinophils primed by supernatants from human nasal epithelial cell cultures [35,36]. Epithelial cells cultured from nasal polyps were found to enhance eosinophil survival more strongly than epithelial cells from healthy nasal mucosa, suggesting that active polyp tissue might be relatively resistant to corticosteroids. This is in keeping with a more aggressive approach to the treatment of polyposis, using higher doses of corticosteroid than commonly required to treat rhinitis [13]. Such an approach is supported by the results of a new, placebo controlled 12-week study, comparing FPND 400 µg o.d. and b.d. treatments in patients with bilateral polyposis: this demonstrated a dose-related improvement in several parameters, including polyp size reduction [20]. Both o.d. and b.d. dosage regimens with FPND 400 µg appear to be well-tolerated. The relatively high incidence of minor epistaxis associated with FPND 400 µg o.d. during the first 12 weeks of the present study did not extend into the open treatment phase and was not expected, since the overall incidence with FP is not different from that of other intranasal steroids [32]. In addition, long-term treatment with FPANS 100 µg b.d. over a year has revealed no deleterious changes in nasal mucosal biopsies from patients with perennial allergic rhinitis [25]. The lack of effect on serum cortisol levels during 24 weeks treatment with FPND 400 µg o.d. in this study exemplifies the negligible systemic corticosteroid effects to be expected from FPND, given the very low mean systemic bioavailability of this formulation, which has been estimated at 0.06% compared with 0.51% for FPANS [17]. Safety is particularly important in view of the long-term topical corticosteroid treatment required for control of nasal polyposis. The only other steroid nasal drops currently available, betamethasone sodium phosphate, have been associated with adrenal suppression [19]. The unit dose presentation of FPND also promotes accurate dosage and avoids accidental overdosage, which has occurred with betamethasone sodium phosphate nasal drops [18].

In conclusion, this study has shown FPND 400 µg o.d. to provide significant clinical benefits to adult patients suffering from mild to moderate bilateral nasal polyposis. The formulation was well tolerated by the patients, and the low systemic bioavailability of FPND ensures local effectiveness and minimizes the risk of steroid side-effects occurring during long-term treatment.

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