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Intranasal beclomethasone dipropionate in the treatment of common cold*

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SUMMARY

Sinusitis is usually considered a complication of viral rhinitis. Virus infections in the upper respiratory tract lead to mucosal swelling, which may obstruct paranasal sinus outflow, resulting in infection in the paranasal sinuses. Topical nasal steroids have been found beneficial in a variety of acute and chronic nasal conditions including allergic and nonallergic rhinitis and chronic rhinosinusitis. The purpose of this study was to examine whether the intranasal inhalation powder beclomethasone dipropionate (BDP) 400 μg/day treatment has a beneficial or harmful effect on symptoms and signs of common cold, and whether or not it can prevent common cold complications. A total of 54 patients were randomized, 26 into the placebo-group and 28 into the BDP group. During the 14-day follow-up, there were on an average10.3 symptomatic days in the placebo group and 10.7 days in the BDP group (p=0.72). The use of intranasal BDP in the treatment of common cold neither reduced symptoms caused by inflammation nor did it shorten the recovery time. On the other hand, because BDP does not increase the risk of complications or significantly prolong the recovery during the common cold, there is no need to discontinue its use in the patients with allergic rhinitis or nasal polyposis.

Key words: beclomethasone, common cold, dipropionate, intranasal inhalation powder, sinusitis, rhinosinusitis

INTRODUCTION

Human rhino viruses are the main cause of common colds, and most of what we know about this symptom complex comes from the studies of these viruses. Although, the pathogenesis of common cold is not fully understood, new research shows that inflammatory mediators and neurogenic reflexes triggered by infection play an important role (Pitkäranta and Hayden, 1998). Sinusitis is usually considered a complication of viral rhinitis. Virus infections in the upper respiratory tract lead to mucosal swelling, which may obstruct paranasal sinus outflow, resulting in the infection of sinuses.

No specific medical treatment so far exists to heal the common cold. Topical nasal steroids are found beneficial in a variety of acute and chronic nasal conditions including allergic and nonallergic rhinitis and chronic rhinosinusitis (DelaFuente et al., 1989). Corticosteroids have traditionally been regarded as contraindicated in infectious conditions because of their immunosuppressive action. However, this issue is complex, and the effect of corticosteroids on the immune system depends on the dose, treatment duration, and the type of infectious agent. In the study by Frey and Speck, the rate of infectious complications was not increased in patients given a daily dose of less than 700 mg prednisone (Frey and Speck, 1992). Puhakka et al., found that intranasal fluticasone propionate treatment tented to prevent paranasal sinusitis, especially in rhino virus-positive subjects (Puhakka et al., 1998).

The purpose of this pilot study was to examine whether the intranasal inhalation powder beclomethasone dipropionate 400 μg/day treatment has a beneficial or harmful effect on symptoms and signs of common cold, and whether or not it can prevent common cold complications.

MATERIALS AND METHODS

The study protocol was approved by the Ethical Committee of Central Hospital of Central Finland and conducted in Autumn 1998.

The patients for this randomized, placebo-controlled double-blind parallel group study were recruited from the staff of the Central Hospital of Central Finland. The inclusion criteria were symptoms of acute common cold, having lasted for 1-3 days. Patients younger than 18 years of age, those with chronic syste-

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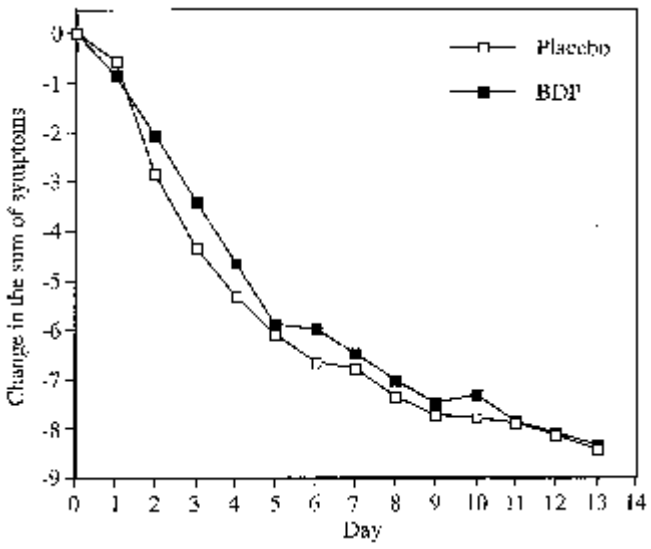

Figure 1. Changes in the sum of symptoms compared to the baseline during the follow-up.

mic diseases, with ongoing treatment of local or systemic corticosteroids, or pregnant women were excluded. The patients were allocated randomly into one of the two groups: the first (placebo group) having placebo and the second active treatment, beclomethasone dipropionate (BDP group) (Beclonasal Easyhaler 100 μg/dose, Orion Pharma, Finland). Placebo contained lactose and the active drug BDP and lactose. Both were administered by Easyhaler® multidose powder inhaler designed for nasal application, once a day, two doses per each nostril (Nuutinen et al., 1995). At the first visit symptoms were recorded, and both the rhinoscopy and ultrasonography of the maxillary sinuses were estimated. This protocol was followed also at the 7th and 14th at the day of the follow-up period. Patients recorded daily the following symptoms: nasal blockage, rhinorrhea, nasal itching, sneezing, cough, sore throat, and hoarseness and graded each symptom into one of the four grades: 0= no, 1= mild, 2= moderate, 3= marked.

The data were entered and edited in a blind mode using the statistical package SPSS (Release 7.7.1). After the clean file was achieved, the randomization code was broken. The sum of symptom scores was calculated for each symptom separately during the first and second week, and for the whole 14-day follow-up period. Also, to get a global measure of the degree of symptoms, the sum of all seven symptoms (sum of symptoms) was calculated for every day, for the first and second week, and for the whole 14-day follow-up period. The number of symptomatic days was also evaluated and healing was achieved when the sum of symptoms was equal to zero. Treatment differences for symptom scores were estimated as arithmetic means with 95% confidence intervals. The groups were compared using the t-test for independent samples. The log-rank test was used to compare the treatment groups with respect to the time to recovery. The study has been analyzed using SPSS (Release 7.5.1).

RESULTS

A total of 54 patients (49 women and 5 men) fulfilling the inclusion criteria were randomised, 26 into the placebo group and 28 into the BDP group. The mean age was 40.3 years, ranging from 23 to 57 years). Two of these patients, one in each group discontinued the study. One patient had bronchial asthma (1.9 %) and three(5.6%) had allergic rhinitis. Maxillary sinusitis had been treated in 19/26 (73%) and 14/28 (50%) patients, respectively in the placebo and BDP groups, in 6/26 (23%) and 3/28 (11%) during the last 12 months. The duration of rhinitis before the enrolment was 2.7 and 2.8 days (range 1-4 days), respectively in the placebo and BDP groups. Symptoms and rhinoscopic and ultrasonographic findings of the beginning of the study are presented in Table 1. No statistically significant differences were found between the groups with respect to the patient characteristics at the baseline. The three most severe symptoms (scale 0-3 for each) were rhinorrhea (means: 1.9 and 2.2), nasal blockage (1.8 and 1.9), and sneezing (1.4 and 1.5) in the placebo and BDP groups, respectively. Corresponding means for the sum of symptoms (scale 0-21) were 9.2 (SD 2.6) and 9.5 (SD 2.3) at the baseline (placebo vs BDP, p=0.65). So, with respect to the symptom variables, there were no statistically significant baseline differences between the groups.

As can be seen in Figure 1, there are no significant differences in the development of the sum of symptoms between the placebo and BDP groups, even though the decrease of symptoms seems to be slower in the BDP group. The same is also true for the individual symptoms. During the 14-day follow-up, there were 10.3 symptomatic days on average in the placebo-group and 10.7 days in the BDP group (p=0.72). The median time to recovery was 12 days in the BDP group and 11 days in placebo group (log-rank test p=0.81). The difference in the individual symptom scores and in the sum of symptoms during the whole two-week period between the placebo and BDP groups are presented in Table 2. No statistically significant differences were found, but there is a trend toward the higher scores for rhinorrhea and sneezing as well as the sum of symptom scores in the the BDP group.

During the follow-up, one patient in the BDP group developed a positive unilateral ultrasonographic sign. The maxillary irrigation was positive confirming the diagnosis of maxillary sinusitis. The clinical recovery was complete. After 2 weeks treatment rhinoscopy was normal in 20/21 (91%) and 20/24 (83%) in the placebo and BDP group, respectively. Ultrasonography was normal in all patients.

DISCUSSION

The patient material of this study does not represent the normal distribution of the adult population in the region but that of the staff of the Central Hospital of Central Finland, with 88 percent women and a mean age of 40 years. On the other hand, common colds, especially if they are prolonged or complicated, can be costly in the active adult population by decreasing the working ability.

Table 1. Symptoms, and rhinoscopic and ultrasonographic signs at the beginning of the study.

	Placebo-group (N=26)		BDP-group (N=28)	
Symptoms	n	%	n	%
Nasal blockage	26	100	27	96
Rhinorrea	24	92	28	100
Nasal itching	18	69	17	61
Sneezing	22	85	24	86
Cough	17	65	16	57
Sore throat	15	58	17	61
Hoarseness	18	69	22	79
Rhinoscopy				
Normal	10	38	6	21
Abnormal	16	62	22	79
Ultrasonography				
Normal	26	100	27	96
Abnormal	0	0	1	4

Our results show that the total recovery from an uncomplicated common cold takes almost two weeks. We did not find any statistically significant difference in the severity of individual or overall symptoms during the follow-up or in the recovery from the common cold between the groups. However, the grade of rhinorrhea, sneezing, and overall symptoms seemed to be slightly more severe in the BDP-group. There was also a trend for both a slower decrease of symptoms and full recovery in the BDP group than in the placebo group. Prophylactic administration of a systemic and intranasal steroid had only a modest effect on the symptoms of experimental rhino virus colds in the study by Farr et al., (1990). Puhakka et al., (1998) presented that a six-day intranasal fluticasone propionate treatment of the common cold tended to prevent paranasal sinusitis, especially in rhino virus- positive subjects. On the other hand, relatively high doses of oral glucocorticoids started before rhinovirus inoculation did not reduce the frequency or severity of cold symptoms or nasal mucus production by Gustafson et al., (1996). They concluded that corticosteroids do not provide clinically meaningful benefit in human rhino virus colds and may serve to increase viral replication.

According to published data (Meltzer et al., 1993; Norlander et al., 1998; Pauwels, 1986; Pipkorn et al., 1987) intranasal corticosteroid treatment in allergic patients reduces inflammation and also decreases the risk for developing paranasal sinusitis. We excluded the patients with ongoing treatment with intranasal or systemic corticosteroids, and we had too few patients with allergic rhinitis in order to have the possible positive effects of BDP on these patients. The required sample size was not estimated at the planning stage of this study because the aim of this study was to look for preliminary evidence of efficacy and possible complications which then must be confirmed in a study with a sufficient number of patients. The observed power was too low to show statistical significance of the treatment difference. The posterior sample size calculations based on the actual data indicated that the required number of patients is 330 per treatment group (power 80%, type I error 5%) to show the difference of 5.7 points statistically significant.

Table 2. The treatment effect of BDP compared to placebo in the sum of each individual symptoms and the sum of symptoms, recorded during the two-week follow-up period.

	BDP		Placebo		BDP compared to Placebo		
Symptoms	Mean	SD	Mean	SD	Mean	95% CI	p-value
Nasal blockage	12.6	7.4	11.9	5.8	+0.7	-3.1 to 4.4	0.72
Rhinorrhea	12.0	7.0	9.3	7.4	+2.7	-1.3 to 6.7	0.19
Nasal itching	4.1	5.5	4.9	4.0	-0.8	-3.6 to 2.0	0.57
Sneezing	6.7	5.4	4.4	4.6	+2.3	-0.4 to 5.1	0.10
Cough	10.6	10.3	10.0	9.1	+0.6	-4.9 to 6.0	0.83
Sore throat	3.6	4.8	3.0	3.7	+0.6	-1.8 to 3.0	0.63
Hoarseness	7.6	6.0	7.9	8.3	-0.3	-4.4 to 3.7	0.87
Sum score	57.3	29.7	51.6	25.9	+5.7	-10 to 21.7	0.48

CONCLUSIONS

Our pilot study shows that the use of intranasal BDP in the treatment of common cold neither reduces symptoms caused by inflammation nor shortens the recovery time. On the other hand, because BDP does not increase the risk of complications or significantly prolong the recovery during the common cold, there is no need to discontinue its use in the patients with allergic rhinitis or nasal polyposis. The effects of intranasal BDP on common cold in patients with allergic rhinitis need to be further studied.

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