Rhinology, 27, 251-255, 1989

Intranasal sodium cromoglycate in post-catarrhal hyperreactive rhinosinusitis: A double-blind placebo controlled trial

Jørgen F. Sederberg-Olsen and Alix E. Sederberg-Olsen

E.N.T. Clinic, Helsingør, Denmark

SUMMARY

A randomized double-blind comparison was made between sodium cromoglycate and a placebo (saline) given as nasal sprays, to control symptoms of post-catarrhal hyperreactive rhinosinusitis. No significant differences were demonstrated between the two test treatments in rhinopharyngeal symptoms, ultrasonic scannings of mucosal thickness in the maxillary sinus, or in the patients' evaluation of rhinitic symptoms. There was an improvement in symptoms in about 50% of the patients in each treatment group.

INTRODUCTION

Catarrhal conditions are characterized by watery nasal secretion, sneezing and nasal blockage. Mucosal oedema obstructs drainage from the maxillary sinus and auditory tube which often gives rise to a feeling of pressure and pain in the affected organs. The condition may be followed by a bacterial infection. The severity of symptoms depends on how rapidly the mucosal oedema resolves. Sodium cromoglycate is thought to stabilize mast cells in the mucosa and thereby prevent both the immediate and the late response of the nasal mucosa to allergen challenge (Pelikan, 1982). The late nasal mucosa response may indeed play an important role in producing symptoms of rhinitis in many patients. This response is frequently overlooked in practice and could be responsible for the treatment failure in some rhinitis patients (Pelikan, 1982).

Encouraged by our favourable clinical experience with intranasal sodium cromoglycate in the treatment of post-catarrhal rhinosinusitis symptoms, we decided to assess the effect of sodium cromoglycate compared with placebo in the treatment of patients with hyperreactive rhinosinusitis, in a formal study.

METHOD

A double-blind consecutive randomized comparison was made between sodium cromoglycate (2.6 mg/per actuation) and placebo applied as nasal spray. The patients were aged 10 years or more with a history of at least one week of nasal secretion referring to the definition of common cold, as reported by Reed (1980) and oedema of the mucosa of more than 2 mm shown by ultrasonic scanning sinuscan as described by others (Matilla et al., 1981; Revonta, 1980; Katholm et al., 1984). The patients administered the nasal spray four times a day for three weeks during the months of February–April 1985. We obtained informed consent from each patient who participated in the study.

Initially we carried out a normal investigation of ear-nose-throat, ultrasonic scanning of maxillary and frontal sinuses, together with a swab taken by carbon inoculation rod from the rhinopharynx which was sent the same day to the regional microbiological laboratory in a Stewarts' transport medium. We had anamnestic information on the patients' personal or family history of allergy. They were asked about asthma, rhinitis, eczema, or other allergic disorders. It is known that asthmatic children show abnormal X-rays in sinus as reported by Zimmerman et al. (1987). At the ENT examination we especially examined the nasal cavity, rhinopharynx, degree of cyanosis of the mucosa and the appearance of the nasal secretion (clear or purulent).

The patients were provided with a daily diary card to record the severity of symptoms such as nasal blockage, nasal secretion, headache, as well as use of other medication. At the second and third visit, after one and three weeks, a control scanning of the thickness of the mucosa was made. We used polaroid photography of the oscilloscope picture. On the same day the patients were asked about severity of symptoms, and the diary cards were checked. At the last visit there was in addition an assessment of the mucosa in the nasal cavity and rhinopharynx. The patient was asked to express an opinion of the overall effect of the treatment. Patients with purulent sinusitis or polyposis nasi and infections caused by pneumococci and/or haemolytic streptococci were excluded from the trial. The patients were not allowed to use local steroids, adrenergic or parasympatholytic therapy during the trial.

MATERIAL

91 patients participated in this study, 29 males and 61 females (no record in one case). 45 patients were treated with intranasal sodium cromoglycate and 46 with an identical placebo spray. Table 1 shows the distribution of age and sex and the duration of symptoms before start of treatment. The distribution of the patients' personal and family history of allergy are listed in Table 2.

Table 1. Patients characteristics.

variable	frequency/value active	placebo
number in treatment group	45	46
age (years):		
mean	39.1	42.5
range	13–82	15–73
sex:		
male	10	19
female	34	27
no record	1	0
duration of present disease (weeks)		
1–2	16	11
3–4	6	8
more than 4	23	27

Table 2. History of allergy.

		active	placebo
allergy	asthma:		
	yes	2	2
	no	43	44
	no record	0	0
	rhinitis:		
	yes	2	4
	no	43	42
	no record	0	0
	eczema:		
	yes	3	4
	no	42	42
	no record	0	0
family allergy	parents:		
	yes	6	7
	no	36	38
	no record	3	1
	sister/brother:		
	yes	7	5
	no	36	40
	no record	2	1
	Children:		
	yes	10	13
	no	32	33
	no record	3	0

MEDICATION

Use of test and other therapy was recorded daily on diary cards. Only one patient had used other nasal therapy, namely Otrivin® during the third week of sodium cromoglycate treatment.

WITHDRAWALS

Eight patients on sodium cromoglycate withdrew from the trial. These included five due to treatment failure and three due to non co-operation. Eleven patients in the placebo group withdrew from the trial with six withdrawals due to treatment failure and five due to non co-operation.

RESULTS

There were no significant differences between the two treatment groups for increased mucosal thickness, assessed by ultrasonic techniques, neither at admission nor changes from admission at visit 2 and 3 (Table 3).

Table 3. Clinical assessments - scanning picture.

increased mucosal thickness (mm)	mean (sample size) active	placebo	Mann-Whitney *U*-statistic	significance
Left				
admission (visit 1)	8.1 (44)	8.8 (45)	958.0	NS
visit 2 - visit 1	−0.2 (40)	0.0 (40)	781.0	NS
visit 3 - visit 1	0.1 (36)	−1.0 (37)	521.0	NS
Right				
admission (visit 1)	9.7 (44)	9.5 (45)	943.5	NS
visit 2 - visit 1	−0.3 (40)	−0.6 (40)	807.5	NS
visit 3 - visit 1	−1.6 (36)	−1.0 (37)	584.0	NS
Mean of left and right				
admission (visit 1)	8.9 (44)	9.1 (45)	981.5	NS
visit 2 - visit 1	−0.3 (40)	−0.3 (40)	764.0	NS
visit 3 - visit 1	−0.7 (36)	−0.1 (37)	611.0	NS

NS = not significant
Visit 2 - after one week of treatment
Visit 3 - after three weeks of treatment

Although results slightly favoured sodium cromoglycate, there were no significant differences between the two treatment groups for change in symptoms or for nasal fossae and rhinopharynx signs.

No significant differences were seen between the two treatment groups for patients' assessment of test treatment, with 24/40 in the active group and 20/38 in the placebo group rating the test treatment to have moderate/good effect.

Both treatments were well tolerated. No adverse or unusual symptoms were reported during the trial.

DISCUSSION

The inability to demonstrate a significant difference between active and placebo may be due to many reasons. Intranasal sodium cromoglycate has mainly been used to treat allergic rhinitis and in our study there were relatively few allergic subjects.

The present of nasal blockage and mucosal oedema may have limited the distribution and penetration of sodium cromoglycate, so if we had combined the test treatments with a nasal decongestant agent we may have obtained a clearer difference between active and placebo groups. With respect to the case material studied, since hyperreactive rhinosinusitis may be complicated by bacterial infection, then if we had entered patients into the trial after one month's rather than one week's duration of nasal symptoms, some spontaneous recovery from bacterial infection could be anticipated and we would have studied a population of more true hyperreactive patients.

Finally, as sodium chloride solution was used as a placebo, we cannot exclude the possible therapeutic effect of saline lavage which is suggested by the equal improvement of symptoms in about 50% of patients in each treatment group. These considerations apart, however, it is concluded from this investigation that the use of intranasal sodium cromoglycate is not indicated in the treatment of post-catarrhal hyperreactive rhinosinusitis.

REFERENCES

1. Katholm M, Sederberg-Olsen J, Thomsen J. Diagnostic ultrasonography in sinusitis. Acta Otolaryngol (Stockh) 1984; Suppl 412: 88–90.
2. Mattila P, Merilainen P, Luukkala M, Revonta M. Sinuscan, a simple ultrasonic instrument to detect maxillary and frontal sinus. Acta Polytechnica Scandinavica 1981; Ph 128.
3. Pelikan Z, Pelikan-Filpek M. The effects of disodium cromoglycate and beclomethasone dipropionate on the immediate response of the nasal mucosa to allergen challenge. Ann Allergy 1982; 49 (5): 283–292.
4. Pelikan Z. The effects of disodium cromoglycate and beclomethasone dipropionate on the late nasal mucosa response to allergen challenge. Ann Allergy 1982; 48: 200–212.
5. Reed S. The etiology and epidemiology of common colds, and the possibilities of prevention. Clin Otolaryngol 1981; 6: 379–387.
6. Revonta M. Ultrasound in the diagnosis of maxillary and frontal sinusitis. Acta Otolaryngol (Stockh) 1980; Suppl 370: 1–55.
7. Zimmermann B, Stringer D, Feanny S, et al. Prevalence of abnormalities found by sinus X-rays in childhood asthma: Lack of relation to severity of asthma. J Allergy Clin Immunol 1987; 80: 268–273.

J. Sederberg-Olsen, M.D.
ENT-Clinic
Strandgade 35
DK-3000 Helsingør
Denmark