

A Randomized, Prospective, Double-Blind Study of the Efficacy of Dexamphenol Nasal Spray on the Postoperative Treatment of Patients with Chronic Rhinosinusitis after Endoscopic Sinus Surgery

Pongsakorn Tantilipikorn MD*,
Prayuth Tunsuriyawong MD*, Perapun Jareonchairsri MD*,
Anan Bedavanija MD*, Paraya Assanasen MD*,
Chaweewan Bunnag MD*, Choakchai Metheetrairut MD, MSc*

* Division of Rhinology & Allergy, Department of Otorhinolaryngology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Objective: To assess the efficacy of dexamphenol nasal spray compared with normal saline spray in the postoperative treatment of patients with chronic rhinosinusitis (CRS) who underwent endoscopic sinus surgery (ESS).

Materials and Method: A prospective, randomized controlled study was conducted in CRS patients who underwent ESS. The enrolled patients had never been operated intranasally. These patients received either dexamphenol or normal saline nasal spray intranasally four times a day for six weeks post-operatively.

Results: Fifty CRS patients were recruited in the present study. Age ranged from 23 to 63 years (means 43.4 ± 11.2 years). Forty-four percent of patients were diagnosed as CRS without nasal polyps (NP) (CRSs NP) and 56% were CRS with NP (CRSw NP). Twenty-five cases were randomly assigned to use dexamphenol nasal spray whereas the other 25 cases used normal saline nasal spray. The preoperative severity of CRS, determined by the computerized tomography (CT) scan scoring system of Lund-McKay was 13.9 ± 6.2 in the dexamphenol group and 13.6 ± 6.9 in the normal saline group, which were not statistically different ($p > 0.05$). The endoscopic scoring was 10.2 ± 2 in the dexamphenol group and 10.7 ± 3 in the normal saline group, which were not statistically different ($p > 0.05$). The mucociliary transit time improvement (time difference between pre- and post-treatment by nasal spray) was 8.4 ± 3.3 minutes in the dexamphenol group and 1.7 ± 1.2 minutes in the normal saline group, which were statistically different ($p < 0.05$).

Conclusion: The majority of the postoperative symptom scores and all of the endoscopic scores of the dexamphenol group were not statistically different from those of the normal saline group. However, dexamphenol nasal spray has superior efficacy compared with normal saline nasal spray on improvement of mucociliary clearance and nasal discharge in the postoperative care of CRS patients after ESS.

Keywords: Rhinosinusitis, Nasal spray, Endoscopic sinus surgery

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Endoscopic sinus surgery (ESS) is a surgical procedure that has been accepted as a standard treatment of chronic rhinosinusitis (CRS) patients who fail to respond to medical therapy. It has been done for more than 500,000 procedures annually in the United States of America. The efficacy of ESS ranges

from 74-98%⁽¹⁻³⁾. Recently, a multi-institutional prospective cohort study reported 15.8 to 21.2% improvement of quality of life after ESS procedure⁽⁴⁾.

In order to determine the predictive factor of ESS outcome, several factors have been analyzed such as asthma, allergy, aspirin intolerance, previous sinus surgery, polyposis and preoperative severity of CRS. Besides those factors, good postoperative care is well accepted as a necessary step to achieve the best outcome. The postoperative care helps to maintain not only the patency of sinus(es) drainage at ostiomeatal unit (OMU), but also the function of ciliated mucosa

Correspondence to:

Tantilipikorn P, Division of Rhinology & Allergy, Department of Otolaryngology, Faculty of Medicine Siriraj Hospital, Bangkok 10700, Thailand.

Phone: 0-2419-8040, 0-2419-7409

E-mail: siptv@mahidol.ac.th

to move the mucous blanket & secretion from sinus cavities toward the OMU.

The isotonic saline is an approved solution for standard postoperative care after ESS. It promotes moisture and humidification, which help the movement of cilia to clear nasal and paranasal sinus discharge. Dexpanthenol is a substance added into the normal saline for further improving mucociliary clearance. The efficacy of dexpanthenol nasal spray was studied by Foonant et al in 2008. They performed an open-label study, comparing the dexpanthenol nasal spray with the normal saline irrigation⁽⁵⁾. They reported comparable efficacy between dexpanthenol nasal spray and normal saline irrigation but the dexpanthenol nasal spray was more convenient.

In this double-blind study, the efficacy of dexpanthenol nasal spray on the postoperative treatment after ESS was assessed by comparing with the isotonic saline nasal spray. The outcome measures were subjective symptoms, objective endoscopic score, and mucociliary transit time (MTT).

Material and Method

A prospective, randomized, placebo-controlled trial was done in the patients who were scheduled for ESS. The present study protocols were approved by the Institutional Review Board-Ethical Committee of Faculty of Medicine Siriraj Hospital. Diagnosis of CRS was made by the criteria of Task Force of American Academy of Otolaryngology Head and Neck Surgery⁽⁶⁾. The present study had been conducted in the department of Otorhinolaryngology between August 2005 and August 2006. The inclusion criteria were CRS with or without nasal polyp (NP) (CRS w NP and CRS sNP, respectively), age more than 18 years old, and the ability to come for postoperative

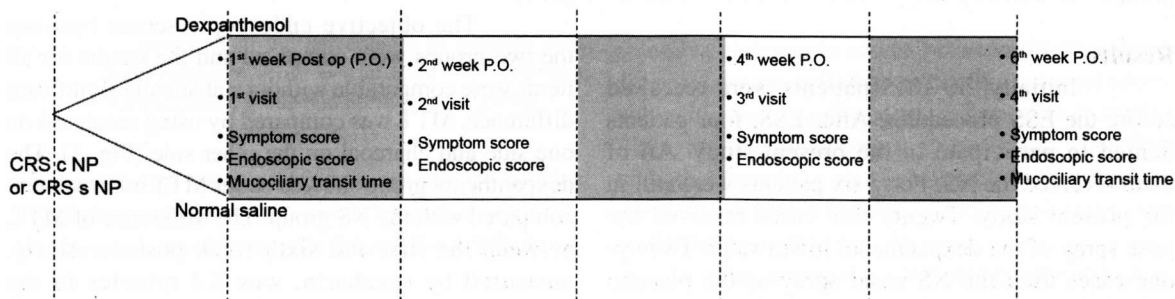
follow-up every week for two weeks and every two weeks for four weeks.

The preoperative computerized tomography (CT) scan of paranasal sinus of each patient was scored according to the grading system of Lund-McKay⁽⁷⁾. The endoscopic pictures of postoperative nasal cavities of each patient were taken and scored unanimously by a single evaluator. The authors used the endoscopic scoring system recommended by Rhinosinusitis Task Force⁽⁶⁾.

All cases had never been operated on intranasally and failed to respond to conventional maximal medical treatment for three months. Preoperatively, the patients who agreed to participate in the present study were randomized to receive either dexpanthenol nasal spray (Mar®Plus, Bad Vilbel, Germany) or normal saline nasal spray. Randomization was done according to age and presence of nasal polyp (Fig. 1).

Postoperatively, the patients were asked to come for nasal toilet four times on the first, second, fourth, and sixth week. Besides dexpanthenol or NS nasal spray, no other nasal spray or oral medication was allowed. Drop out was defined as failure to follow the postoperative schedule or having the evidence of wound infection which required oral antibiotic treatment.

The efficacy of postoperative treatment by both nasal sprays was assessed by subjective symptom; objective-endoscopic score every week for two weeks and every two weeks for four weeks, and MTT in the first and fourth visit postoperatively. The patients in both groups were asked to report their symptoms of nasal obstruction, nasal discharge, headache, facial pain, problem of smell and overall symptoms. The severity of each symptom was categorized into no symptoms (score = 0), mild



P.O. = postoperative; CRS = chronic rhinosinusitis; NP = nasal polyp

Fig. 1 Experimental protocol and study design

(score = 1), moderate (score = 2) and severe (score = 3). For nasal blockage, 0 = no nasal block, 1 = mild nasal block, 2 = moderate nasal block and 3 = complete nasal block. For nasal discharge item, scoring as 0 = no discharge, 1 = clear, 2 = white/thick and 3 = mucopurulent was applied. For headache/facial pain, scoring as 0 = no headache/pain, 1 = mild headache/pain, 2 = moderate headache/pain and 3 = severe headache/pain. For problem of smell, scoring as 0 = no problem, 1 = mild/minimal problem of smell, 2 = moderate problem of smell and 3 = severe problem of smell.

All patients underwent endoscopic exam for each postoperative visit and pictures were taken and graded (0 to 3) by a single evaluator who did not recognize the name and diagnosis of the patients. Three points grading for each endoscope score had been utilized. "Good clinical efficacy" was defined as grade 0 (no symptom or normal endoscopy) on the fourth visit postoperatively.

MTT were evaluated by applying saccharin on one side of the nose and charcoal on the other side. Both saccharin and charcoal were placed on the anterior end of inferior turbinate. The patient was asked to report the taste sensation of sweet and the investigator then examined the oropharynx for the visibility of charcoal. The time that the patient recognized the sweet taste and the time that the investigator saw charcoal were then recorded.

Statistical analysis was performed with SPSS version 11.5 (SPSS Inc., Chicago, IL). The Chi-square for trend test was used for comparison of the symptom score and endoscopic score between the dexampanthenol and NS groups. For comparison of the change of MTT, the pair t-test was used for pre- and post-treatment comparison. The independent sample t-test was used for the comparison of MTT between groups. A p-value of less than 0.05 was considered statistically significant. The comparison between groups was made by the "intention-to-treat" analysis.

Results

Initially, 50 CRS patients were recruited before the ESS procedures. After ESS, four patients denied to participate in the present study. All of them received the NS. Forty-six patients were still in the present study. Twenty-five cases received the nose spray of the dexampanthenol in seawater. Twenty-one cases used the NS nasal spray as the placebo group.

Nineteen patients were male and 27 patients were female. The mean age group was 43.4 ± 11.2 years.

Table 1. Patients' demographic data at 1st visit (n = 46)

	Dexampanthenol group (n = 25)	Normal saline group (n = 21)
Age (years)	43.9 ± 11.3	42.8 ± 12.6
Number of patients:		
CRS w NP	16	10
CRS s NP	9	11
Endoscopic score	10.2 ± 2	10.7 ± 3
CT score	13.9 ± 6.2	13.6 ± 6.9

CRS = chronic rhinosinusitis; NP = nasal polyp

All of them were diagnosed CRS and have been operated for ESS. Forty-four percents of cases were CRS without NP (CRS s NP). Fifty-six percent were CRS with NP (CRS w NP) (Table 1).

Thirty-three patients (71%) completed the present study protocol. Six patients in the dexampanthenol group did not come for the last (fourth) visit. Seven patients in the NS group lost their postoperative appointment. Three of seven patients (in the NS group) reported nasal burning sensation and discontinued the present study protocol. Four of seven patients missed their last postoperative appointment.

At final visit, nineteen patients (57.6%) finished using dexampanthenol nasal spray without interruption. Fourteen patients (42.4%) used NS nasal spray for 6 weeks postoperatively. Subjective symptoms (nasal blockage, rhinorrhea, headache, facial pain, problem of smell, and overall symptom) were compared between groups (Table 2, Fig. 2). Dexampanthenol nasal spray significantly improved nasal discharge compared with NS nasal spray ($p < 0.05$) whereas NS nasal spray significantly improved the problem of smell compared with the dexampanthenol nasal spray group ($p < 0.05$). The effects on other symptoms were comparable between the dexampanthenol and NS group.

The objective endoscopic scores between the two groups were compared and the results for all items were comparable without statistically significant difference. MTT was compared by using saccharin on one side and charcoal on the other side (Fig. 3). The dexampanthenol group showed better MTT improvement compared with the NS group. The difference of MTT, between the first and sixth week postoperatively, measured by saccharin, was 8.4 minutes in the dexampanthenol group and 1.7 minutes in the NS group, which were statistically different ($p = 0.016$). The difference of MTT between the first and sixth week

Table 2. Comparison of the percentages of patients who had symptom score or endoscopic score = 0 between dexpanthenol group and normal saline group at 4th visit (n = 33)

	Dexpanthenol group (%), n = 19	Normal saline group (%), n = 14	p-value
Symptom score			
Nasal blockage	68	66.7	1.000
Nasal discharge	74	50.0	0.031*
Headache	82	78.6	0.881
Facial pain	70	81.0	0.334
Problem of smell	44	71.4	0.015*
Overall	44	57.1	0.295
Endoscopic score			
Polypoid swelling	74	83.3	0.408
Discharge	54	59.5	0.748
Edema	70	78.6	0.488
Adhesion	90	88.1	1.000
Crusting	78	73.8	0.823

* Indicates statistical significance between groups

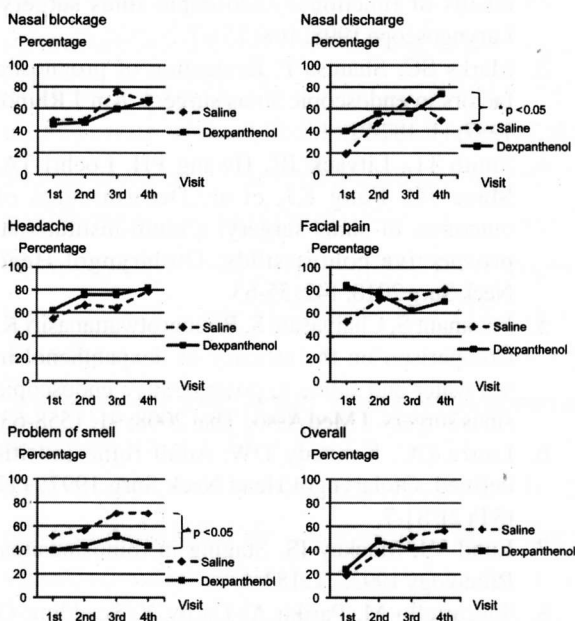


Fig. 2 Comparison of the percentages of patients who had symptom score = 0 at each visit between dexpanthenol group and normal saline group

postoperatively, measured by charcoal, was 8.4 minutes in the dexpanthenol group and 1.7 minutes in the NS group, which was statistically different ($p = 0.018$).

Discussion

The Mar[®]Plus spray is composed of isotonic saline mixed with dexpanthenol. Unsurprisingly, the

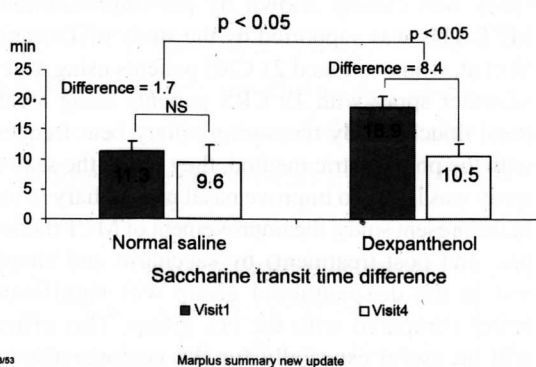


Fig. 3 Comparison of mucociliary transit time difference (pre- and post-treatment) between groups assessed by saccharine. The X axis indicates study groups as specified on the abscissa. The Y axis indicates means and standard error of mean of mucociliary transit time

objective endoscopic scores between the two groups did not show any difference including mucosal edema, polypoid swelling, discharge, adhesion and crusting. Both groups showed comparable efficacy. The effects of both treatments on the subjective symptoms of nasal blocking, headache, and facial pain were comparable as well.

The patients in the dexpanthenol group significantly had less nasal discharge compared with patients in the NS group. Fooananat et al showed that the dexpanthenol nasal spray had inferior

efficacy more than the NS irrigation to reduce postnasal dripping in the first visit only and had the same efficacy in their last visit⁽⁵⁾. It should be noted that their study was conducted in open-label design and the comparison was done between dexpanthenol nasal spray and NS irrigation, which may explain the different results compared with the present study.

In terms of improvement of olfactory symptom, the patients in the dexpanthenol group showed inferior efficacy than the NS nasal spray. However, that is the subjective report of patients without the semi-objective test such as the University of Pennsylvania Smell Identification Test (UPSIT). The further study is needed for evaluation of the effect of dexpanthenol on sense of smell. Theoretically, dexpanthenol is the substance without odor.

The striking property of dexpanthenol nasal spray was clearly shown by the improvement of MTT. This was supported by the study of Taccariello M et al, who compared 21 CRS patients using a sterile seawater spray with 19 CRS patients using alkaline nasal douche⁽⁸⁾. By measuring ciliary beat frequency with the photometric method, they found the seawater spray was likely to improve nasal mucociliary *in vitro*. In the present study, the improvement of MTT (between pre- and post-treatment) by saccharin and charcoal test in the dexpanthenol group was significantly better compared with the NS group. This efficacy will be useful especially for the postoperative care in the condition that may impair ciliary function such as ciliary dyskinesia or extensive loss of mucosal surface.

Conclusion

In this prospective study, dexpanthenol nasal spray showed superior efficacy compared with NS nasal spray on improvement of mucociliary clearance and nasal discharge. Its efficacy on other symptoms and objective nasal endoscopic scores postoperatively was comparable to NS nasal spray.

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Potential conflicts of interest

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