LETTER TO THE EDITOR

Functional recovery in subjects undergoing nasal surgery: a new therapeutic strategy

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To the Editor,

The histological layer covering the nasal cavities entails a series of strata in the craniocaudal sense: epithelial layer, basal membrane, lymphoid layer, glandular layer, and vascular layer (1). The epithelial component is the most sensitive to the traumatic damage induced by surgical interventions on the nasal area. The nasal mucosa is constituted by a pseudostratified richly vascularized, ciliated columnar epithelium, and includes numerous muciparous goblet cells and glands of the lamina propria (2). The nasal mucosa's importance entails the high functional specificity of its constituent elements, including inspired air climatization and filtration, defense against pathogens and pollutants, and olfaction. The different cellular and glandular elements are typically differentiated into i) ciliated columnar cells, arranged in the pseudostratified columnar epithelium, based on the double level stratification of the nuclei, with cilia that arise from the apical membrane, ii) non-ciliated cells, iii) muciparous goblet cells, producing mucus, with a defensive action, and with the well-developed endoplasmic reticulum, characterized by intense secretory activity, iv) basal cells, with modest shape and mitotic activity, and mucous glands. Nasal surgery frequently causes mucosal damage, which may have relevant functional consequences. Moreover, patients experience disturbing symptoms after sinonasal surgery (3). Consequently, the therapeutic strategy should be addressed to relieve symptoms and restore mucosal integrity and nose functions (4, 5). In this regard, a new multi-component medical device (Rinocross®; DMG Italia, Pomezia, Italy), containing D-panthenol, hyaluronic acid (HA), vitamin E, vitamin A, and biotin, has been proposed for the topical treatment of post-surgical complications. The device was tested on patients with atrophic rhinitis. The rationale of its use in patients who underwent sinonasal surgery is based on the multi-functional activities exerted by the different components which exert anti-inflammatory, antioxidant, repairing, hydrating, and lubricating activities. The current study therefore investigated the efficacy and safety of this compound's "eutrophic" property in patients who had undergone sinonasal surgery.

MATERIALS AND METHODS

The study enrolled 40 subjects (22 males and 18 females, aged between 21 and 59 years) subjected to various surgical interventions involving the nasal area. The patients were divided into two groups, A and B, each consisting of 20 people, which differed in the treatment methods following surgery. The study was performed according to the Helsinki Conference's ethical rules, and the internal review board approved the procedure. Each patient signed informed consent.

Key words: sinonasal surgery; treatment; D-panthenol; hyaluronic acid; vitamin A; vitamin E; biotin

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Group A included patients subjected to septoplasty surgery (6 patients), turbinate decongestion surgery (8 patients), and nasal polypectomy surgery (6 patients), using functional endoscopic sinus surgery (FESS). Group A was treated with Rinocross® nasal spray, two sprays per nostril, two times a day for one month.

Group B included patients who underwent septoplasty surgery (5 patients), turbinate decongestion surgery (9 patients), and nasal polypectomy surgery, using FESS (6 patients). Group B was treated with saline isotonic solution nasal spray, two sprays per nostril, two times a day for one month.

At baseline (T0), the investigators performed: anamnestic assessment, administration of a specific questionnaire, with subjective evaluation scale by visual analogic scale (VAS) of nasal obstruction, nasal dryness, hyposmia/anosmia, and presence of epistaxis. Investigators performed nasal endoscopy, anterior rhinomanometry, and mucociliary transport time. The score obtained by the VAS was categorized in 5 severity grades: 0= absent; 1-2= mild; 3-5= moderate; 6-8= severe; 9-10= very severe. At the end of the treatment (T1), investigators re-evaluated the patients performing the same procedures.

The statistical analysis was performed using the *chi*-squared test. With a p-value less than 0.05, the differences were selected as significant, and Graphpad analyzed data.

RESULTS

Baseline data (T0)

Endoscopic findings. In Group A, 5 (15%%) patients had mild mucosal hyperemia, 8 (40%) moderate, and 7 (35%) intense hyperemia. One patient (5%) had mild septal deviation, 3 (15%) moderate, and 2 (10%) intense septal deviation. Two patients (10%) had mild turbinate hypertrophy, 3 (15%) moderate, and 3 (15%) intense turbinate hypertrophy. Two patients (10%) had moderate polyposis, and 4 (20%) intense polyposis. In Group B, 3 (25%%) patients had mild mucosal hyperemia, 8 (40%) moderate, and 9 (45%) intense hyperemia. Two patients (10%) had mild septal deviation, 3 (15%) moderate, and 3 (15%) intense septal deviation. Five patients (25%) had mild turbinate hypertrophy, 2 (10%) moderate, and 1 (1%) intense turbinate hypertrophy. Four patients (20%) had moderate polyposis.

Anterior rhinomanometry. In group A, 5 (25%) patients had mild reduction of nasal airflow (700-870 cm^3/sec), 6 (30%) had moderate (500-700 cm^3/sec), and 9 (45%) severe nasal obstruction (300-500 cm^3/sec). After decongestion with an adrenergic agent, 3 patients had moderate, and 9 had severe obstruction. In Group B, 8 (40%) patients had a mild reduction of nasal airflow, 6 (30%) had moderate, and 6 (30%) severe nasal obstruction. After decongestion with an adrenergic agent, 6 patients had moderate and 6 had severe obstruction.

Mucociliary clearance. In Group A, the mucociliary clearance time was mildly reduced (17.1 minutes) in 7 patients, moderately (18.8 min) in 9, and intensely (19.2 min.) reduced in 4 patients.

In Group B, the mucociliary clearance time was mildly reduced (17.6 minutes) in 5 patients, moderately (18.5 min) in 11, and intensely (19.7 min.) reduced in 4 patients.

Symptom perception. In Group A, the nasal obstruction was evaluated as mild by 5 (25%) patients, moderate by 9 (45%), intense by 5 (25%), and severe by 1 (5%) patient. The nasal dryness was considered mild by 2 (10%) patients, moderate by 12 (60%), intense by 3 (15%), and severe by 3 (15%) subjects. The olfaction impairment was evaluated mild by 6 (30%) patients, moderate by 8 (40%), and intense by 6 (30%) patients. Epistaxis was considered mild by 5 (25%) patients and moderate by 1 (5%) patient. In Group B, the nasal obstruction was evaluated as mild by 7 (35%) patients, moderate by 9 (45%), and intense by 4 (20%) patients. The nasal dryness was considered mild by 5 (25%) patients, moderate by 9 (45%), intense by 4 (20%), and severe by 2 (10%) subjects. The olfaction impairment was evaluated mild by 7 (35%) patients, moderate by 10 (50%), and intense by 3 (15%) patients. Epistaxis was considered mild by 3 (15%) patients and moderate by 2 (10%) patients.

End of treatment data (T1)

Endoscopic findings. In Group A, 2 (10%) patients had mild mucosal hyperemia, and 1 (5%) moderate hyperemia. In Group B, 1 (5%%) patient had mild mucosal hyperemia, 3 (15%) moderate, and 1 (5%) intense hyperemia.

Anterior rhinomanometry. In group A, 1 (5%) patients had a mild reduction of nasal airflow, and 1

(5%) patients had a moderate nasal obstruction. In Group B, 2 (10%) patients had a mild reduction of nasal airflow, and 1 6 (5%) had a moderate nasal obstruction.

Mucociliary clearance. In Group A, the mucociliary clearance time was normal (13.9 min) in 16 patients and moderately (18.1 min) reduced in 4 patients. In Group B, the mucociliary clearance time was mildly reduced (17.1 min) in 9 patients, and moderately (18.3 min) in 11 patients.

Symptom perception. In Group A, the nasal obstruction was evaluated as mild by 9 (45%) patients, moderate by 7 (35%), intense by 3 (15%), and severe by 1 (5%) patient. The nasal dryness was considered mild by 2 (10%) patients and moderate by 3 (15%) subjects. The olfaction impairment was evaluated mild by 10 (50%) patients, moderate by 6 (30%), and intense by 4 (20%) patients. No patient reported epistaxis. In Group B, the nasal obstruction was evaluated as mild by 2 (10%) patients and moderate by 3 (15%) patients. The nasal dryness was considered mild by 3 (15%) patients, moderate by 3 (15%), and intense by 1 (5%) subject. The olfaction impairment was evaluated mild by 3 (15%) patients and moderate by 5 (25%) patients. No patient reported epistaxis.

Intergroup comparison. Nasal endoscopy findings improved more significantly ($p=0.009$) in Group A than in Group B, nasal airflow increased ($p=0.008$) in Group A than in Group B, the mucociliary transport time more significantly improved ($p<0.01$) more in Group A than in Group B, nasal obstruction was more significantly reduced ($p<0.0001$) in Group A than in Group B, nasal dryness was more significantly improved ($p=0.008$) in Group A than in Group B, and olfaction more significantly improved ($p<0.0001$) in Group A than in Group B.

All treatments were well-tolerated by all patients, and no clinically relevant adverse events were reported.

DISCUSSION

Surgical trauma can induce clinical consequence attributable to the mucosa's structural "fragility" and the impaired nasal functions associated with surgical wounds. The symptom severity and functional impairment are related to the surgery abrasiveness; in fact, FESS is scarcely demolitive, thus safeguarding the nose's structural and functional structures also in children (6).

In the post-surgical period, treatment aims to restore the structural and functional integrity of the nasal mucosa. Various types of treatment have been proposed over time, using the compounds available at that time. A revolution in the field of epithelial eutrophism has been offered by HA, the main constituents of the extracellular matrix, endowed with numerous hygroscopic, rheological, and viscoelastic properties (7). HA modulates the cascade of inflammatory events, provides antioxidant activity and dampens cytokine overload (8). HA also exerts an intense tissue repair activity, achieved by cellular migration and proliferation. HA limits collagen's conversion from soluble to an insoluble form, representing a lubricating factor capable of promoting the fibrous component's sliding. The tested medical device contains other components able to repair and restore the damaged mucosa, namely D-panthenol (9), vitamin E (10), vitamin A (11), and biotin (12).

The current study showed that the new multi-component medical device significantly improved the macroscopic features, nasal airflow, mucociliary transport time, and symptom perception in patients who underwent sinonasal surgery. Moreover, Rinocross® nasal spray was significantly more effective than a comparative compound. The efficacy was also associated with optimal safety as the new medical device was well-tolerated by all patients, and no clinically relevant adverse events occurred during the intranasal administration period. On the other hand, this study has some limitations, including the open design, the lack of biomarker assessment, and the limited number of enrolled patients, therefore, the outcomes should be considered as preliminary. Consequently, further studies should be performed to bridge these gaps. In conclusion, the new multi-component medical device could be a promising treatment for patients after sinonasal surgery as it provided rapid symptom relief, mucosal repairing, and functional restoring.

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