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Highlighting the New Advancements in Rhinitis Medicamentosa: A Review Article

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ABSTRACT

highlighting the In this review, we're most advancements in the diagnosis and management of rhinitis medicamentosa. A topic which has not reviewed recently. Rhinitis medicamentosa is relatively common condition resulting from longer than recommended use of nasal decongestant. There still no clear diagnostic criteria to diagnose RM. In addition, the pathophysiological explanation to RM has been researched, however with no solid conclusion has been developed. Rhinitis medicamentosa can be prevented by proper management of the primary disease. The important goals in treating RM is to first, stop nasal decongestant then to treat the underlying condition properly. Corticosteroids also has been used and are effective in reliving RM symptoms. Other new less invasive techniques has been developed recently in treating nasal congestion caused by RM, however, part of them are still under research and has to be proved on accurate samples. Refractory cases that are not responsive to previously mentioned management can benefit

from more advanced inferior turbinate reductions surgeries and every case has to be assessed separately in choosing the best surgical technique.

Keywords: Rhinitis Medicamentosa, Decongestants, Nasal Obstruction, Turbinoplasty.

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INTRODUCTION

In this review, a thorough literature searches were made using MEDLINE, Google Scholar and the reference list of congruent articles, pointing out recent updated information on the pathophysiology, diagnostic points, medical and surgical management of rhinitis medicamentosa (RM). The term "Rhinitis medicamentosa" has been used regularly to define one of unwanted outcome of the prolong use of nasal decongestant. Which usually result in persistent nasal symptoms after a period of relief. Until now, there is no clear diagnostic criteria for RM. Rebound effect which usually observed following nasal decongestants discontinuation has to be differentiated from RM as these two entities get confused.1

Nasal decongestants addiction has been reported in many patients with non-allergic rhinitis as well as patients with rhinitis medicamentosa as they enter a circle of rebound and relief.² Rhinitis medicamentosa (RM) which also has been described as "chemical rhinitis", usually develop after exaggerated use of nasal decongestant.³

With regular use of nasal decongestant, time of onset of RM has

not yet been strictly defined. Some studies have shown that it can happen up to 4 to 6 weeks of use and not after the third or fourth day as it usually described.⁴ Generally, even with no definitive evidence in this regard, the use of nasal decongestant more than 10 days is not recommended.⁵

During pregnancy, RM tend to increase as these patients tend to prefer more topical options over oral or systemic medications.⁶ In regards to incidence of RM, a study conducted on 300 participants in Takrit, Iraq showed that (13.3%) participant complained from rhinitis medicamentosa.⁷

Rhinitis medicamentosa was more in male 60% than female 40%. Around 30% of patients with history of viral rhinitis developed rhinitis medicamentosa while 10% of patients of total participants had allergy, whereas 60% of patients of the whole number of rhinitis medicamentosa had history of chronic nasal obstruction. Depending on clinical duration, rhinitis medicamentosa distribution was prominent after 30 days of nasal decongestants use (69.4% vs. 65.3%) and no significant difference among patients with infectious and allergic rhinitis (P>0.05) (Fig. 1).8

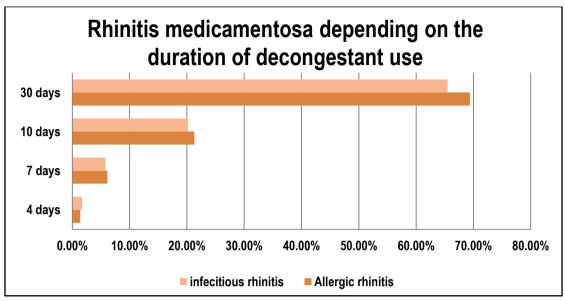


Figure 1: Rhinitis medicamentosa depending on the duration of nasal decongestant use. 8

PRESENTATION

The increasingly rapid development of isolated persistent nasal congestion after trial of nasal decongestant use is the classic presentation of rhinitis medicamentosa. Reddish and thickened nasal mucosa what usually found on examination, however not specific.¹ Hypertrophic Turbinates with a "beefy red" look of mucosa are usually found. In addition, local examination can reveal congested, granular mucosa, with spots of punctate bleeding caused by tissue fragility. Perforation of the nasal septum can result however it's considerably rare. 9,10 Also, a scanty mucus can be seen in such patients. Collectively, no specific findings of RM has been described ,however, inability to decongest, cobblestone look and erythema being the most common. 11

PHYSIOLOGY OF NASAL CONGESTION

One of the most common complaints to be encountered in general care or otolaryngology clinics is nasal congestion and it carries a large burden on the patient. The primary pathophysiological mechanism behind allergic rhinitis, rhinosinusitis and nasal polyposis is mucosal inflammation leading to prominent congestion. ¹² Eventually, the inflammation will lead to venous engorgement, increase secretions and edema predisposing to all factors of congestion. ¹³ The physical size of nasal cavity will be limited as a result of such factors. ¹⁴ One of the factors that may alter the perception of nasal congestion and volume of nasal cavity either in normal or patients with rhinitis is recumbent position. ¹⁵

Other pathological defects like nasal septum deviation, concha bullosa, adenoid hypertrophy and choanal atresia can predispose to nasal pathway obstruction either by direct effect or by making the area prone to infection and inflammation. ¹⁶ In addition, on of the most significant factors in the pathophysiology is the neurogenic mechanisms and may affect the primary signaling leading to the sensation of congestion even without any nasal inflammation or any other pathology affecting the airflow. ¹² Other associated conditions that may present with symptoms of congestion like otitis media and asthma has to be sort out, also, congestion could worsen the symptoms of obstructive sleep apnea. ¹⁷

MECHANISM OF ACTION OF NASAL DECONGESTANT

Nasal decongestants, a symptomatic relief type of medication are commonly used by diverse groups of patients and are available in topical and oral forms.¹⁸ Decongestants may contain pseudoephedrine. phenylephrine. oxymetazoline xylometazoline. Table.1 showing a list of nasal decongestants have been reported to cause RM. They are available over the counter and can be utilized as a nasal spray, drops or oral form. 19 Nasal decongestants can be categorized as sympathomimetic amines as they act by stimulating the alpha-adrenergic receptors causing vasoconstriction to capillaries supplying the upper respiratory tract structures.20 The resultant action will be significant decrease of edema and secretions and improvement of breathing process.¹⁸ In regards to age restriction, generally they should not be given to patients under six years old21. Even though their spectrum of action is mainly local, they may cause other systemic effects like hypertension. Headache, nausea, insomnia and dizziness also has been reported as a side effects of such medication. And to the purpose of this discussion, people should not use a decongestant for longer than five days to avoid the risk of rhinitis medicamentosa21

Table 1: Decongestants causing rhinitis medicamentosa

Sympathomimetics

Amphetamine

Benzedrine

Ephedrine

Phenylephrine

Phenylpropanolamine

Imidazolines

Naphazoline

Oxymetazoline

Xylometazoline

PATHOPHYSIOLOGY OF RM

Up to this day, there is no clear answer as to why it happens and several hypothesis has been developed in this regard. One say it may be a result of the negative feedback to the endogenous

sympathetic norepinephrine leading to rebound effect after prolonged use or the sympathetic nerves may no longer able to maintain vasoconstriction because of the suppression of norepinephrine release.^{22,23,} The 2011 French Society of Otorhinolaryngology guidelines suggests that this effect might be no more than continuum of the disease process as it has been described in the context with healthy volunteers only upon their use of nasal decongestant. Other hypotheses suggest either repeated alpha-2 receptor stimulation, provoking intense vasoconstriction with mucosal ischemia and interstitial edema, or else alpha-2 receptor down-regulation, leading to relative dilation and a tachyphylaxic effect resulting in increased need of more decongestants, or an affinity for alpha receptors which, when stimulated, induce secondary vasodilation once the alpha effect has abate.24 The most recent model has been studied is the effect of oxidative stress in RM, which has been studied on rats by Dokuyucu & his colleagues.²⁵ They found That the total oxidative status was prominent in Rhinitis medicamentosa rat model, indicating an imbalance of oxidative stress and production of oxidants. Also, they detected a relationship between oxidative stress and RM in rats. And they concluded that The significant effect of Erdosteine (ED) (which was used in their study) on the advancement of nasal mucosal changes suggest that oxidative stress may be of an important role in the pathophysiology of RM.25

HISTOLOGY

Histopathological examination of nasal mucosa after the development of rhinitis medicamentosa can show areas of epithelial metaplasia and epithelial hyperplasia, also some areas of lost cilia , increase of goblets cells number and submucosal glands. In addition, increased expression of the epidermal growth factor receptor, and inflammatory cell infiltration has been described. Functionally, lost epithelial ciliated cells will lead to the decrease the ability of nasal clearance. Moreover, increased vascular permeability with interstitial edema has been described as one of ultrastructural changes to vascular endothelium. However, Graf suggests that RM results from interstitial edema rather than from vessel dilatation.

PREVENTION

In a recent randomized controlled study done by Thongngarm & his colleagues, the combination of INS and Oxymet (oxymetazoline) provided the advantage beyond INS monotherapy in relieving nasal congestion in subjects with chronic rhinitis. Subjects with allergic rhinitis appeared to have a greater response to the combination compared with those with chronic rhinitis. In the Oxymet group, subjects with allergic rhinitis significantly improved nasal congestion score compared to non-allergic individuals. In addition, the combination of INS and Oxymet was not associated with rhinitis medicamentosa.29 Zhumambayeva & his colleagues demonstrated that those who receive specific immunological treatment for their allergic rhinitis are less likely to develop RM. their results demonstrated that rhinitis medicamentosa developed only in 5 (17.2%) patients with advanced specific immunotherapy to the end of pollination season. Thus, this substantial finding is consistent with previous research30 and is an additional evidence for the statement that specific immunotherapy is reliable, etiology based treatment of allergic rhinitis, playing another significant role in rhinitis medicamentosa prevention.8

TREATMENT

Rhinitis medicamentosa usually managed medically with great improvement, however, RM, in many cases can be challenging and resistant to traditional treatment: a multiple unsuccessful treatment attempt, enduring drug addiction for many years usually the highlight in RM disease course.

The crucial aims of rhinitis medicamentosa treatment are firstly to stop the use of nasal decongestants and secondly to cure the underlying cause of condition that led to the initial use of vasoconstrictor nasal drops. Topical Corticosteroids therapy has been well documented to be effective in reliving the symptoms of rhinitis medicamentosa. A randomized, double-blind, placebocontrolled study done on 19 healthy participants treated with oxymetazoline 200 g three times a day for 2 weeks showed that their nasal congestion abate significantly after administration of fluticasone 200 g twice daily for 3 days, even without discontinuing the nasal decongestant.31 One suggestion has been made by the authors that this observation might be due the increased expression of alpha-adrenergic receptors provoked by administration. thereby downsizing corticosteroids tachyphylaxis effect of nasal decongestant.31 In addition, topical corticosteroids can accelerate the recovery from RM.32 In refractory cases, Surgical options i.e. Turbinate surgery has a major role in the management of nasal congestion caused by mucosal edema. Different approaches and technical modalities like (turbinoplasties, radiofrequency, laser, microresection) can be proposed as options for such management¹. Diode laser reduction of hyperplastic Inferior Turbinate in outpatient settings has been used in treating cases of refractory RM.33 Caffier in his study has suggested this modality as highly effective, safe, and welltolerated treatment option in rhinitis medicamentosa refractory cases. He used a laser in his trial that creates a controlled superficial coagulation zone that degenerate into necrotic tissue and separate from the underlying viable tissue within 6 weeks after his intervention. His intervention has resulted in great restoration of function with minimal invasive harmful effects, in addition, long-lasting effect Also described to be positive in reliving nasal congestion symptoms and preventing the addiction circle to nasal decongestants.33 Another new intervention has been conducted is kinetic oscillation stimulation (KOS). The core idea behind this treatment or intervention is to introduce mechanical oscillations similar to the naturally occurring turbulence to enhance a positive effect on the inflammatory status in the mucosal surface layer.² The results of this intervention has been promising, after one nasal mucosa trial with Kinetic oscillation stimulation (low frequency mechanical vibrations), participants with Non-Allergic Rhinitis and Rhinitis Medicamentosa had reported noticeable decrease of their nasal symptoms, both overall Median Rhinitis Questionnaire Symptom Score (RQSS) and specifically of stuffiness, in comparison to placebo-treated patients. Moreover, the effect was more prominent in the first days after treatment but was still present after 2 weeks as well. The advantages of such intervention that were reported to be easy to administer, well tolerated by the patient, and side effects were few and mild. Considering that available treatments like (steroids and vasoconstrictors) are not always successful and can be addictive,

this intervention by Juto and his colleagues has a promising potential for viable alternative in treating rhinitis medicamentosa.² When medical therapy and other less invasive interventions fails, there are various available surgical techniques can be used to manage inferior turbinate hypertrophy (ITH), including but not all, turbinectomy, turbinoplasty, extramucosal or submucosal electrocautery, radiofrequency ablation (RFA), laser-assisted resection or ablation, and cryosurgery. However, there is still no clear data indicating which option has the optimal results and better long term effects.³⁴

Mucosal sparing techniques like submucus microdebriderassisted and RFA technique has been studied thoroughly in the recent literature and has become a favorable trend in recent years. In terms of long-term outcome, MAIT offered better longterm results than RFA also didn't has any significant adverse outcome on nasal mucosa.34 Farmer & his colleagues emphasizes the short term beneficial outcome of inferior turbinate coablation. 16 participants with the lowest pre-operative nasal air-flow conduction gain much greater objective improvement and benefits from IT coablation, and this has to be one of the markers in selecting patients for such surgeries. Such observation highlights the significance obtaining of objective assessment of nasal obstruction before surgery.16 In regards to partial inferior turbinectomy, the observed collective data has shown that partial IT is as effective as total inferior turbinectomy with high success rate reaching up to 80%.35,36

CONCLUSION

Rhinitis medicamentosa is relatively common condition resulting from longer than recommended use of nasal decongestant. There still no clear diagnostic criteria to diagnose RM. In addition, the pathophysiological explanation to RM has been researched, however with no solid conclusion has been developed. Rhinitis medicamentosa can be prevented by proper management of the primary disease. The important goals in treating RM is to first, stop nasal decongestant then to treat the underlying condition properly. Corticosteroids also have been used and are effective in reliving RM symptoms. Other new less invasive techniques has been developed recently in treating nasal congestion caused by RM and turbinate hypertrophy however part of them are still under research and has to be proved on accurate samples. Refractory cases that are not responsive to previously mentioned management can benefit from more advanced inferior turbinate reductions surgeries and every case has to be assessed separately in choosing the best surgical technique.

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