REVIEW ARTICLES

Rhinitis medicamentosa

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Rhinitis medicamentosa, the syndrome of rebound nasal congestion secondary to prolonged topical intranasal use of vasoconstrictors, is reviewed. In this condition the nasal airway is very obstructed; atrophic rhinitis is the most serious complication. Management consists of withdrawing the offending nasal spray and alleviating the nasal obstruction by means of any of several treatment modalities.

On passe en revue la rhinite médicamenteuse, le syndrome de rebond de la congestion nasale secondaire à l'usage topique prolongée des vasoconstricteurs nasaux. En cette affection l'obstruction des voies aériennes est prononcée; la rhinite atrophique s'avère la complication la plus grave. On a effectué la cure de sévrage en supprimant le vasoconstricteur en cause et en soulageant l'obstruction nasale par n'importe laquelle de plusieurs modalités du traitement.

Both the otolaryngologist and the family practitioner are frequently confronted by the patient troubled by a "stuffy" nose. The most common causes of this problem are acute viral rhinitis (the common cold), allergic rhinitis, anatomic defects and purulent sinusitis.[1] After careful consideration of these disorders during history-taking and physical examination a different condition may reveal itself. The patient tells of the frequent use of nosedrops to gain relief of the nasal obstruction, and the physician discovers a hyperemic, edematous nasal mucosa that shrinks little after the intranasal administration of vasoconstrictors. The condition of rebound nasal congestion secondary to prolonged topical intranasal use of vasoconstrictors is appropriately termed rhinitis medicamentosa.[2]

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History of the condition

Vasoconstrictors have been available for intranasal use since the 19th century. The alkaloid ephedrine was first isolated in 1887 from the Chinese herb Ma-huang.[3] Shortly afterwards Oliver and Schafer[4] discovered epinephrine in the adrenal medulla, and 10 years later Stolz[5] and Dakin[6] produced it synthetically. The commonly used phenylephrine was discovered 5 years later by Barger and Dale.[7] The discovery of amphetamine followed in 1930 and that of naphazoline in 1941.[3] Early in the 1930s work began in an effort to determine the adverse effects of these agents in humans. In 1931 Fox[8] described the chronic effect of epinephrine and ephedrine on the nasal mucosa of rabbits. His work was followed by that of Lierle and Moore,[9] Walsh and Cannon,[10] Kully,[3] Lake,[2] Ryan[11] and Fabricant.[12]

Despite the early evidence of ill effects of the intranasal use of vasoconstrictors, advertising continued to illustrate the benefits of this practice without sufficient mention of the deleterious effects associated with prolonged use. Kully[3] reported in 1945 that no class of drugs was more widely distributed and used than the vasoconstrictors. At that time there were 240 products of this kind available.

Addiction to nosedrops was well documented in 1946 by Lake,[2] who described how one patient "had become so addicted to the use of nosedrops that it was necessary to hospitalize her and then get her out of the room while one of the first assistants went through her belongings and removed numerous bottles of nosedrops". Following these publications little appeared in the literature until 20 years later, when Stride[13] reported that up to 5% of outpatient consultations in many ear, nose and throat units were for rhinitis medicamentosa — "a direct consequence of misguided topical nasal therapy". Subsequent reports were presented by Blue,[14,15] May and West[1] and Baldwin.[16] Despite the past and recent work describing rhinitis medicamentosa, the intranasal use of vasoconstrictors is increasing steadily.[16]

Intranasal use of vasoconstrictors

As Kully[3] wrote: "The nasal mucosa responds to infection as do other body tissues, with swelling, augmented blood supply, increased exudation and diapedesis. Shrinking the tissues with medication reverses this physiologic response. In no other tissue of the body is infection treated by diminishing the blood supply and shrinking the collateral edema. Such treatment lessens neither the severity nor the duration of the infection. On the contrary, the typical cause of an acute rhinitis may be altered and prolonged." Boies,[17] in his textbook of otolaryngology, stated that decongestion is required to promote drainage of the purulent fluid within the nasal or sinus cavities associated with an infectious process in the nose or paranasal sinuses. He claimed that topically administered vasoconstrictors are useful for this purpose but advised that the duration of their use be limited to 1 week. Fabricant[18] suggested that, when judiciously employed, nasal vasoconstrictors aid in promoting adequate drainage from paranasal sinuses by opening obstructed ostia, and that "a number of sympathomimetic amines have come to assume a legitimate place in the otolaryngologist's treatment schedule. They afford symptomatic relief for the patient with acute coryza, but probably have no therapeutic value. Intranasal vasoconstrictors should be used only temporarily — five days' use, as stated on prescriptions, with no refills."

Nasal vasoconstrictors are used therapeutically in preparation for nasal operations, as an adjunct in treating serous otitis media, and for acute and chronic sinusitis, and are used prophylactically to prevent the barotrauma associated with air travel and scuba diving. They are also used in nursing infants suffering from a cold. However, of 22 patients with rhinitis medicamentosa recently studied by Baldwin[16] only 3 initiated drug therapy on the basis of the indications cited. Of the remaining 19 patients 16 had allergic rhinitis, 4 had a deviated nasal septum and 3 had an upper respiratory tract infection.

The obvious disparity between the therapeutic indications and the actual use of this class of drug evinces the need for better physician and patient awareness of the limitations of nasal vasoconstrictors.

Physiology of the upper respiratory tract[2,19]

The nose serves as a physiologic air-conditioner, performing three main functions: filtering the inspired air and regulating its temperature and humidity. Anatomically the nose is well suited to this purpose as the nasal mucous membranes, folded over the turbinates, create a large surface area for imparting warmth and moisture to the inspired air. The nasal mucosa consists of mucus-secreting pseudostratified ciliated columnar epithelium and a highly specialized form of ciliated epithelium in the olfactory sensory area. The ciliated columnar epithelium is rich in goblet cells, which secrete approximately 1 litre of mucus per day. The mucus is transported by the cilia as a continuous blanket backward toward the choanae, from where it passes into the nasopharynx. Here it is carried to the lateral pharyngeal wall and is swallowed, lubricating the pharyngeal and laryngeal mucosal surfaces. The cilia beat approximately 200 times per minute, and the mucus blanket moves at a rate of about 0.5 cm/min.

The two nasal chambers vary in their activity, with alternating congestion of the inferior turbinate on one side and decongestion on the opposite side. The change occurs every 20 to 120 minutes in this so-called nasal cycle. The cavernous tissue on the medial surfaces of the turbinates becomes more or less congested with variations in the temperature and humidity of the inspired air. These changes vary the effective surface area of the nasal mucosa and, in so doing, adapt the nasal chambers to changes in the environment.

Pathophysiologic effects of nasal vasoconstrictors

Currently nasal vasoconstrictors are of two main classes: the sympathomimetic amines and the imidazole derivatives (incomplete sympathomimetics). The latter include naphazoline, xylometazoline and oxymetazoline.[13,20] Drugs of either group, when applied intranasally, will cause local vasoconstriction. The imidazoles, however, lack the systemic effects on the myocardium and bronchioles associated with the sympathomimetics.[20] For this reason the use of the imidazoles is preferred.

Sympathomimetics are divided into two groups on the basis of their action on the hypothetical α- and β-receptors in the affected tissues. The α-receptors mediate vasoconstriction and the β-receptors are responsible for vasodilatation.[20] The decongestion afforded by these agents is a direct consequence of their vasoconstrictive action. The subepithelial capillaries and arterioles, together with the venous sinuses of the erectile tissue, undergo vasoconstriction. If the vasoconstriction is severe or prolonged a reversal reaction, secondary vasodilatation, occurs and the mucosa becomes increasingly less sensitive to subsequent applications of vasoconstrictors; the result is the drug habituation characteristic of rhinitis medicamentosa.

The cause of the secondary vasodilatation is not fully understood, but a number of theories have been advanced. In 1945 Kully[3] suggested that it was due to either fatigue of the constrictor mechanism or the presence of an active vasodilator in the drug. He and others[14,21,22] believe that "overconstriction might produce local submucosal hypoxia and reactive hyperemia manifested as vasodilatation. Soon after Kully's report was published Ryan,[11] working with rabbits, demonstrated complete absence of epithelial cell cilia following the intranasal administration of either desoxyephedrine (methamphetamine) or naphazoline hydrochloride. These dramatic changes developed just 5 to 8 days after the start of daily use of the drug. Ryan also observed subepithelial thickening and fibrosis after 3 weeks and epithelial cell metaplasia into stratified squamous cells by the end of 60 days. Boies[17]

postulated that the mucus cells of the nasal epithelium "may be unduly stimulated and may increase nasal blockage by excess secretion". Finally, a current concept of Baldwin's[16] is that "the beta effects [of topical sympathomimetics], although not so pronounced, outlast the alpha effect and thereby lead to secondary vasodilatation and tissue congestion".

The complications of rhinitis medicamentosa, described long ago by Kully[3] and Fox,[8] include the development of atrophic rhinitis, sinusitis and otitis media. The persistent nasal vasodilatation and congestion may impede sinus drainage and predispose to sinusitis. Similarly, congestion about the eustachian orifices may lead to retraction of the tympanic membranes and its consequences.[3] It is suspected that the epithelial "denudation" associated with the prolonged use of certain vasoconstrictors manifests itself in atrophic rhinitis.[8,16] Another possible complication is the exacerbation of hypertension in susceptible individuals.[23] Patients receiving β-blockers may be more prone to this complication.[24]

Diagnosis and management of rhinitis medicamentosa

Rhinitis medicamentosa should be considered in the differential diagnosis of nasal obstruction. The diagnosis becomes more apparent when anatomic, allergic and infectious causes have been excluded. History-taking is of the utmost importance; the patient must be thoroughly questioned concerning the type and concentration of nasal medication used, and the frequency and duration of use.

The physical signs of rhinitis medicamentosa tend to vary with the duration of vasoconstrictor use and the underlying condition that led to the initiation of therapy. Baldwin[16] reported that the nasal mucosa is typically hyperemic, congested and granular, with areas of increased tissue friability and punctate bleeding; the mucus is clear and often scanty unless there is an associated sinus infection. "In one patient", Baldwin wrote, "who had used nasal sprays daily for over twelve years, the mucous membrane was pale and anemic looking." This is in contrast to Stride's finding of profuse, stringy, mucoid nasal discharge, narrowed airways and edematous mucosa.[13] Blue[14] described congestion of the turbinates during the early stages, with the mucosa becoming pale and boggy with long-term use of the agents. May and West[1] told of atrophic and crusted mucous membranes and an abnormally patent airway associated with prolonged nasal decongestion. Walker[25] included poor shrinkage of the nasal mucosa on examination as a key finding, and Lewis and colleagues[22] reported a "rubbery" nasal mucosa on palpation.

The goals in the treatment of rhinitis medicamentosa are twofold: curtailment of the drug therapy to allow the nasal epithelium to return to normal, and treatment of the underlying disorder that led to the original use of nasal vasoconstrictors.

Probably the simplest and least comfortable method for the patient is complete withdrawal of nasal medication. As complete bilateral cessation of the use of vasoconstrictive agents promptly results in rebound congestion and total nasal obstruction, Baldwin[16] suggested discontinuance in only one nostril initially. The patient is permitted to spray as often as desired in the other nostril, but once the rebound phenomenon subsides (in approximately 1 to 2 weeks) total withdrawal is advocated. A variation of this technique is placement of a nasal pack in the resting nostril to ensure that no nasal spray will be introduced into that chamber.

Another method described by May and West[1] is the patient's use of a saline nasal spray in lieu of the vasoconstrictor. They maintained that this has the dual function of moisturizing the nasal mucosa and providing a psychologic boost to those in need of a substitute medication.

A recent technique, described by Baldwin[16] and by Saunders and Gardier,[26] is the intranasal application of dexamethasone with decreasing frequency over a period of 2 to 4 weeks. Baldwin[16] cited three advantages to this method: steroids aid in controlling underlying allergy, they aid in reducing rebound congestion, and they provide a psychologic boost to the patient during withdrawal.

In our clinic we have been trying the topical use of nonabsorbed steroids — for example, flunisolide (Rhinalar) and beclomethasone dipropionate (Beconase). These provide the local effect without the possible systemic effects. Our initial results have been promising, and controlled studies are under way.

When these methods have failed, systemic therapy with analgesics, antihistamines, decongestants and corticosteroids has been used.[2,16,20,25-27] Such therapy is not appropriate at present.

Essential to success in the use of any of the protocols mentioned is the patient's total understanding of his or her condition. The cause and effects of the condition must be explained, and the patient should be told that after an initial 4 to 7 days of extreme discomfort the nasal obstruction will progressively subside.

Recently Baldwin[16] compared treatment regimens in three groups: one using corticosteroids topically, another using decongestant–antihistamine combinations systemically, and the third ceasing the use of a nasal spray as previously described. He claimed success in all three groups: all the patients were able to discontinue the use of vasoconstrictive agents within 2 weeks and did not use the drugs during 6 months of follow-up.

Conclusion

We have described a common clinical problem that confronts the general physician and the otolaryngologist. The diagnosis of rhinitis medicamentosa should be considered in all patients presenting with a stuffy nose.

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L'hyperglycémie et les complications du diabète de type adulte

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Dans cet article on analyse les principaux travaux ayant étudié les effets de l'hyperglycémie et de son traitement sur les complications associées au diabète de type adulte. Deux constatations s'imposent. D'abord, il n'y a pas encore de consensus sur les valeurs diagnostiques de la glycémie; quelques diabétologues recommandent un retour à la glycémie à jeun. Ensuite, un rapport de causalité précis entre l'hyperglycémie (et son contrôle) et les principales complications du diabète n'a pas été établi.

Tant que l'histoire naturelle du diabète de type adulte et l'efficacité du traitement sur le pronostic à long terme ne seront pas mieux compris, il ne saurait y avoir de place pour le dépistage systématique du diabète chez les adultes asymptomatiques. Aussi, les individus présentant de légères anomalies de la glycémie devraient être suivis annuellement afin de surveiller l'apparition d'un diabète clinique ou de tout autre facteur de risque de maladie cardiovasculaire. Ils ne devraient être ni étiquetés comme diabétiques ni soumis à un traitement strict.

In this paper the principal investigations into the effects of glycemia and its treatment on the complications associated with maturity-onset diabetes are analysed. Two points are stressed. First, a consensus is lacking on the diagnostic levels of blood glucose; some diabetologists recommend a return to the use of fasting blood glucose values. Second, a definite causal relation between hyperglycemia (and its control) and the main complications of diabetes has not been established.

Until the natural history of the condition and the effectiveness of hypoglycemic treatment on the long-term prognosis are better understood, systematic screening for maturity-onset diabetes in asymptomatic adults is not justified. In addition, patients with mildly abnormal blood glucose levels should be followed yearly to monitor the development of overt diabetes or other cardiovascular risk factors. They should be neither labelled as diabetics nor compelled to comply with a strict therapeutic regimen.

En 1970 le University Group Diabetes Program publiait les résultats d'une expérience clinique portant uniquement sur le diabète de type adulte.[1,2] Ces résultats mettaient en doute l'importance de l'hyperglycémie dans la pathogénèse des complications associées au diabète et l'efficacité du traitement. Cette étude a soulevé une polémique qui dure encore, et le médecin de famille reste souvent indécis quant à la conduite à prendre devant un individu présentant un diabète de type adulte modéré. La question fondamentale reste la même: dans quelle mesure l'hyperglycémie est-elle responsable des complications

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