

# Recent progress in the treatment of nasal allergy, intranasal steroid treatment

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Topical steroids have been used in the treatment of nasal disorders for about ten years. This presentation is a short review based on the experience gathered during these years. The mode of action of the steroids will be discussed, actual preparations presented as well as their efficacy in allergic rhinitis. Indications, contraindications and side effects will be brought up and finally also the need for a thorough patient instruction.

## MODE OF ACTION

Corticosteroids have since many years a well documented beneficial effect in allergic disorders. They have also, when given systemically, a number of serious side effects. This has raised the question whether it is justified to take these risks in treatment of nasal allergy, which in a way can be said to be a harmless disease. The only way to avoid answering this question is to give the steroids topically. Almost every cell in the body has receptors for steroids, and every treatment with injections and tablets affects the whole body to some extent. The positive effect of steroids in allergic diseases has been ascribed mainly their anti-inflammatory capacity. Today our knowledge of this mechanism on the cellular plane has improved very much. This has been summarized in Figure 1. The steroid binds to the receptor on the cell membrane, and this induces the formation of new proteins inside the cell. One of these, macrocortin, has been thoroughly characterized. It inhibits the enzyme phospholipase A<sub>2</sub> which transforms phospholipides to arachidonic acid. By influence of other enzymes, e.g. lipoxygenase and cyclooxygenase, arachidonic acid is transformed to leucotrienes and prostaglandins respectively. These substances are known to have strong inflammatory properties. With this mechanism in mind it is easy to understand why steroids are lacking immediate effects. It takes hours until the formation of macrocortin can affect the concentration of these mediators. When performing clinical trials with topical steroids it is possible to choose differ-

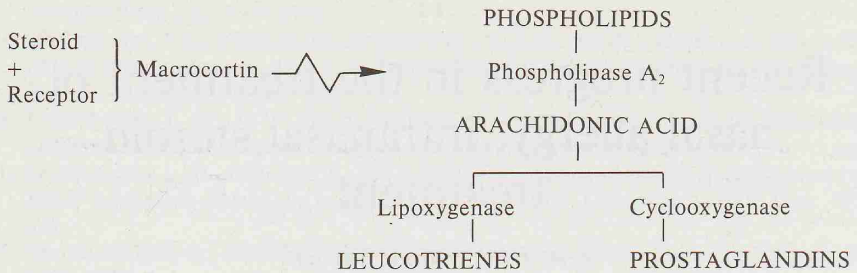


Figure 1. Basal effector mechanism of steroids.

ent parameters in a way which improves the knowledge of how steroids act. Studies by prof. Okuda have focused the interest on the mucosal surface. There is an increased number of basophilic cells (mast cells and basophile leucocytes) in allergic rhinitis. These cells are biologically active and can still release histamine in the secretion. This is the explanation for allergic symptoms to appear already a few seconds after allergen exposure. Recent studies have shown that the number of basophilic cells decrease in the secretion during topical steroid treatment. Maybe as a secondary effect to this the number of eosinophile leucocytes also decreases. The nasal mucosa is hyperreactive in nasal allergy partly because of an increased activity in the irritant receptors. There are signs of a reduced sensitivity in these receptors during local steroid treatment. Hypersecretion induced by metacholine provocation has also been shown to decrease during topical treatment. Finally the steroid treatment increases the nasal patency by affecting the vessels. There is a stabilization of endothelial- and epithelial barriers which decreases the oedema and also the content of albumin in the secretion. All these findings can help us to understand the pathogenesis of nasal disorders. The action of steroids seems to be more profound than just anti-inflammatory.

#### PREPARATIONS

Corticosteroids for topical use have to possess certain qualities. There is a demand for a high anti-inflammatory capacity, and also for a high metabolic rate. Most of the stuff given to the nose is passed to the pharynx by the mucociliary transport mechanism and then swallowed and absorbed. To avoid systemic effects this has to be inactivated by the first passage of the liver. Most of the preparations used today are poorly soluble in water. There is a continuous investigation work going on changing the steroid molecule in direction to higher potency and lower tendency to systemic effect.



Today there are mainly four preparations in clinical use in Europe:

*Beclomethasone dipropionate* (Glaxo, Schering Corp). This steroid derivate was first tested on skin diseases where it was shown to have an effect 5000 times stronger than hydrocortisone measured as the ability to cause cutaneous vasoconstriction. It was later introduced as a freon driven spray in treatment of bronchial asthma. Since almost ten years the same kind of spray has been used intranasally. Most of our present knowledge is based on the use of this preparation which still dominates the market.

*Flunisoide* (Syntex Corp) came 1978. It is like the other preparations for topical use poorly soluble in water, why it is dissolved in a mixture of propylene- and polyethylene glycole and delivered from a pump spray.

*Budesonide* (Astra) is a new nonhalogenated steroid which is approved for inhalation treatment of bronchial asthma. It is just about to be introduced for the treatment of nasal disorders as a freon spray. It has in animal studies shown to be a bit more potent than beclomethasone dipropionate without increased risk for systemic effects.

*Fluocortin butylester* (Schering AG) is produced as a powder for insufflation in the nose by help of a so called rhinolator. It seems to be less potent than the others but probably just as effective if the dose is increased. This seems to be possible without risks for systemic side effects as the substance is said to be inactivated immediately when absorbed. For the moment this preparation is on the market only in Western Germany.

The therapeutic effect of all these substances seems to be as good, and controlled comparative studies done so far have not been able to show any difference of clinical importance.

#### EFFICACY

After several years of experience there is now overwhelming evidence that local steroid treatment is highly effective in allergic rhinitis. A great number of clinical trials have proven this. In seasonal allergic rhinitis many studies also give an indirect proof of the lack of systemic effects in ordinary doses as the level of eye-symptomes is unchanged. Over all hay-fever studies on both children and adults have shown a control of symptoms in 60-90% of the patients.

In perennial rhinitis the role of allergy is often more difficult to prove. Patients included in trials of this disease can differ considerably both in the severity and origin of the symptoms. The average success rate in published trials is ranging from 55-80%.

#### SIDE EFFECTS

The serious side effects of systemic steroid treatment have caused that every possible side effect has been looked for when the use of intranasal steroid treatment

was introduced. Based on the results of a great number of clinical trials it can now be stated, that there are no general side effects if the local steroid treatment is used in ordinary therapeutic doses. This does not exclude that there is a systemic influence to a certain low extent. If the dose is increased the risk of side effects is also increased. This has been shown in a study where dogs developed cushingoid symptoms on high doses of inhaled steroid.

Local side effects are few and very seldom of such a magnitude that the treatment has to be interrupted. Immediate irritation can appear in the beginning, but decreases often after some days of treatment. Dryness and haemorrhagic crusting in the anterior part of the nose is sometimes seen especially when the steroid is administered by help of a pressurized freon gas. There is no proof for a risk of nasal infections during long-term treatment. Repeated cultivation tests have neither shown increased numbers of pathogenic bacteria nor appearance of candida in the nose, which can be seen in the throat in inhalation therapy. No signs of a decrease in the concentration of IgA in nasal secretion have been found.

Continuous treatment for at least three years with repeated biopsies has not shown signs of tissue damage or atrophy. This does not prove that the treatment is completely without risk, why it is wise to check patients on long-term therapy with rhinoscopy with some intervals.

#### INDICATIONS-CONTRAINDICATIONS

Which cases of nasal allergy should be treated with local steroids? From what has been said before there are no absolute contraindications. This does not mean that every patient with nasal allergy should be offered this treatment. It must not replace a careful allergy investigation. Especially in children the possibility to find the causing allergen and start specific steps is high. On the other hand, no patient should be withhold this treatment because of the old fear for steroid side effects. Patients with infrequent acute allergic spells are not suitable for intranasal treatment because of its lack of immediate effects. Sometimes the time needed for full effect is 7-10 days. Patients with hay-fever symptoms also from eyes and throat often have to add eye drops and antihistamines to the intranasal steroid treatment.

#### PATIENT INSTRUCTION

A good therapy result is only reached if the patient has got a careful information. At least a few weeks of treatment is necessary to be able to judge the effect in perennial rhinitis. Administration morning and evening has been shown to give as good results as four times daily. The dose recommended by the manufactor is suitable to start with, but in perennial rhinitis it is often possible after some weeks to reduce the dose. Patients on long-term treatment shall always be advised to try to find their own lowest effective dose. In hay-fever it is sometimes necessary

to increase the dose temporarily during days with heavy pollen exposure. The patient needs an active instruction in how to use the spray. To avoid dryness and crusting the nozzle of the freon spray should not be pointed against the septal wall, but straight backwards. One puff should be given in the upper and one in the lower part of the nose to get the best distribution.

If side effects appear, it is often possible to avoid them by changing preparation. The risk for dryness is highest with the freon spray and the immediate irritation is more frequent with the glucole solution. Probably there will soon be a water solution on the market which should solve this problem.

#### CONCLUSION

The local steroids are effective in the treatment of nasal allergies. They have almost all the advantages of systemic steroid treatment, but seem to have none of its disadvantages if used in a correct way.

Since this presentation was given a comprehensive review on the same topic has been published by Niels Mygind. The interested reader is referred to study: Topical steroid treatment for allergic rhinitis and allied conditions. *Clinical Otolaryngology* 1982, 7, 343-352.

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