Nonfluorinated corticosteroid topical preparations in children

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SUMMARY

Topical treatment of babies and little children with corticosteroids (CS) may provoke various side effects. Such a treatment should be carried out by experienced dermatologists or general practitioners educated in pediatric dermatology. In principle nonfluorinated preparations are advocated, as they cause less side effects than the fluorinated. A 10-year experience obtained with the alcloderm (Afloderm®) is discussed more in details.

KEY WORDS

corticosteroids, nonfluorinated, children, treatment

Introduction

Corticosteroids (CS) applied topically in the form of ointments, creams, lotions, solutions or even applied intradermally seem to be an ideal drug for treatment of various inflammatory skin conditions. CS reduce or even completely suppress the symptoms of inflammation and alleviate accompanying symptoms such as pain, itching and paresthesia. CS inhibit the release of phospholipase 1, the enzyme responsible for liberation of arachidonic acid from phospholipids which are constituents of the cell membranes. As a consequence formation of prostaglandin's (PG) and other derivatives of arachidonic pathway is inhibited. PG derive from arachidonic acid via the cyclooxigenase pathway, they contribute to the inflammation of the skin in contact allergic eczema, psoriasis and UV induced inflammation. They also enhance the itch induced by histamine. In addition the CS exhibit also antiproliferative and immunosuppressive effects. In view of such excellent therapeutic achievements a broad field of indications is open to the application of CS in pediatric dermatology: seborrheic dermatitis, atopic dermatitis, various forms of hereditary and acquired erythroderma, as well as further inflammatory conditions.

Main characteristics of corticosteroids

The anti-inflammatory action of CS is on the molecular level still not completely clarified. According to a simplified theory free CS diffuse across the cell membrane and become bound to cytoplasmatic receptors which then become translocated into the nucleus. The hormone-receptor complex binds to a receptor site on one DNA strand associated with a particular gene, activating transcription of that gene. The specific messenger RNA is then exported from the nucleus and translated to the ribosomes (1). The latest investigations indicate however that the process is by far more complicated and

that in addition to receptors various signal transducing and transcription molecules e.g. AP-1, NF- κB, 1-κBχ are involved (2).

Unfortunately CS, especially if administered not carefully enough, may cause a number of side effects. The risk is greater when treating children, which fact necessitates that the therapeutist be familiar with the untoward effects. These are both local and systemic.

Local side effects include development of skin atrophy, persistent erythema, teleangiectasia, papules and pustules, steroid acne, striae distensae, gluteal granulomas, hypertrichosis, pigmental changes and seldom a contact sensitization. A delayed healing of erosions and wounds may also be observed.

Systemic side effects are Cushingoid appearance, dwarfism, dysbalance of electrolytes, steroid diabetes, increased catabolism of proteins, arterial hypertension and osteoporosis. Systemic Addisonian crisis (nausea, anorexia, postural hypotension, vascular collapse) has been reported with the use of topical CS. One has to be especially careful when treating large or eroded surfaces with fluorinated CS in small children.

Basic structure of CS consist of the 21 carbon-atom ring structure of sterols (Fig. 1). The activity of CS is dramatically enhanced by the introduction of an unsaturated bond between the first two carbon atoms, by the nature of the side chains, particularly on the 21 C position, and by fluorination of the 9α position. The first CS available for clinical use (cortisone) did not contain halogens. Halogenation of the basic steroid structure in the 9α position improves the activity, but also increases the side effects (3). For better penetration through the skin, a lipophilic component was added to CS, with the binding of a chemical group e.g. acetonide, valerate or propionate, and by the substitution of the hydroxyl group at the C 21 with chlorine.

Nonfluorinated corticosteroids

Pediatric dermatologists prefer to use nonfluorinated CS as they are less prone to provoke local or systemic side effects taking into account the long-term application. The majority of the little patients are referred to dermatologists because of chronic skin disorders: seborrhea, atopic dermatitis, various erythemas, acquired and hereditary erythroderma, various eczemas, hereditary bullous epidermolysis and others.

Among the factors promoting the frequency and extent of side effects should be mentioned the following: magnitude of the treated area of the skin, inflamed or eroded surface, delicate skin of babies, intertriginous areas, scalp, scrotum and specially application of occlusive dressings (diaper area), but also addition of keratolytics and quality of the vehicle. Compounds that contain

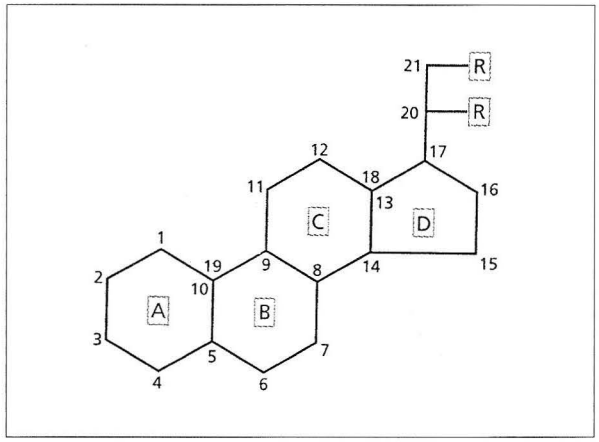

Figure 1. The configuration of the basic corticosteroid structure.

higher amounts of propylene glycol tend to be more potent. According to the potency of their action measured mainly as their vasoconstrictive effect, various CS may be assigned to one of the following classes: i) mildly potent, ii) moderately potent, iii) potent or iv) very potent (4). Other authors recognize a classification into seven classes (5). These differences in the pharmacological activities depend mainly on the chemical structure and the concentration of CS, but also on the quality of vehicle. It is generally accepted that nonfluorinated CS cause fewer side effects than the fluorinated ones. The nonfluorinated CS are in principle less potent than the fluorinated and may be assigned to one of the first two above-mentioned classes. Hydrocortisone, prednisolone and alclometasone were among the first used for topical application in dermatology. Some of nonfluorinated CS are presented in Table 1.

Clinical experience with alclometasone

In principle all the nonfluorinated CS listed in Table 1 have certain advantages but also minor shortcomings. Experienced clinicians know that a balanced judgement concerning the efficiency and safety of a drug can be offered only after it had been in use for a number of years. This is the reason why we decided to make this short report on our experience with *alclometasone dipropionate (Afloderm®*)*, which we have been using in pediatric dermatology for years.

We started to use Afloderm® in our department more than ten years ago. During the following years other nonfluorinated CS became available. We however still use Afloderm® in our daily work with patients. In such a way we have been able to gather ample experience

* *Afloderm®* Belupo, Koprivnica, Croatia

Table 1. Generic and proprietary names of some topical nonfluorinated corticosteroids used in Slovenia

Potency	Generic names	Proprietary names
Mild	alclometasone dipropionate	Afloderm® cream, ointment
Moderate	hydrocortisone valerate hydrocortisone probutate mometazone furoate	Westcord® cream, ointment Pandel® Elocom® cream, ointment

concerning the activity and safety of this drug. Afloderm® is available as a cream or ointment in various concentrations, which fact is important in choosing the appropriate preparation. Nonfluorinated CS are in principle safer compared to the fluorinated compounds, nonetheless one should be careful when using them in children, especially in babies, as their skin is not fully developed. When planning such a treatment a correct diagnosis should be made first, the stage of inflammation should be recorded (acute, sub-acute, chronic), and the appropriate preparation chosen (cream, ointment).

The pharmacodynamic characteristics, the mode of penetration into the skin (transepidermal or transfollicular) as well as the absorption of the preparation should also be considered. The amount of the drug absorbed depends on the quality of the skin and the specific area of the skin surface involved. The delicate skin of babies in general and specially in intertriginous areas (even in adults) is much more prone to absorption compared to the skin of palms or soles, where it is reduced. Further factors also enhance the penetration. Humidity has a similar effect as occlusive dressings. Hyperemia of the skin, the number of hair follicles (scalp or pubic area) as well as the form of the preparation (emulsion or gel) or the content propylene glycol also increase the absorption. All these guidelines have to be considered before applying the treatment with CS.

The disorders in which we frequently use alclometasone are atopic dermatitis, allergic and irritant dermatitis as well as other acquired and hereditary skin inflammations. In the majority of our children erythema of the skin was observed; a skin infiltration, in some instances scales and itch were expressed too. In most cases the cream or ointment was applied once daily, always without an occlusive dressing. In our initial experiences with Afloderm® the level of cortisol was assessed in plasma and the patients were carefully observed for the appearance of eventual side effects. At the end of the treatment with alclometasone we were able to confirm that we observed neither variation in plasma cortisol nor side effects on the skin.

After more than 10 years' lasting experience with Afloderm® we have basically observed no serious side effects, like skin atrophy, striae or telangiectasias. Such manifestations were recorded only in a few patients with chronic illness whose parents chose on their own initiative to use other CS preparations additionally to Afloderm®

Conclusions

At the end of our short experience-report on the use of nonfluorinated CS in pediatric dermatology we would like to draw the following conclusions:

1. Nonfluorinated CS are definitely preferred to fluorinated CS.

2. Before starting the treatment the diagnosis and the stage of the disease have to be specified.

3. The appropriate form of the preparation should be selected.

4. The application of CS shouldn't last too long.

5. The preparation should be applied two times a day only in the acute stages of the condition, during a few days only.

6. As a rule CS should be applied once daily and as soon as possible the treatment switched to preparations not containing CS.

7. In the cases where a longer lasting treatment is planned the so-called *alternating* scheme is advocated: one-week nonfluorinated CS, one-week preparation not containing CS.

8. When treating chronic conditions the dilution of proprietary preparations with the pure base (Belobase®, Diprobase®, Linola® or other) and water should be considered.

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REFERENCES

1. Ebbling FJG. Functions of the skin. In: Rook A et al, Textbook of Dermatology, 5th ed, Champion et al eds, Blackwell, Oxford, 1992, 140-6.

2. Werth VP, Lazarus GS. Systemic Glucocorticoids. In: Fitzpatrick's Dermatology in General Medicine, 5th ed, Freedberg et al eds, McGraw Hill, New York,1999, 1783-9

3. Bauman L,Kerdel F. Topical Glucocorticoids. In: Fitzpatrick's Dermatology in General Medicine,5th ed, Freedberg et al eds, McGraw Hill, New York 1999; 2713-7.

4. Griffiths WAD, Wilkinson JD. Topical Therapy. Topical steroids. In: Rook A et al, Textbook of Dermatology,6th ed, Champion RH et al eds, Blackwell, Oxford 1998, 3547-53.

5. Werth VP, Lazarus GS. Systemic Glucocorticoids. In: Fitzpatrick's Dermatology in General Medicine, 5th ed, Freedberg et al eds, McGraw Hill, New York 1999; 278-9.

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