REVIEW

Department of Dermatology, University Hospital Schleswig-Holstein, Campus Kiel, Germany

Topical hydrocortisone 17-butyrate 21-propionate in the treatment of inflammatory skin diseases: pharmacological data, clinical efficacy, safety and calculation of the therapeutic index

R. Fölster-Holst, D. Abeck, A. Torrelo

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Prof. Dr. Regina Fölster-Holst, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Dermatologie, Venerologie und Allergologie, Schittenhelmstr. 7, 24105 Kiel
rfoelsterholst@dermatology.uni-kiel.de

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Hydrocortisone 17-butyrate 21-propionate (hydrocortisone buteprate, HBP) is a medium potent, non-halogenated double-ester of hydrocortisone with a favorable benefit/risk ratio for the treatment of inflammatory skin disorders. HBP is available as a 0.1% cream or ointment formulation. Good results were obtained with a once-daily topical treatment. HBP is characterized by a strong topical anti-inflammatory activity and weak systemic action. It is considered to have potency comparable to that of betamethasone 17-valerate (BV), but its systemic effects are less pronounced. HBP was shown to have a good efficacy in the treatment of various oozing and lichenified eczematous skin diseases including atopic dermatitis (AD) and in the treatment of psoriasis vulgaris. Even in very young children, HBP proved successful as an effective and safe drug. A therapeutic index of 2.0 can be attributed to this glucocorticoid. In this respect, there is no difference between topical HBP and other topical glucocorticoids with increased benefit/risk ratio, e.g. prednicarbate (PC), methylprednisolone aceponate (MPA) and mometasone furoate (MM).

1. Introduction

For more than five decades, topical glucocorticosteroids have been used in the treatment of skin diseases for their anti-inflammatory potency (Korting et al. 1992; Surber et al. 1995; Hughes and Rustin 1997), antimitotic activity (Korting et al. 1995) and immunosuppressive effects (Hughes and Rustin 1997). The long-term use of topical glucocorticoids is still limited by topical and systemic side effects such as skin atrophy (Korting et al. 1995). Research focuses on the strategy to optimize the anti-inflammatory and immunosuppressive potency of these agents while minimizing adverse effects (Surber et al. 1995). Members of this new generation of topical glucocorticoids with an increased benefit/risk ratio are mometasone furoate (MM), prednicarbate (PC), methylprednisolone aceponate (MPA), alclometasone dipropionate, and carbothioates such as fluticasone propionate as well as 17,21-hydrocortisone aceponate (HA) and hydrocortisone-17-butyrate-21-propionate (hydrocortisone buteprate, HBP) (Brazzini and Pimpinelli 2002).

This article reviews the activity, efficacy and safety profile of HBP and calculates its therapeutic index (TIX), a useful tool to compare topical glucocorticoids quickly in terms of their benefit/risk ratio according to the guidelines of the German Dermatological Society (DDG) (Luger 2009).

2. Molecular structure

HBP is a fourth generation (Reich and Schmidt 2006) medium potent non-halogenated double ester of hydrocortisone (HC) – a class II-steroid according to Niedner (Werfel 2009) – in which butyric acid is bound at position 17 and propionic acid at position 21 (Fig. 1). The additional esterification increases the natural lipophilicity of the molecule and improves percutaneous absorption (Traulsen 1997). Furthermore, HBP is released easily from topical preparations (Tanaka et al. 1986). HBP is available as a 0.1% cream or ointment. Rapid metabolization in liver to the inactive congener HC contributes to its low systemic activity (Fig. 1, Mizushima 1984). Drugs of this type are considered the ideal dose form for topical corticosteroids (Harada 1983).

3. Pharmacodynamics

3.1. Effects at the molecular level

Most physiological effects of glucocorticoids are the result of their specific binding to an intracellular receptor (Higgins et al. 1973; Ballard et al. 1974; Muramatsu et al. 1986) in which the relative potency of glucocorticoids correlates with their affinity to the receptor (Muramatsu et al. 1986; Dausse et al. 1974; Luzzani et al. 1983). Data from experimental systems indicates that the affinity of HBP was several times higher compared to the parent molecule HC (Muramatsu et al. 1986, 1985). Additionally, HBP strongly binds to leucocytes (Otomo et al. 1981; Mizushima et al. 1986). These factors together with the increased lipophilicity of HPB may explain its strong anti-inflammatory activity.

3.2. Effects at the cellular level/vasoconstrictor effect

The pharmacologic action of HBP is similar to that of other topical corticosteroids, including anti-inflammatory,

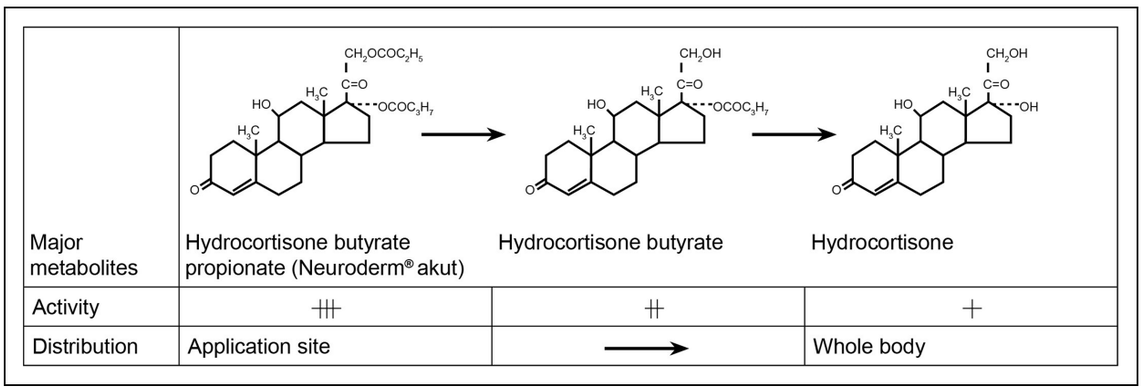

Fig. 1: Chemical structure of HPB and major metabolic pathway of HBP and activity of metabolites (Mizushima 1984).

antiproliferative and immunomodulating effects (Brazzini and Pimpinelli 2002). Animal studies on the metabolism of HBP in the skin suggest that HBP remains in its active unmodified form at this site (Takeda 1982) explaining the good clinical response to HBP, comparable to that of betamethasone 17-valerate (BV) (Takeda 1984).

Vasoconstriction, a measure of the anti-inflammatory activity of glucocorticoids, is more pronounced with molecules esterified in position C17 than in position C21, but esterification in both positions – as with HBP – even increases activity compared to esterification only in position C17 (Takeda 1982). For HBP, the vasoconstricting activity measured by the pale change score was higher compared to HC and BV (Mizushima 1984). Data gained from both animal experiments and clinical studies suggest that the vasoconstrictor effect of HBP is comparable to that of clobetasol 17-propionate (CP) or fluocinonide, both classified as "very strong" glucocorticosteroids (Tachi et al. 1983). In a double blind study, 0.1 % HBP quickly induced a distinct pale skin reaction due to vasoconstriction compared with ten other commercially available topical corticosteroids (0.1 % halcinonide, 0.05 % CP, 0.05 % fluocinonide, 0.12 % BV, 0.025 % beclomethasone propionate, 0.064 % betamethasone dipropionate, 0.1 % diflucortone valerate, 0.1 % hydrocortisone butyrate (HCB), 0.025 % fluocinolone acetonide, and 0.3 % prednisolone valerate acetate) (Tachi et al. 1983).

When applied to experimentally induced edema and dermatitis in rats, the anti-inflammatory activity of HBP was superior to that of hydrocortisone 17-butyrate (HB) and BV (Otomo et al. 1981). In standard models for testing topical glucocorticoids (skin blanching/vasoconstrictor assay, ultraviolet-induced erythema), HBP was at least equipotent to 0.25 % PC and 0.1 % BV, but superior to HC. Among all tested glucocorticosteroids, HBP and HA showed the most pronounced skin blanching activity, and HBP showed best results in terms of suppression of skin redness induced by UV irritation (Schäfer-Korting et al. 1993).

4. Safety and tolerability

The principal systemic adverse effects associated with topical corticosteroids are body weight gain, Cushing's syndrome, growth retardation, electrolyte imbalance, and hypertension (Brazzini and Pimpinelli 2002). Although the local anti-inflammatory activity of HBP is strong, its systemic action is weak representing a clear difference compared to several reference drugs (Otomo et al. 1981; Takeda 1982; Ito and Mizuno 1982; Kukida 1982).

4.1. Toxicity

Subacute and chronic percutaneous toxicity studies in rats and dogs revealed that the changes induced by HBP ointment were reversible and common to corticosteroids (Tarumoto et al. 1981a, b, c). Its toxicity was comparable to HB ointment and weaker compared to BV ointment (Tarumoto et al. 1981b, c; Ohshima et al. 1981). A comparative toxicity study of HBP ointment and other topical glucocorticosteroids (0.05 % CP ointment, 0.1 % prednisolone 17-valerate 21-acetate (PVA) ointment and 0.1 % diflucortone valerate (DV) ointment) in rats demonstrated that the systemic effect of HBP ointment (e.g., body weight gain suppression, increased serum concentration of total cholesterol and triglycerides, atrophy of lymphatic tissues and skin) was weaker compared to the other drugs (DV > CP > PVA > HBP). This was also the case for the dermal atrophic effect. Thus, HBP ointment was less toxic compared to other topical corticosteroids (Kimura et al. 1986). In another animal study, the systemic effects of HBP were less severe than those of BV and comparable to those of HB (Ohshima et al. 1981).

4.2. Safety index

For topical glucocorticoids, the ratio of vasoconstrictive index in humans (VI) to thymolytic activity in mice (MT) may be used as a safety index (VI/MT), an indicator for assessing the clinical benefits of these drugs. An analysis based on this indicator showed that the safety index of HBP was comparable to that of CP, BV, and beclomethasone 17,21- dipropionate (Takeda 1984).

4.3. Local adverse effects

4.3.1. Skin irritation

For topical drugs, formulation and active ingredient are of crucial importance. Therefore, patch tests were carried out with HBP ointment, cream, and both formulations on 40 patients with skin diseases. The skin safety could be demonstrated by a very good skin irritation index (SSI) according to Sugai (1985) for both HBP ointment (2.5) and cream (1.25). Excluding two patients sensitized by parabens, the index of the cream formulation reached a tolerable range of 18.42 while the index for the ointment formulation was at 17.5 (Hayakawa and Matsunaga 1984). HBP ointment and cream formulations did not differ from non-steroidal agents concerning incidence of skin

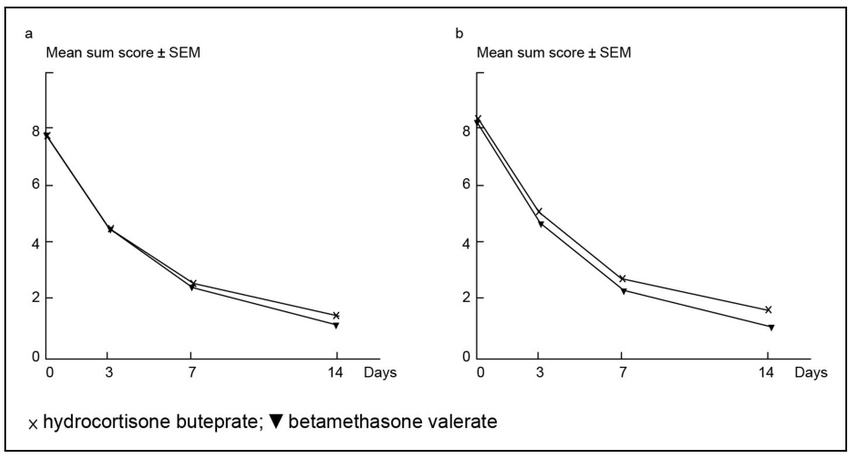

Fig. 2: Plasma cortisol levels in adult patients with psoriasis treated with 10 g/day HBP, HB or BV (Takeda 1984a).

irritation (Hayakawa and Matsunaga 1984), demonstrating that skin irritation is minimal with HBP – regardless of whether applied as a cream or ointment.

4.3.2. Skin atrophy

Skin atrophy is mostly related to repeated doses of strong topical glucocorticosteroids over a long period of time or to drugs with medium or stronger activity applied under occlusion. It is more common in the inguinal region, the skin surrounding the anus, and the axillary region (Takeda 1984). Topically applied non-halogenated double esters of prednisolone or HC have a low atrophogenic potential (Kerscher and Korting 1992; Korting et al. 1992b). Furthermore, agents such as HBP and PC show more moderate effects on fibroblast metabolism *in vitro* than the fluorinated glucocorticoids dexamethasone and BV (Hein et al. 1994). This is important because the severity of skin atrophy induced by topical glucocorticosteroids can be predicted to some extent by the results of fibroblast suppression tests (Takeda 1984). In a comparative study in rats, the dermal atrophic effect of HBP was slight, comparable to that of PVA, and weaker compared to CP and DV (Kimura et al. 1986). In rats treated with topical HBP, HB, and BV, skin thickness decreased comparably in all groups of animals (Ohshima et al. 1981).

4.4. Systemic adverse effects

4.4.1. Plasma cortisol levels

The decrease in plasma cortisol is a measure of an unwanted systemic effect from absorption of a glucocorticosteroid through the skin. A double-blind study compared the general effect of 0.1 % HBP ointment, 0.12 % BV ointment and 0.1 % HB ointment in adult psoriatic patients under occlusive conditions. The decrease in plasma cortisol was dependent on the drug and respective dosage: at 10 g/day, plasma cortisol did not fall significantly compared to pre-treatment baseline in patients receiving HBP; however, it fell slightly in patients receiving HB and markedly in those receiving BV (Fig. 2). At 30 g/day, plasma cortisol decreased significantly from pre-treatment baseline levels in all groups; the decline was particularly pronounced for BV. Accordingly, suppression of the pituitary-adrenal cortical function is less pronounced for HBP than for BV and HB (Takeda 1982). In other studies, plasma cortisol levels did not change abnormally, even in cases where HBV was used over a long period (Takahashi et al. 1984) or applied extensively over a period of one to two weeks (Nakayama et al. 1987).

4.4.2. Delayed type hypersensitivity

Topical glucocorticosteroids can cause delayed type hypersensitivity reactions after application to mucous membranes and skin. Hypersensitivity reactions following application of HBP formulations can mostly be attributed to ingredients of the vehicle system. An observational study of 12,000 patients treated with HBP cream or ointment demonstrated two cases of sensitization to paraben (cream) and one case of contact eczema induced by propylene glycole (ointment). No substance specific effects of HBP cream or ointment have been documented (Wendt and Stähle 1990). Sensitization against HBP only appears to be possible in rare cases, as two case reports suggest (Hisa et al. 1993; Tohgi et al. 2009).

4.5. Tolerability

In an observational study of 12,000 patients conducted in Germany, 90 % of both patients and investigators rated the tolerability of HBP cream and ointment as "excellent" or "good" (Wendt and Stähle 1990). Among 3,439 patients with atopic dermatitis (AD), 80 % assessed the tolerability as "excellent" and 17 % as "good," thus demonstrating the high acceptance of HBP. Treatment with topical HBP was even safe for toddlers: in a study of 142 pediatric patients, 50 children with atopic dermatitis aged < 2 years tolerated the treatment either "well" (n = 4) or "very well" (n = 46). In most cases (even if symptoms were moderate to severe), application over a two-week period was sufficient to considerably improve symptoms of atopic dermatitis or to achieve healing, but a longer period of application did not increase side effects. Burning sensations were the most frequent adverse events (about 1 %), followed by redness and pruritus (< 1.0 %). Three cases of telangiectasia, two of sensitization to paraben and one of steroid rubeosis were likely associated with the application of HBP cream. For the ointment, a probable association with one case of contact eczema against propylene glycole and with one case of steroid acne were documented. These findings are in agreement with the low incidence of adverse reactions found in early clinical studies of HBP conducted in Japan (Kukida et al. 1982; Kyushu 1984).

5. Clinical efficacy

Clinical studies in Japan showed a clinical effect of 0.1 % HBP cream and ointment in eczema (Hayakawa and Matsunaga 1984; Takahashi et al. 1984; Yoshida et al. 1984; Harada et al. 1985; Fukushiro et al. 1984; Takeda et al. (1984), Harada et al. 1981; Yasuhara et al. 1984) and psoriasis (Takeda et al. 1982;

Takeda 1982; Ito and Mizuno 1982; Kukida et al. 1982) similar or slightly superior to HB and BV. A good clinical response was also obtained in palmoplantar pustulosis, prurigo, lichen ruber planus and chronic discoid lupus erythematosus (Harada et al. 1982). Utility rates in different diseases ranged from 70 to 100 %. The drug acted rapidly, with significant improvement after one to two weeks of treatment, even in chronic lesions (Takahashi et al. 1984; Yoshida et al. 1984) and on sites usually more refractory to treatment such as the palm, elbow or knee (Harada et al. 1985).

The efficacy and safety of HBP cream and ointment were also demonstrated in an observational study among 12,000 patients with contact dermatitis, nummular dermatitis and atopic dermatitis. Patients were treated for one to 119 days (mean treatment duration: 14 days) with HBP cream or ointment; both medications were applied nearly equally often. About 90 % of the patients rated the efficacy as "very good" or "good." Individual symptoms such as desquamation, rhagades, lichenification, exudative eczema and flare-ups were favorably affected (Wendt and Stähle 1990).

5.1. Treatment of psoriasis

Topical corticosteroids are the most commonly prescribed medications for the treatment of psoriasis (Gerdes and Mrowietz 2006). In patients with mild to moderate psoriasis, efficacy, safety, and cosmetic acceptability of 0.1 % HBP cream versus the cream base (placebo) were studied in a multicenter, double-blind, randomized trial (Sears et al. 1997a). Topical treatments were applied twice daily for 21 days. Compared with placebo, significantly more investigators and patients rated HBP to produce excellent or good responses. Additionally, changes from the baseline for most psoriatic signs and symptoms and the total signs score (sum of scores for erythema, skin thickening, and scaling) on day seven significantly favored HBP. The cosmetic acceptability of both treatments was comparable, and both were well tolerated producing generally mild to moderate adverse events.

In another double blind study, the superiority of HBP ointment over BV and HB ointments in the treatment of psoriasis was demonstrated (Kukida et al. 1982). Adult patients with psoriasis vulgaris responded significantly better to HBP ointment than to BV and HB ointments given two to three times daily for three weeks and significantly better than to HB when drugs were additionally applied under occlusion during the night. The incidence of adverse reactions was 3.3 % with all drugs in the simple application (particularly acne-like rash) and 10.0 % with both drugs under occlusive conditions (particularly folliculitis) (Kukida et al. 1982).

In a further double-blind study of adult patients with psoriasis vulgaris, the clinical response did not differ significantly between HBP, BV, and HB (10 g/day or 30 g/day each) under occlusive conditions for 5 days. However, the decrease in plasma cortisol levels was least pronounced with HBP (Takeda 1982). Mild adverse reactions were observed with all drugs in both doses.

5.2. Treatment of atopic dermatitis

Topical steroids are the mainstay of anti-inflammatory treatment of atopic dermatitis and to prevent eczema flares (Korting et al. 1992; Surber et al. 1995; Hughes and Rustin 1997). Low or mild potency agents are often prescribed, but in severe episodes more potent preparations may be used (Sears et al. 1997b). Atopic dermatitis primarily occurs in infancy and childhood (Leung et al. 2004). Since prolonged treatment periods and repetitive treatments are often necessary, especially at these age topical formulations with good tolerability are recommended (Takeda 1984a). In early Japanese studies, good efficacy in the treatment of patients with atopic dermatitis was shown for 0.1 % HBP ointment by subgroup analysis (Takahashi et al. 1984; Yoshida et al. 1984; Harada et al. 1985; Fukushiro et al. 1984; Takeda et al. 1984; Yasuhara et al. 1984). In these open-label trials, utility rates ("useful" or better) from 70 % (Takeda et al. 1984) to 100 % (Yoshida et al. 1984) were obtained, with better results for the exudative type (Fukushiro et al. 1984; Yasuhara et al. 1984). This data was confirmed by later clinical trials with a double-blind design. In a multicenter, double-blind, placebo-controlled, randomized study, HBP 0.1 % cream was significantly more effective than placebo in alleviating signs of atopic dermatitis over 14 days. 194 adult patients with atopic dermatitis were treated topically with HBP 0.1 % cream or placebo once daily for 14 days. The severity of signs of dermatitis improved significantly in patients treated with HBP versus patients receiving placebo. Both physicians and patients judged HBP to be more effective and tolerable than placebo. Most adverse effects were mild to moderate in both groups with burning sensations (4 % placebo, 2 % HBP) being most prominent. Patients judged HBP to be cosmetically acceptable for daily use (Sears et al. 1997b). These results agree with the findings of a broad observational study where a good or very good efficacy of the treatment was reported in 88 % of patients with atopic dermatitis. Tolerability – even in very young children – was mostly assessed as very good (Wendt and Stähle 1990). In comparison with BV, HBP showed a similar efficacy in once-daily treatment when used in a cream formulation (Fig. 3, Traulsen 1997). Two separate studies comparing ointment and cream preparations of HBP and BV were

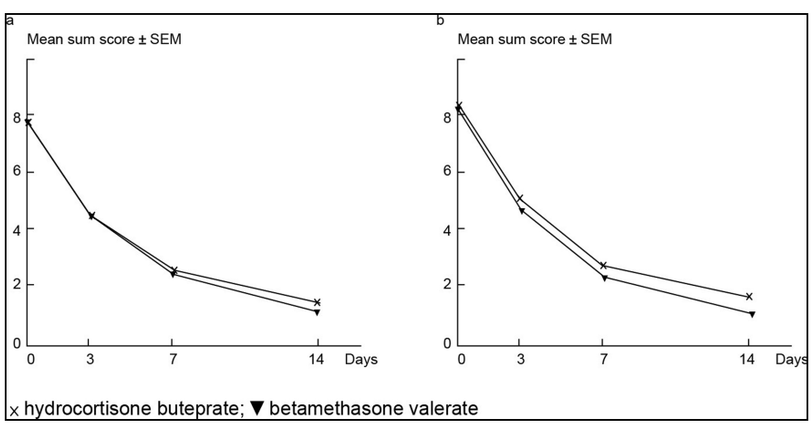

Fig. 3: Efficacy of HBP versus BV in patients with atopic dermatitis. Change in the sum of scores of erythema, scaling, vesicles, papules and pruritus over time: (a) cream study, (b) ointment study (Traulsen 1997).

Table 1: Clinical data on efficacy and tolerability of hydrocortisone butyrate propionate in children and elderly patients

Patients	Diseases	Treatment	Response rate	Utility rate*	Tolerability	Publication
37 children ≤ 5 years	Oozing and lichenified eczematous dermatitis including AD, acute eczema, nummular eczema, seborrheic dermatitis and Vidal's lichen	0.1 % HBP ointment in simple application once daily for 2-3 weeks	91.9 % "considerable improvement" or better	83.8 % "useful" or better	No separate evaluation	Fukushiro (1984)
69 children ≤ 5 years	AD, contact dermatitis, seborrheic dermatitis, hand eczema, acute eczema, chronic eczema	0.1 % HBP ointment in simple application once daily for 3 weeks	91.3 % "moderate improvement" or better	87.0 % "useful" or better	No separate evaluation	Harada (1985)
17 children 6-9 years	AD, contact dermatitis, acute eczema	0.1 % HBP ointment in simple application 2 or 3 times daily for 3 weeks	100 % "moderate improvement" or better	100 % "useful" or better	No separate evaluation	
142 children < 2 years	AD and different types of allergic, toxic, microbial induced and dysregulative eczema	0.1 % HBP ointment or 0.1 % HPB cream median duration of application 14 days	No separate evaluation	No separate evaluation	90.16 % very good 9.02 % good 0.82 % moderate	Wendt and Stähle (1990) Observational study
23 children 6 years	AD, contact dermatitis, hand eczema, acute eczema, other types of eczema, insect bites	0.1 % HBP ointment or 0.1 % HPB cream in simple application for 3 weeks or more	91.3 % "moderate improvement" or better Rate of cure: 56.5 %	Not determined	No adverse reactions seen	Unpublished data, Prof. Mitsuaki Uchiyama, Department of Dermatology, Yokohama City University University Medical School, Japan
20 elderly patients ≥ 65 years	Contact dermatitis, acute eczema, chronic eczema, seborrheic dermatitis, other types of dermatitis, insect bites	0.1 % HBP ointment or 0.1 % HPB cream in simple application for 3 weeks or more	Rate of cure: 70,0 % 95,0 % "moderate improvement"	Not determined	No adverse reactions seen	Unpublished data, Prof. Mitsuaki Uchiyama, Department of Dermatology, Yokohama City University University Medical School, Japan

*The utility rate was assessed by considering both clinical response and adverse reactions.

Table 2: Calculation of therapeutic index of HBP compared with other commonly prescribed topical glucocorticoids according to the guidelines of the German Dermatological Society (Deutsche Dermatologische Gesellschaft) (Luger 2009)

Drug	BV	CP	HC	HCB	MM	MPA	PC	TRI	HBP
Vasoconstriction	8	12	4	8	8	8	8	8	8[a]
Efficacy in the treatment of AD in comparison to other glucocorticoids	10	15	5	10	10	10	10	10	10[b]
Sum 1	18	27	9	18	18	18	18	18	18
Skin atrophy	12	12	6	6	6	6	6	12	6[c]
Suppression of the hypothalamic pituitary axis	2	4	2	2	2	2	2	4	2[d]
Allergenic potential	1	1	1	1	1	1	1	1	1[e]
Sum 2	15	17	9	9	9	9	9	17	9
Therapeutic index (sum 1/sum 2)	1.2	1.5	1.0	2.0	2.0	2.0	2.0	1.06	2.0

The attribution of scores to HBP based upon the following references: a: Mizushima (1984); Tachi et al. (1983); Schäfer-Korting et al. (1993). b: Traulsen (1997); Takeda (1984). c: Takeda (1984); Kimura et al. (1986); Hayakawa and Matsunaga (1984); Kerscher and Korting (1992); Korting et al. (1992b); Hein et al. (1994). d: Takeda (1982); Takahashi et al. (1984). e: Luger (2009); Wendt and Stähle (1990); Hisa et al. (1993); Tohgi et al. (2009).
Abbreviation: triamcinolone acetonide (TRI)

conducted as randomized, double-blind right/left comparisons of symmetrical skin lesions. Patients in the cream study applied HBP 0.1 % cream to affected skin lesions on one side and BV 0.1 % cream to lesions on the opposite side over 2 weeks. Both treatments proved effective and obtained complete healing in half of the patients. In the respective ointment study, complete healing was documented in 38 % of HBP-treated lesions versus 48 % of the BV-treated skin areas. In terms of local adverse reactions (dry skin, itching), no differences between the treatments were documented. The results of other comparative studies showed a similar clinical efficacy of HBP and BV in the treatment of patients with exudative and lichenified eczema, both common signs of atopic dermatitis (Takeda 1984).

5.3. Treatment of children and elderly patients

The clinical value of HBP cream and ointment also became apparent in the therapy of babies, infants, children, and elderly patients with various skin diseases (Table 1). For both children and elderly patients, safe drugs with an improved risk/benefit ratio usable over a prolonged period of time are recommended. HBP seems to meet these requirements. In an open clinical study, more than 90 % of treated patients – both children (< 6 years old) and elderly patients (≥ 65 years) with various skin diseases – improved moderately or better (unpublished data, Prof. Mitsuaki Uchiyama, Department of Dermatology, Yokohama City University University Medical School, Japan). In this study, the symptoms/signs of the respective skin diseases improved within one or two weeks and no relevant acute adverse reactions developed during the three-week treatment period. Additionally, a pronounced efficacy of a once-daily application of HBP in young babies and infants (Harada et al. 1985; Fukushiro et al. 1984) was shown. In a broad observational study with 142 children below 2 years of age, treatment with 0.1 % HBP cream or ointment proved effective and well tolerated (Wendt and Stähle 1990).

6. Calculation of TIX

New generation topical corticosteroids such as HBP have a high anti-inflammatory activity, a reduced skin atrophogenic potential and a high clinical efficacy compared with established drugs (Brazzini and Pimpinelli 2002). The safety profile of newly developed molecules is so favorable that a classification system of topical corticosteroids based on risk/benefit ratio would be desirable (Brazzini and Pimpinelli 2002; Wendt and Stähle 1990). To follow this issue, the German Dermatologic Society (DDG) developed the therapeutic index (TIX) as a useful quality marker to compare the commonly prescribed topical corticosteroids (Luger 2009). The TIX puts the therapeutic effect of a drug (vasoconstriction, efficacy in the treatment of AD in comparison to other glucocorticosteroids) in relation to its potential to induce unwanted effects (skin atrophy, suppression of the hypothalamic pituitary axis, allergenic potential). A topical glucocorticoid with a high TIX has high efficacy that clearly outweighs its systemic and local adverse effects with 2.0 being the highest currently found TIX. Based on these calculation criteria and the data of the literature mentioned above, the TIX of topical HBP was determined at 2.0 (Table 2). This indicates that HBP combines high efficacy with a low incidence of systemic and local adverse effects making topical HBP a safe and potent topical glucocorticoid for the treatment of inflammatory skin diseases.

7. Conclusion

HBP is a medium potent (Werfel 2009), non-halogenated double-ester of hydrocortisone with a favorable benefit/risk ratio for the treatment of inflammatory skin disorders. The substance is characterized by a strong topical anti-inflammatory activity comparable to that of BV but exhibits only weak systemic action. HBP was shown to have a good efficacy in the treatment of various skin diseases including atopic dermatitis and psoriasis vulgaris. Even in very young children, HBP is an effective and safe topical drug. Correspondingly, a TIX of 2.0 can be attributed to this glucocorticoid.

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