Review paper

Acitretin, a systemic retinoid for the treatment of psoriasis – current state of knowledge

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Abstract

Acitretin, a synthetic retinoid, is a pharmacologically active metabolite of etretinate. It replaced etretinate for the treatment of severe psoriasis (e.g. psoriatic erythrodermia and pustular psoriasis) because of its more favourable pharmacokinetic profile. Acitretin is 50 times less lipophilic than etretinate and has a shorter elimination half-life. However, there is evidence that small amounts of acitretin (especially in the presence of alcohol) are converted to etretinate. In psoriasis acitretin normalizes epidermal cell proliferation, differentiation and cornification. Acitretin appears to be as effective as etretinate (the effective dose of acitretin varies between 25 mg/day and 50 mg/day) and can be used in the same combination regimens. Teratogenicity is the most important safety issue (acitretin is FDA pregnancy category X). Other adverse effects are strongly related to the dose. It is unique compared to other systemic therapies for psoriasis (such as methotrexate and cyclosporine) in that acitretine is not an immunosuppressive agent.

Key words: acitretin, psoriasis, efficacy, safety.

Introduction

Retinoids belong to the group of natural and synthetic analogues of vitamin A: tretinoin, isotretinoin, acitretin and etretinate differ in terms of pharmacokinetics, toxicity profile and their clinical use [1].

The first studies on the effectiveness of etretinate (aromatic ester) in the treatment of psoriasis were published in 1975, while regarding acitretin in 1984. Acitretin (in Poland known as Neotigason) is a synthetic retinoid, which is an active metabolite of etretinate (the latter being a prodrug). Due to its short period of half-life (approximately 2 days), nearly 50-fold lower lipophilicity and comparable efficacy in psoriasis treatment, acitretin virtually replaced etretinate in 1997 [2].

Mechanism of action

The mechanism of action (like other drugs of this group) is not yet fully understood. It is believed that retinoids connect to a specific cellular carrier protein, CRABP (cellular retinoic acid binding protein), which functions in two subtypes: CRABP I and II (in psoriatic epidermis expression of CRABP II dominates). Then transportation to the nucleus with the activation of specific receptors RARS (retinoic acid receptors) and RXRs (retinoid X receptors) takes place. There are three subtypes of these receptors (α, β and γ) and regarding their construction they show similarity to glucocorticoid and thyroid hormone receptors. Retinoid receptors are expressed within the epidermis, sebaceous glands, hair follicles and also within the immune system.

It is noteworthy that in psoriatic epidermis mainly RAR-γ and RXR-α receptors are observed, acting as transcription factors and resulting in activation of specific, short DNA sequences (RAREs and RXREs), located in the promoter regions of certain genes (including genes responsible for cell growth and differentiation), which in consequence stimulates or inhibits their transcription [3].

It should be emphasized that acitretin leads to the normalization of all pathological processes responsible for psoriatic lesion formation: it reduces excessive keratinocyte proliferation and their abnormal differentiation, and diminishes accumulation of inflammatory infiltrate. Anti-inflammatory action of acitretin is associated with the inhibition of chemotaxis of polymorphonuclear leukocytes from blood vessels into psoriatic skin lesions and also with the release of inflammatory mediators from neutrophils. In addition, it exhibits immunomodulatory prop-

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Table 1. Comparison of the pharmacokinetics: acitretin and etretinate

Parameter	Acitretin	Etretinate
Molar mass [g/mol]	326	354
Plasma transport proteins	Albumins	Lipoproteins, albumins
Oral bioavailability [%]	36-95	30-70
Active metabolites	13-*cis*-acitretin etretinate	All-trans acitretin 13-*cis*-acitretin
Half-life [days]	2-3	80-175
Necessary time for the prevention of pregnancy after discontinuation of therapy [years]	2	2
Areas of storage:		
Liver	No	No
Adipose tissue	No	Yes
Adrenals	No	Yes

erties and inhibits angiogenesis (both in a direct mechanism, by inhibiting endothelial cell migration and formation of new vessels, as well as indirect, by reducing production of vascular endothelial growth factor (VEGF) by human keratinocytes) [4, 5].

Pharmacokinetics of acitretin

The following issues of acitretin pharmacokinetics are important (Table 1):

- The bioavailability of orally administered acitretin increases as much as twofold if it is taken with food (especially fat). It should be emphasized that there is considerable individual variation in absorption of this drug (therefore in its serum concentration) which does not affect body weight. Serum concentration of acitretin after oral administration reaches a maximum after 4 h [6].
- More than 99% of acitretin binds to plasma proteins, and the main fraction is transporting albumins [7].
- It is nearly 50-fold less lipophilic than etretinate [8]. Thus, in contrast to etretinate, acitretin does not accumulate in fat tissue, which translates into a much shorter period of its life (etretinate accumulates in adipose tissue and is slowly released from it) [9].

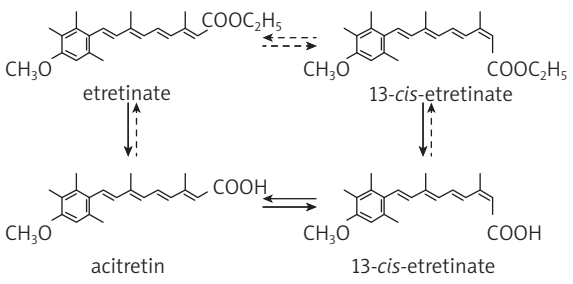

Fig. 1. The chemical structure of acitretin, etretinate and their metabolites

- The half-life of acitretin is about 2 days, that of etretinate 80-175 days [10].
- It is metabolized by the liver (with cytochrome P-450 involvement) and excreted in urine and faeces. Its main active metabolite is 13-*cis*-acitretin (Fig. 1), but it can also undergo transformation to etretinate (see below) [11].
- After introduction of acitretin to the treatment of psoriasis, it seems that the period of effective contraception can be shortened to 2 months (in case of etretinate it is 2 years), corresponding to the time of elimination of the drug from the organism [12]. Based on numerous studies, it appears that acitretin may be converted to etretinate (especially after consumption of alcohol). A correlation between the amount of consumed alcohol and the concentration of etretinate in the serum of patients treated with acitretin has been found. However, there was no relationship between the length of treatment (total dose) and the detectability of etretinate [13, 14]. Based on chromatographic studies, it should be emphasized that the described transformation concerns only acitretin and not its major metabolite, 13-*cis*-acitretin.
- The drug crosses the placenta, and as animal studies show, it can also be excreted in breast milk. It was calculated that the dose of acitretin received by an infant breastfed by a mother treated with this formulation is about 50 mg/day [15].
- Acitretin has no effect on the metabolism of endogenous vitamin A in the skin. After withdrawal of the drug, it is rapidly eliminated from the epidermis, resulting within a few days in resolution of adverse skin and mucosal symptoms [16].

Effectiveness of acitretin in various forms of psoriasis

Acitretin is most effective in the treatment of pustular psoriasis (both generalized as well as located within

palms and soles) and psoriatic erythroderma. In the case of psoriasis vulgaris to obtain satisfactory clinical improvement, combination therapy with, for example, UV irradiation is indicated. Beneficial effects of this retinoid in psoriatic arthritis have also been observed.

Psoriasis vulgaris

The efficacy of monotherapy

Murray *et al.* conducted an open, multi-centre clinical trial, where patients with severe psoriasis received acitretin at doses of 25 mg to 50 mg. After 12 months of therapy PASI 50 was achieved by 76% of patients, and PASI 75 by 46% [17]. Similar results were also observed in another multi-centre trial where after 12 weeks of acitretin therapy at a mean dose of 40 mg/day, PASI 50 was noted in 85% of patients, and PASI 75 in 52% [18].

Lassus *et al.* performed a randomized clinical trial on 80 psoriatic patients and compared the effectiveness of the retinoid depending on its dose (10 mg, 30 mg or 50 mg). After 8 weeks of treatment the mean decrease in the PASI index was, respectively, in the groups receiving 10 mg, 30 mg and 50 mg, 61%, 79% and 86% (in the placebo group 30%) [19]. In another randomized trial, Goldfarb *et al.* compared the clinical effects of acitretin at doses of 10 mg, 25 mg, 50 mg and 75 mg. After 8 weeks of treatment, it turned out that the effectiveness of acitretin at 10 mg or 25 mg did not differ significantly from placebo. A significant clinical improvement was observed in patients treated with acitretin at doses of 50 mg and 75 mg (in both these groups the efficacy of acitretin was similar) [20].

Randomized clinical trials comparing efficacy of etretinate and acitretin (e.g. study by Gollnick *et al.*) showed no statistically significant differences [21].

Take-home message and practical advice: acitretin and etretinate show comparable efficacy. Clinical effects of therapy with acitretin are proportional to the applied doses. Treatment is usually started at a dose of 25 mg/day, which after 2-4 weeks can be increased to 50 mg/day (treatment usually lasts several months).

The effectiveness of combination therapy

The use of combination therapy in patients with psoriasis usual leads to faster remissions and at the same time to limitation of retinoids intake. Acitretin is usually associated with:

- PUVA therapy (retinoids + PUVA = Re-PUVA) – Re-PUVA seems currently to be the most effective form of treatment in severe cases of psoriasis vulgaris; this allows one not only to achieve clinical remission, but in comparison to the PUVA treatment, to reduce the total dose of UVA radiation by 30-50% and shorten the treatment period by an average of 18 days [22];
- UVB phototherapy (retinoids + UVB = Re-UVB) – combination therapy of UVB and acitretin allows one to obtain satisfactory clinical results more slowly than in the case of Re-PUVA, but much faster, and in a greater percentage of cases, than when used in monotherapy with acitretin or UVB irradiation [23]; 3 months long Re-UVB therapy causes a 75% reduction in the PASI index, compared with 35% in the group treated with UVB irradiation and 42% for the monotherapy with acitretin [24];
- derivatives of vitamin D_3 – marked effectiveness of such combination is confirmed by two randomized clinical trials, based on large patient groups. In one of them (the study group consisted of 154 patients with psoriasis and healthy control) treated with acitretin (at a dose of 20 mg/day to 70 mg/day) and topical calcipotriol, a significant improvement/clinical complete remission in 67% of patients was obtained (in the group using placebo – 41%) [25];
- biologicals – acitretin is not an immunosuppressive drug; therefore, theoretically it could be used in combination with biological agents; Gisondi *et al.* conducted a randomized, controlled, blinded clinical trial in 60 patients with plaque psoriasis, in which they compared the efficacy of monotherapy with etanercept (25 mg 2× a week) or acitretin (0.4 mg/kg daily) with the combination therapy with these drugs (etanercept – 25 mg 1× a week + acitretin – 0.4 mg/kg/day); in 24 weeks of therapy PASI 75 was achieved, respectively, in 45%, 30% and 44% of patients [26]; excellent results were also obtained in 7 patients with psoriasis vulgaris, treated with infliximab and acitretin [27].

General rules of Re-PUVA and Re-UVB therapies rely on the use of acitretin at a dose of 50 mg/day for about 2 weeks, then the dose is usually reduced to 25 mg/day and combined with PUVA or UVB. On the other hand, in cases when treatment with PUVA or UVB did not deliver the expected results, acitretin 25 mg/day may be added, after 1-2 weeks of 30-50% reduction of the radiation dose. Thus, the method of Re-PUVA or Re-UVB reduces both the total dose of acitretin (better tolerance of treatment) and the applied UV radiation (and thus the risk of distant side effects) as well as the duration of therapy.

During systemic treatment with retinoids other topical preparations (corticosteroids, anthralin) may be added, while retaining considerable caution because of the thinning of the skin.

It is not recommended to combine acitretin with the following drugs:

- methotrexate – in the literature there are descriptions of toxic hepatitis as a result of combined use of methotrexate and etretinate [28];
- cyclosporine – in the metabolism of both of these drugs cytochrome P-450 is involved, and thus their treatment should be carried out alternately (beginning with cyclosporine, followed by maintenance therapy with acitretin), for a period of less than 1 year [29].

Erythroderma

Efficacy in monotherapy

The basic principle of the treatment is the initiation of low doses of acitretin, usually 10-30 mg, which are usually sufficient to achieve remission.

The effectiveness of combination therapy

Sometimes Re-PUVA or Re-UVB is used just like in psoriasis vulgaris, but with the use of lower doses of retinoid and UV.

Palmoplantar pustulosis

Efficacy in monotherapy

Significantly higher efficacy of acitretin vs. placebo in the treatment of palmoplantar pustulosis was demonstrated in two randomized clinical trials. In the first one after 4 weeks of therapy, with a dose of 50 mg/day 5× reduction in the number of skin lesions was achieved (in the placebo group 1.4×) [30]. Similar clinical effects were also observed in the second study, which additionally showed that the effectiveness of acitretin is comparable to etretinate therapy [31].

The effectiveness of combination therapy

Usually, a combination with local PUVA irradiation (PUVA-soak) is used, yielding a remarkable improvement in clinical outcome.

Conclusions and practical advice – although monotherapy with acitretin effectively alleviates symptoms in patients with palmoplantar pustulosis, to maintain the remission continuous retinoid administration in high doses (50 mg/day) should be recommend. Moreover, during combination therapy it is difficult to predict the duration of clinical improvement; sometimes exacerbations are observed in the actively managed therapy.

Generalized pustular psoriasis

Efficacy in monotherapy

In a large group of patients, monotherapy with acitretin allowed complete clinical remission to be achieved and also inhibition of eruption of new skin lesions was observed within several hours. Treatment is usually started at a dose of 50 mg/day. Length of treatment is usually 1-4 months [32].

Psoriatic arthritis

Efficacy in monotherapy

Treatment starts with a maximum dose of retinoid, which can then be reduced to 0.2-0.3 mg/kg/day and it is usually long lasting therapy.

The effectiveness of combination therapy

The most frequently used method is Re-PUVA.

Clinical application of acitretin in other skin diseases

To prevent the development of non-melanoma skin cancers in transplant recipients

Numerous observations (including three randomized clinical trials) suggest that the use of acitretin in transplant recipients prevents the development of skin cancers (both squamous and basal cell carcinoma). In one randomized clinical trial acitretin was administered to 44 patients after transplantation of solid organs at a dose of 30 mg/day for 6 months, in the second at a dose of 25 mg/day for 12 months (23 patients after kidney transplants). In both studies, the incidence of skin cancer was significantly lower than in patients after transplantation, but not treated with acitretin [40]. Among 26 patients who participated in the third study, there was no such correlation, whereas regression of actinic keratosis was evident (acitretin was used at a dose of 0.2-0.4 mg/kg/day) [33].

Congenital ichthyosis

In one clinical trial, which involved 29 children with various forms of congenital ichthyosis, acitretin at a dose of 0.5 mg/kg/day proved to be very effective (only in 3 children clinical improvement was slight) and relatively safe (among the most commonly reported adverse events, dryness of skin and mucous membranes, and a slight increase in triglyceride levels and liver enzymes were observed) [34]. Similar results were also obtained in another study in which 33 patients were treated with acitretin (21 adults and 12 children) because of severe disorders of keratinization: various forms of congenital ichthyosis, keratoderma of palms and soles, Darier disease (duration of treatment was 4 months) [35].

Keratoderma of palms and soles

The available data (although based on small numbers of patients) confirm the efficacy of therapy with acitretin of different varieties of keratoderma of palms and soles, e.g. Vohwinkel syndrome, punctuate palmoplantar keratoderma, epidermolytic keratoderma, Papillon-Lefèvre syndrome [36, 37].

Darier's disease

The efficacy of acitretin in the treatment of Darier's disease was confirmed in randomized clinical trial conducted by Christopherson *et al.* The study revealed that the clinical results of the acitretin treatment are comparable to those after etretinate [38]. On the basis of other available studies, it appears that in patients with

Darier disease acitretin is effective already at a dose of 10-25 mg/day [39].

Pityriasis rubra pilaris

In patients with pityriasis rubra pilaris (PRP) acitretin is applied usually at a dose of 25-35 mg/day and treatment should be carried out for many months (up to 40), which may provoke side effects. Trials to use Re-PUVA and Re-UVB are also being conducted.

The efficacy of acitretin in patients with PRP confirms a retrospective clinical study, in which 9 patients treated with the dose of 0.5 mg/kg/day for about 19 months achieved a complete/significant clinical improvement and there were no serious adverse events [40].

Lichen planus

In a randomized clinical study conducted by Laurberga *et al.* a significant clinical improvement was achieved in 64% of patients with lichen planus (LP), who received 30 mg/day of acitretin (vs. 13% in the placebo group) [41]. Efficacy of this drug in the treatment of LP was also confirmed by a meta-analysis conducted by Cribiera *et al.* (on a group of 86 patients with LP) [42]. This therapy seems to be particularly beneficial in patients with hypertrophic LP form.

Discoid lupus erythematosus

In one randomized clinical trial the efficacy of acitretin (50 mg/day for 8 weeks) and hydroxychloroquine (400 mg/day) was compared in 58 patients with discoid lupus erythematosus (DLE). Clinical improvement was observed in 46% of patients treated with retinoid and in 50% of patients receiving hydroxychloroquine. Adverse events were reported more frequently in patients who received acitretin (even necessitating discontinuation of therapy in 4 cases) [43]. In another clinical study, acitretin proved to be effective in 15 of 20 enrolled subjects with DLE.

Lichen sclerosus

The effectiveness of acitretin (at a dose of 20-30 mg/day) in the treatment of lichen sclerosus was demonstrated in a randomized clinical trial on 78 patients [44].

Other conditions

In the literature there are single studies indicating a beneficial effect of acitretin in the case of hyperkeratotic eczema of the palms (one randomized clinical trial conducted on 29 patients) [45], mycosis fungoides [1], viral warts (in one study the resolution of skin lesions was observed in 16 of 20 children undergoing therapy with the retinoid) [46] and in patients with giant condylomata of Buschke-Loewenstein and epidermodysplasia verruciformis (in both cases as adjuvant therapy) [47].

Contraindications for the use of acitretin

Contraindications for the use of acitretin include pregnancy, lactation, lack of patient consent to use effective contraception, severe liver or kidney failure and significant hyperlipidaemia.

Recommended tests before introduction of acitretin therapy

– Women of childbearing potential:
  - Due to the teratogenicity of acitretin, the physician should be convinced that the patient understands and accepts the need for continuous effective contraception, starting from 4 weeks before treatment, during the whole period of treatment and for 2 years after its completion (with signed consent). In the U.S. it is recommended to use contraception for 3 years after completion of treatment [48]. Also women with infertility in their history should use effective contraception.
  - The therapy can be started only on day 2-3 of the next normal menstruation after the initiation of contraception. At the same time two weeks before the therapy pregnancy must be excluded by a negative pregnancy test.

– All patients:
  - Before starting therapy it is necessary to perform the following tests: peripheral blood counts, liver function tests (levels of transaminases, bilirubin and alkaline phosphatase), glucose, urea, creatinine, and lipid profile (with the designation of HDL and LDL) [1].

Recommendations during treatment with acitretin

– Women of childbearing potential:
  - No alcohol during acitretin therapy and 2 months after its completion (due to the risk of formation of etretinate).
  - Use of effective contraception (as above) and performance of pregnancy tests every month during the entire treatment period.

– All patients:
  - Monitoring of laboratory tests (liver enzymes, lipids, glucose) every 2-4 weeks (the first 2 months), then though they are normal, every 3 months [1]. Treatment should be discontinued if transaminase activity rises 3× the upper normal limit, cholesterol is higher than 300 mg/dl or triglyceride level is above 500 mg/dl (due to the risk of acute pancreatitis).
  - Patients with diabetes, alcoholism, or disorders of lipid metabolism in the personal/family history should be monitored more frequently because of the increased risk of hypertriglyceridaemia.
  - It should be avoided/special care should be taken in case of parallel use of acitretin with the following

drugs: methotrexate (a potentially harmful effect on the liver), tetracycline (risk of pseudotumour cerebri), phenytoin (acitretin reduces its ability to bind to proteins), antidiabetic medications (hypoglycaemic risk – retinoids may increase sensitivity to insulin; necessity, especially at the beginning of therapy, of frequent blood glucose measurements), corticosteroids (risk of hyperlipidaemia), low-dose progesterone preparations (acitretin reduces its effectiveness) and preparations of vitamin A or other drugs from the group of retinoids (risk of hypervitaminosis A).

- Patients during therapy with acitretin and for 1 year after its completion cannot serve as blood honor donors.
- Avoidance of alcohol (because it interferes with lipid metabolism and leads to increased levels of liver transaminases).
- Reduction of exposure to UV radiation (the recommendation is not due to the photosensitizing properties of the drug, but is dictated by the skin thinning observed during retinoid therapy).
- Avoidance of laser treatments and waxing as a method of hair removal (due to the skin thinning and fragility).
- Use of special moisturizing lipsticks and emollients. Because of the possibility of dryness of the conjunctiva, patients should not wear contact lenses.
- Acitretin is not recommended for the treatment of children. In special cases (the ineffectiveness of other methods), parameters of growth and ossification should be monitored. In children under 12 years of age acitretin is usually used at a dose of 0.5 mg/kg (total dose should not exceed 35 mg/day).

Side effects during acitretin therapy

Teratogenicity

The most serious risk associated with treatment of all retinoids, including acitretin, is teratogenicity (in FDA classification the drug belongs to category X). The use of the drug during pregnancy can lead to the development of fetal malformations, spontaneous abortion or premature birth.

Defects observed in retinoids embryopathy (retinoic acid embryopathy) include the following: defects of the central nervous system (hydrocephalus, microcephaly), defects in the outer ear (congenital absence of the auricle, absence/hypoplasia of the external auditory meatus), cardiovascular (e.g., septal defects), eyes (microphthalmia), skeletal, craniofacial, and thymic as well as parathyroid anomalies [49].

The typical post-retinoid fetal defects have not been described yet in relation to a father treated with acitretin [50].

Mucocutaneous symptoms

These are the most common and are very troublesome for patients. They include the following: dryness of skin and mucous membranes, erythema (especially facial); thinning of the skin and increased fragility (seen among 50-75% of patients within a few days of starting therapy, apparently within the hands and soles, sometimes accompanied by symptoms similar to abortive Nikolsky sign); erythematous and scaly lesions of a few centimetres in diameter within the dorsal surfaces of the forearms and hands (retinoid dermatitis), increased sweating, inflammation of the nasal mucosa (rhinitis sicca), bleeding of nasal mucosa and sometimes of the rectum, blepharitis and conjunctivitis, cheilitis, changes in the nails, which become brittle and soft (in as many as 25-50% of patients), paronychia, sometimes granulomatous tissue proliferation is observed, resembling pyogenic granuloma (usually within the nail folds of the toes), hair loss (affects as many as 50-75% of patients treated with acitretin and is more common in women; after discontinuation of therapy regrowth is usually observed) [51, 52]. In addition, during the first 4 weeks of acitretin therapy, the exacerbation of psoriasis may be presented, which often (and erroneously) leads to withdrawal of therapy.

It should be noted that these symptoms are dose dependent; when their intensity is large, dose reduction should be performed.

Effects on liver and lipid metabolism

A transient increase of liver enzyme levels is observed in approximately 15% of patients treated with this retinoid. Controlled clinical trials, during which patients received acitretin for 2 years and liver biopsies were performed (the study group consisted of 83 patients), revealed that this therapy was not associated with the risk of permanent liver damage [53].

Acitretin also affects lipid metabolism. Hypertriglyceridaemia occurs in 25-50% of patients, while hypercholesterolaemia is observed in 10-30% of patients (typically an increase of LDL level and decrease of HDL). These disturbances are more commonly presented in individuals with risk factors such as diabetes, obesity, alcohol abuse, smoking and a personal/family history of hyperlipidaemia [54]. In patients with high levels of triglycerides and/or cholesterol it is recommended to follow a diet: eating foods rich in fibre, natural plant sterols contained in nuts and vegetable oils, fish (salmon, sardines, herring, mackerel), restriction of meat, poultry and veal, reduced consumption of carbohydrates with a high glycaemic index (sweets, white bread) and a ban on drinking alcohol. Changing the diet can reduce LDL cholesterol by up to 20-30%.

It should be noted that both the liver enzymes and triglyceride and cholesterol levels return to baseline usually 4-8 weeks after discontinuation of acitretin treatment.

Changes in bone

During acitretin treatment scattered calcification of ligaments and ossification within the vertebrae may develop. Frequently they appear within the anterior cervical ligament or lumbar spine (diffuse idiopathic skeletal hyperostosis – DISH), but also calcification of the Achilles tendon was reported, and tibial tuberosity and the development of heel spurs [55]. According to some authors, the risk of DISH syndrome is dependent on the length of therapy and dose. Not all studies, however, confirm the existence of such a relationship [56]. For this reason radiographic monitoring should not be routinely performed, even in patients treated with acitretin for a long time [1]. Tests designed to detect any abnormalities of ossification should be performed in those patients who present atypical musculoskeletal symptoms.

Acitretin in children should be used with caution – isolated cases of bone disorders during long-term treatment with etretinate (including premature overgrowing of epiphysis of long bones, skeletal hyperostosis, extraskeletal calcification, and in one child osteopenia and pathological fractures) have been reported. At the same time it should be emphasized that one study, which monitored 42 children treated with retinoids for more than 11 years, showed no incidence of bone disorders [57].

Other side effects

Other side effects include muscle and joint aches, itching, yeast vulvovaginitis, fatigue, drowsiness, malaise, nausea, and very rarely a mild increase in intracranial pressure was observed – pseudotumour cerebri (symptoms: headache, nausea, vomiting and visual disturbances; in the literature there is a description of one case of this disorder after acitretin) [58].

Although experiments on experimental mice showed that acitretin leads to prolongation of wound healing, observations in humans have not confirmed this. Therefore, there is no need for discontinuation of treatment before surgery [59].

Summary

Acitretin should be considered in patients with pustular psoriasis (both generalized as well as within palms and) and psoriatic erythroderma. In the case of psoriasis vulgaris, combination with UV irradiation is indicated. A beneficial effect of this retinoid in psoriatic arthritis was also found.

Doses greater than 50 mg/day (irrespective of body weight) are not recommended. This allows one to reduce the incidence of adverse events (better tolerance of treatment) and provides greater safety during both short- and long-term therapy.

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