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Modern cosmetic product for acne therapy in children

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The article presents a clinical trial indicating efficacy and safety of a new cosmetic product – topical antiseptic – as monotherapy and in combination therapy with benzoyl peroxide and topical retinoid adapalene for acne treatment in children and adolescents of 8-18 years of age.

The trial revealed high anti-inflammatory and antibacterial activity and an almost complete absence of systemic and local side effects; this makes use of this topical antiseptic preferable and advisable for pediatric practice.

Keywords: *acne, children, adolescents, efficacy, safety, topical antiseptic.*

Acne is a chronic polymorphic multifactor skin diseases occurring due to hyperproduction and imbalance of sebaceous glandular secretion's lipids, follicular hyperkeratosis with narrowing of ducts of sebaceous glands, propagation of bacteria and development of inflammation [1].

Acne is the most widespread skin affection in children and adolescents – it usually manifests itself at the age of 8-12 years; the incidence rate peak is observed between 14 and 16 years of age (it occurs in girls earlier than in boys). It was confirmed by a retrospective cohort trial aimed at assessing contribution of different skin diseases to the total morbidity of this group of patients. Thus, acne spread is 28.6%; it is more widespread than dermatitis (19.4%) and warts (16.2%) [2]. According to some data, comedones occur in all adolescents at least once [3]; acne spread in this age group reaches 70-90% [4, 5].

Manifestation of the process is usually characterized by occurrence (in response to the androgen-mediated hyperstimulation of sebaceous glands) of preclinical stigmas, such as seborrhea and microcomedones. Open and closed comedones and inflammatory elements in the form of papules, pustules and nodules form soon. Gender morbidity spread is virtually the same, although the disease more often takes a severe and longer course.

Acne pathogenesis is based on 4 factors: hypertrophy of sebaceous glands, follicular hyperkeratosis, microbial (*Propionibacterium acnes*) colonization and inflammation. Acne develops in the setting of seborrhea – a special condition connected with hyperproduction of sebum and alteration of its composition [6].

Clinically, common acne are distinguished by an intense polymorphism of elements. Open and closed comedones appear on facial skin (nose, cheeks, forehead, chin) in the setting of increased sebaceous excretion (seborrhea). Some of them transform in papules and pustules. Papulopustular rashes may localize not only on face, but also on neck, shoulders, breast and upper back (seborrheic zones).

The main groups of drugs for treating acne are sebostatic, antibacterial, anti-inflammatory and the drugs suppressing follicular hyperkeratosis. External therapy is prescribed to the patients regardless of the disease severity.

Thus, high acne morbidity and spread among children and adolescents sets several difficult problems connected with timely selection of both a safe and effective therapy with simple

dosage scheme and convenient-for-children method of application for pediatricians and dermatologists. However, it ought to be remembered that it is important to reasonable provide specialized acne treatment to children of different age groups depending on the disease severity. The refusal to undergo therapy motivated by the doctor's/parents' doubts of the child's unwillingness may result in complication of the disease, wider spread of the elements and psychoemotional sphere disorders in the patients [7]. All these facts call for the search for new topical remedies, which could be used effectively and safety to treat acne in children and adolescents.

The aim of this study was to evaluate efficacy and safety of a local cosmetic product (topical antiseptic) in children of 8-18 years of age with mild and moderate acne.

PATIENTS AND METHODS

The open comparative clinical study of efficacy, safety and tolerance of a topical antiseptic – Kvotlan gel – was conducted at the FSBI “Scientific Center of Children’s Health” on the basis of the medical rehabilitation department for children with skin diseases of the research institute of preventive pediatrics and medical rehabilitation and the consultative-diagnostic center.

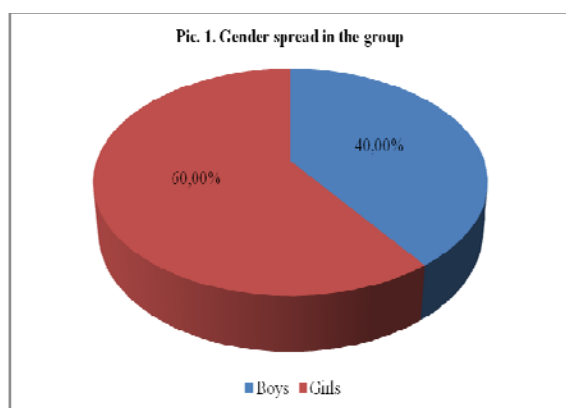
Description. The cosmetic product under study consists of cetylpyridinium chloride monohydrate, glycolan, triethylene glycol, ethylcarbitol, polyethylene glycol, deionized water and a perfume flavor. Pharmaceutical form: 20 ml tubes.

Pharmacological action. Cetylpyridinium chloride monohydrate – a quaternary ammonium compound antiseptic – features antimicrobial, antifungal and viricidal effect. Such components as glycolan, polyethylene glycol, triethylene glycol and ethylcarbitol provide bactericidal, anti-inflammatory, wound-healing, regenerating and analgesic action.

Thus, this topical antiseptic features antimicrobial activity against gram-positive and, to a lesser extent, gram-negative bacteria, variable anti-fungal activity. It is approved for use in children.

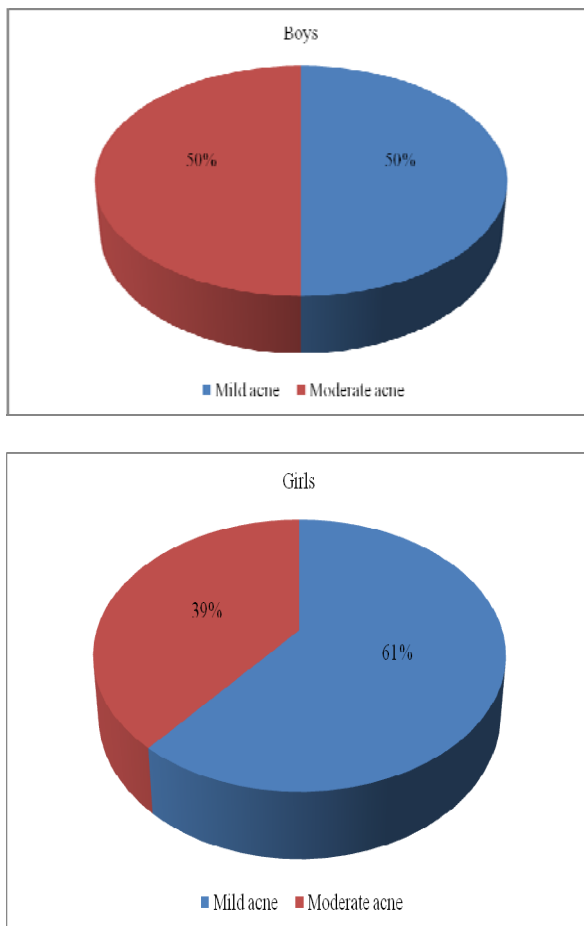
For 1 year, we had been observing 30 children of 8-18 years of age with mild and moderate acne treated with the topical antiseptic under study for at least 8 weeks. The gender spread (18 girls and 12 boys; 60 and 40%) is given in pic. 1.

Pic. 1. Gender spread in the group



17 (57%) children out of them had mild acne, 13 (43%) – moderate. 50% of the boys had mild acne, 50% - moderate acne; 61% of girls had mild acne, 39% - moderate acne (pic. 2).

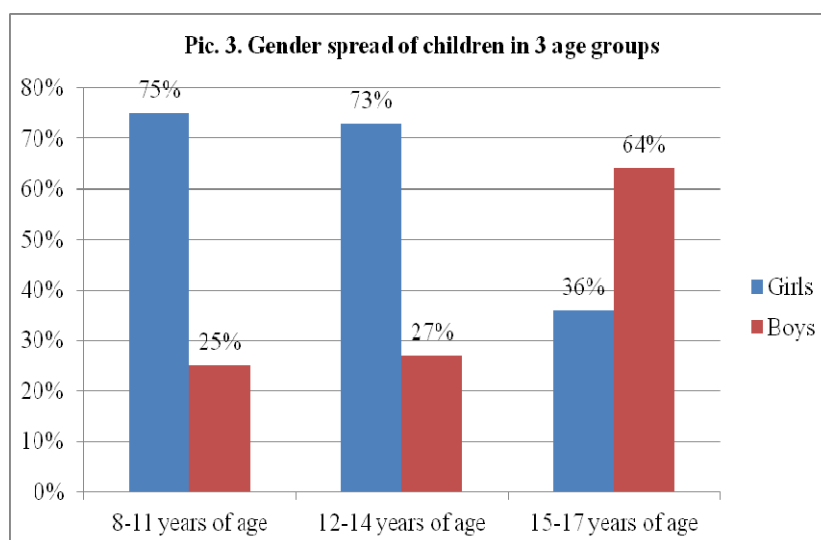
Pic. 2. Gender and acne severity spread



According to the study protocol, all patients were divided into 3 age groups: 8-11 years of age (n=8), 12-14 years of age (n=11) and 15-17 years of age (n=11). Acne was verified in all children (100%). All 8 (100%) patients in the group of children of 8-11 years of age had mild acne; 1 (9%) patient in the group of children of 12-14 years of age had mild acne, 10 (91%) – moderate acne; 1 (9%) patient in the group of children of 15-17 years of age had mild acne, 10 (91%) – moderate acne. The control group (n=5) was comprised of the children of 15-17 years of age with moderate acne (100%) who had been treated with the topical antiseptic under study BID – in combination with adapalene (OD) and benzoyl peroxide (OD) – for 8 weeks.

25% of the group of children of 8-11 years of age were boys, 75% - girls; 27% of the group of children of 12-14 years of age were boys, 73% - girls; 64% of the group of children of 15-17 years of age were boys, 36% - girls (pic. 3).

Pic. 3. Gender spread of children in 3 age groups



Clinical presentation in children with mild acne was characterized by chronic inflammatory skin lesion and a few rashes localizing primarily on skin of forehead, temples, nose and chin; rarely – on skin of breast and back. Rashes were represented by singular inflammatory (papules, pustules) and non-inflammatory (closed and open comedones) elements.

Pathological process in children with moderate acne had a more widespread nature, with localization on skin of face, breast and back. Multiple papular and pustular elements, closed and open comedones were observed.

Inclusion and exclusion criteria. The trial did not involve children under 8 and over 18 years of age and children of 8-18 years of age with severe acne. According to the trial protocol, the therapy using cosmetic products and drugs was forbidden within 14 days before the trial.

Patients were excluded from the trial unless they had positive dynamics in the setting of 4-6-week-long treatment with a topical antiseptic, if there occurred an undesirable reaction or condition requiring withdrawal of the cosmetic product under study or if we observed low compliance, failure to comply with the trial protocol or frequency of application.

Children of the 3 groups had been taking a topical antiseptic externally for 8 weeks; they applied it to the elements on skin of face, breast and back BID; the number of days of treatment until clinical effect was different in different patients depending on the severity of acne symptoms and presence/absence of any previous therapy at the moment of prescription of the drug under study. That is why we recommended the average treatment duration to be 8 weeks and the average daily drug dosage – 1.5 ± 0.3 and 2.5 ± 0.3 at mild and moderate acne, respectively.

Using a quantitative method of performance evaluation in the course of the trial, we measured the amount of inflammatory and non-inflammatory elements before and after treatment and duration of therapeutic effect. In order to objectively evaluate acne severity, we used the dermatological acne index (DAI) and the Cook et al. scale. We appraised life quality of all children before and at the end of trial using the Dermatology Life Quality Index (DLQI) for children.

The drug's safety was evaluated by the degree of reduction in the manifestation of the disease's clinical symptoms in such parameters as clinical remission, considerable improvement, improvement, no effect and given in the form of a graph of the average number of inflammatory (papules, pustules) and non-inflammatory elements (closed and open comedones), the average DAI, the Cook et al. scale and the DLQI value before the treatment and after 8 weeks of the treatment in all groups of patients.

Tolerance was appraised daily on the basis of subjective feelings and objective data both by the doctor and the patient/parents throughout the therapy course (good, satisfactory, unsatisfactory).

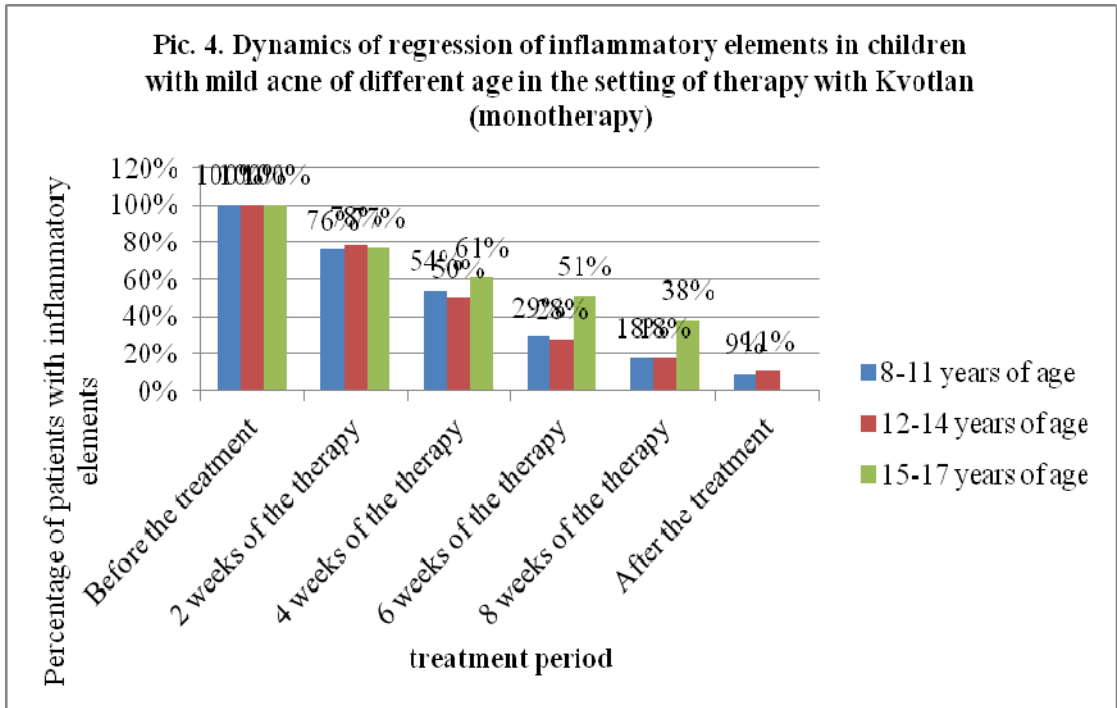
The drug's safety was evaluated on the basis of analysis of frequency and intensity of the undesirable reactions observed in the patients during the therapy. The obtained results were

processed using application software package IBM SPSS, Statistics-20. Quantitative data are presented in the form of the average values with the standard deviation.

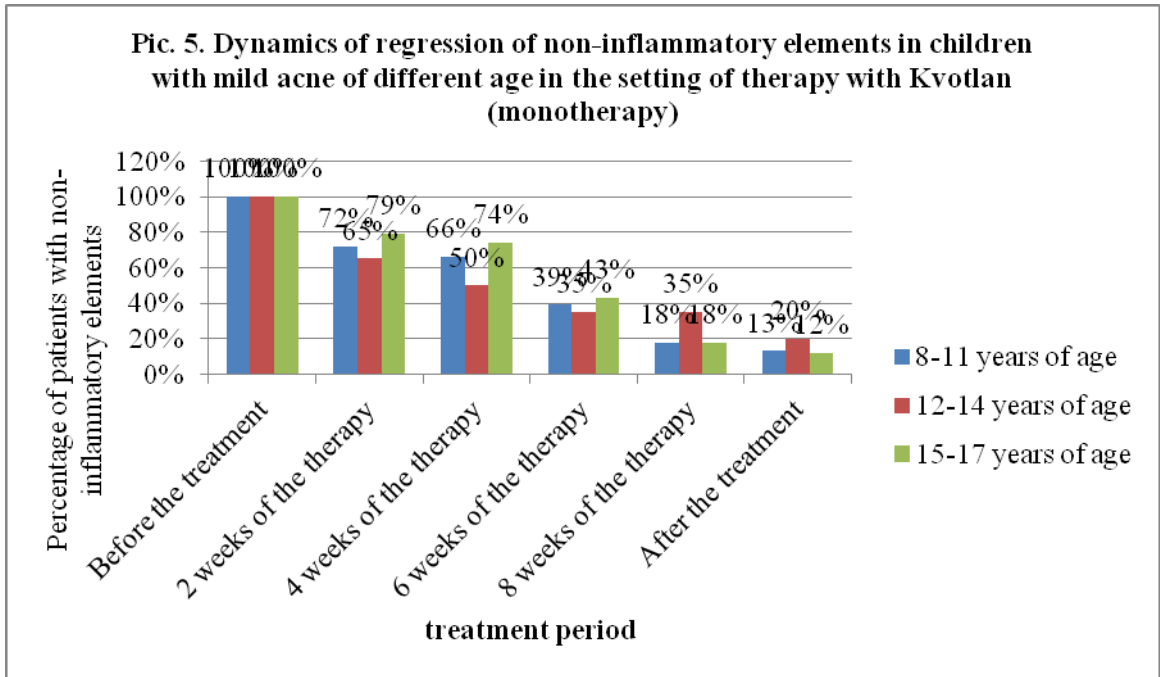
STUDY RESULTS

Regardless of the age at the moment of treatment with a topical antiseptic, regression of both inflammatory and non-inflammatory elements in children with mild acne was $\geq 80\%$: 91 ± 3.0 and $87\pm 2.0\%$ at the age of 8-11 years, 89 ± 1.0 and $80\pm 1.0\%$ at the age of 12-14 years and 81 ± 1.0 and $88\pm 2.0\%$ at the age of 15-17 years, respectively (pic. 4, 5).

Pic. 4.

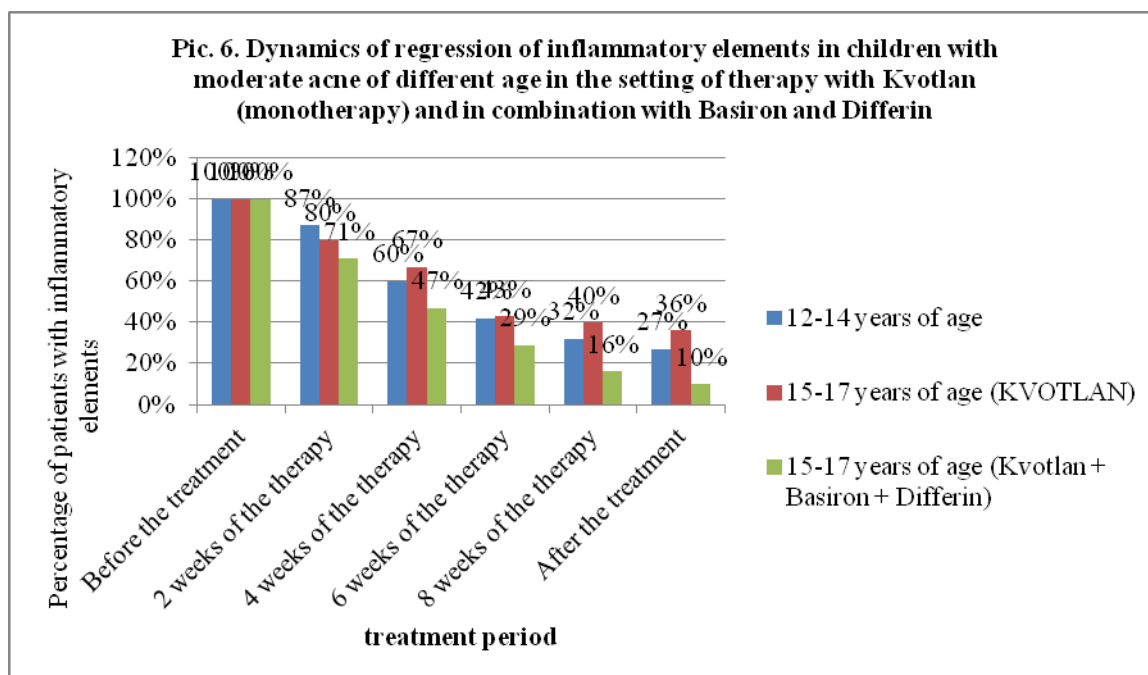


Pic. 5.

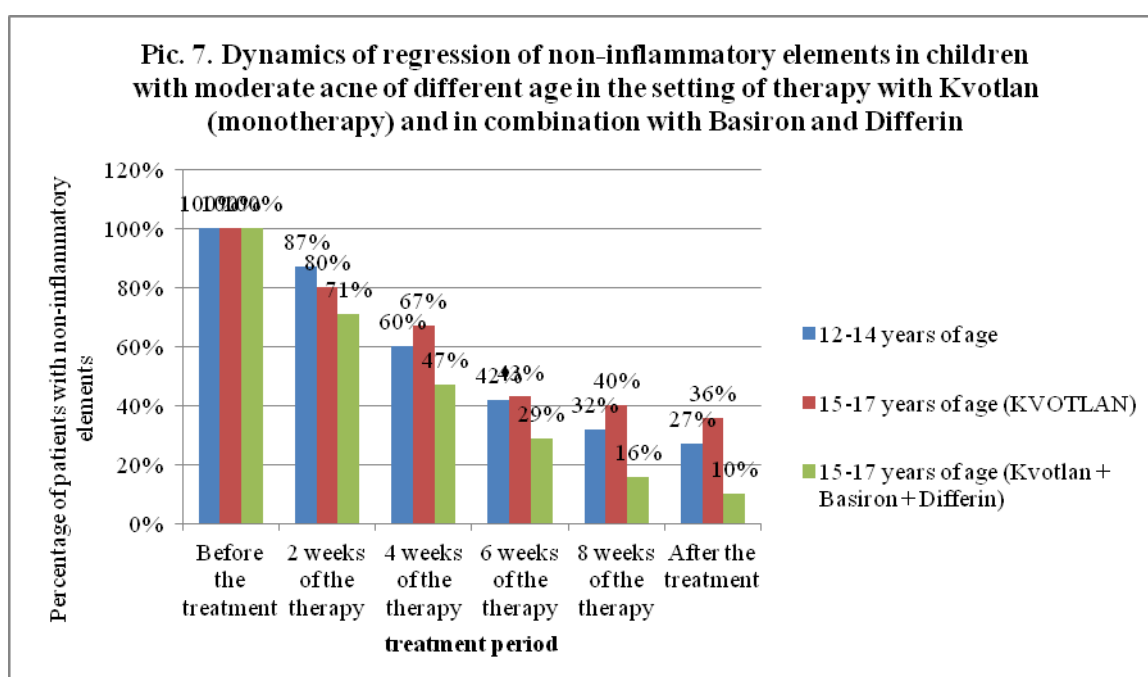


Regression of elements at moderate acne, which was observed only in the children of 12-14 and 15-17 years of age, was significantly weaker: regression of inflammatory elements at the age of 12-14 years was $77\pm 4.0\%$, of non-inflammatory elements - $80\pm 1.0\%$; in the children of 15-17 years of age – 64 and 77% ($p<0.05$), respectively, given more pronounced androgen-mediated hyperstimulation of sebaceous glands, which peaks at that age, and a more intense clinical presentation of the disease. Apart from the therapy with a topical antiseptic, it is reasonable to use a combination of drugs containing benzoyl peroxide (Basiron) and adapalene (Differin) at moderate acne; it will allow increasing the regression rate of inflammatory elements up to 90%, of non-inflammatory elements – up to 95% [compare with the aforementioned 64 and 77%, respectively] (pic. 6, 7).

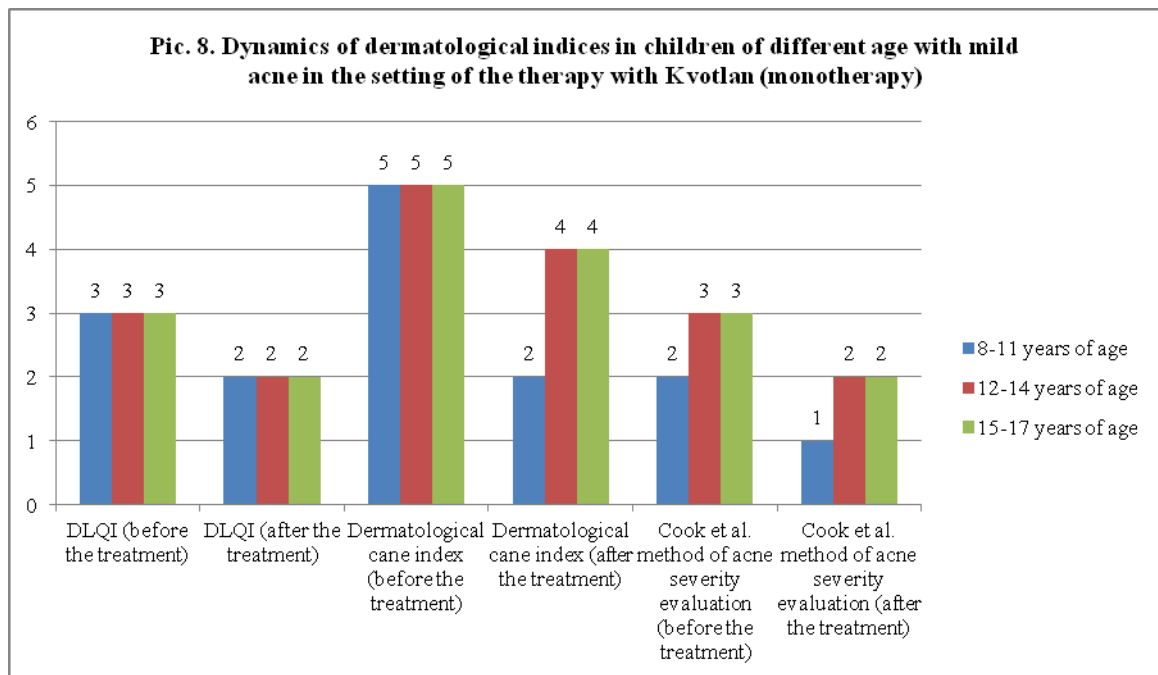
Pic. 6.



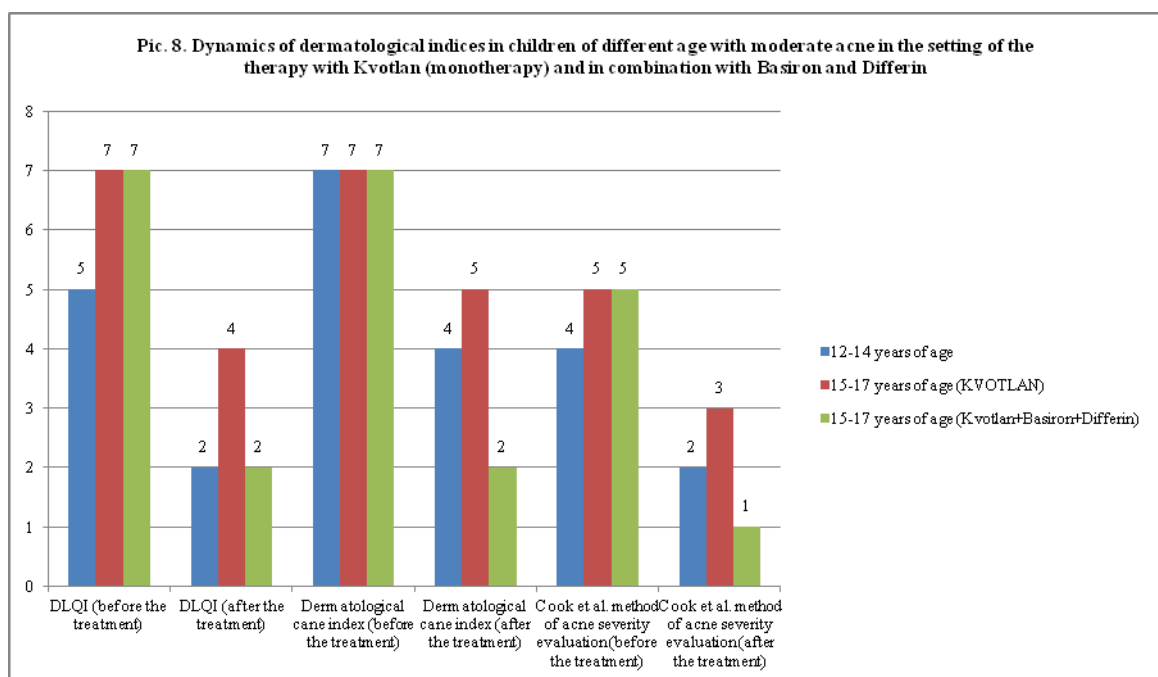
Pic. 7.



Pic. 8.



Pic. 9.



Evaluating DLQI, DAI and the clinical therapy efficacy by means of the method by C.H. Cook et al., we observed the dynamics presented in pic. 8, 9 in all children in the setting of the therapy. Regardless of the age, evaluation of the average life quality index (DLQI) of the children with mild acne reduced from 3 to 2 points, the DAI rate reduced from 5 to 2 points in the children of 8-11 years of age, the average DAI rate reduced from 5 to 4 points in the children of 12-14 and 15-17 years of age. Evaluating the clinical therapy efficacy by means of the method by C.H. Cook et al., we observed the average rate reduction from 2 to 1 point in the children of 8-11 years of age. The average rate in the children of 12-14 and 15-17 years of age reduced from 3 to 2 points; statistical data manipulation did not reveal any significant differences in terms of the children's age ($p>0.05$).

Life quality evaluation (DLQI) in the children of 12-14 years of age with moderate acne revealed the average rate reduction from 5 to 2 points, of 15-17 years of age – from 7 to 4 points. Those children who underwent combined treatment (topical antiseptic + adapalene + benzoyl peroxide) had a worse average DLQI rate reduction than their peers; $p<0.05$ (see pic. 9).

The average DAI rate at the treatment beginning reached 7 points in all children of 12-14 and 15-17 years of age; the DAI rate reduced down to 4 points in the setting of the therapy in the children of 12-15 years of age; the average DAI rate in the group of the children of 15-17 years of age undergoing monotherapy with a topical antiseptic by the end of the treatment was 5 points. The average DAI rate in the children of 15-17 years of age undergoing combined acne treatment by the end of the treatment was 2 points; this confirms reasonability of combined treatment for moderate acne in older children ($p<0.05$). Evaluation of the clinical therapy efficacy by means of the method by C.H. Cook et al. showed that the average rate in the children of 12-14 years of age was 4 points before the treatment and 2 points at the end of the treatment. The average rate in the children of 15-17 years of age of both groups at the beginning of the therapy was 5 points; in the group of children undergoing therapy with a topical antiseptic only, the average rate reduced down to 3 points, while in the group of children undergoing combined therapy (topical antiseptic + adapalene + benzoyl peroxide), the average rate was 1 point ($p<0.05$).

Thus, it is reasonable to treat children with moderate acne with a combination of drugs: such an approach to treatment increases its efficacy more than twice and allows achieving a long-term remission of the disease.

Analysis of the treatment results revealed good therapeutic effect in all 3 groups of patients: clinical remission was observed in 9 patients with mild acne after 8 weeks of application of the antiseptic gel under study.

Significant improvement was observed in most (15) patients: no new papulopustular elements and significant reduction in the number of open and closed comedones by the 4th-8th week of treatment. Although therapeutic effect was observed in the other 6 patients with moderate acne either, papulopustular elements continued to appear from time to time, though in a far lesser amount (tb. 1).

Table 1. Results of the treatment with the topical antiseptic under study

Treatment result	Therapy duration (in weeks), n=30, $p\leq 0.05$						Total (%)	2 weeks after the end of the treatment
	1	2	3	4	6	8		
Clinical cure	-	-	-	3	5	9	9 (30)	No relapse
Considerable improvement	-	-	2	10	13	15	15 (50)	No relapse
Improvement	13	22	21	14	12	6	6 (20)	No relapse
No effect	17	8	7	3	-	-	-	-

Without any doubt, skillful combination of various drugs and combined methods of therapy provides good therapeutic results in patients with acne. Thus, we observed clinical remission and considerable improvement in 4 and 1 patients of the control group, respectively. Consecutive prescription of drugs allowed avoiding unidirectional activity of several drugs, while prescription of a special cosmetic product – a topical antiseptic for facial care – allows reducing dosage and frequency of drug application, provides remedial and protective effect on skin (which is especially important in pediatric practice) in case of external treatment.

Tolerance towards the topical antiseptic was considered both by doctors and children/parents (n=30) good (tb. 2). The drug's safety was considered high; no undesirable reactions were registered in any of the 3 groups of patients.

Table 2. Evaluation of tolerance of the topical antiseptic under study

Tolerance	Group of patients		
	Group I	Group II	Group III
Good	8 (100%)	11 (100%)	11 (100%)
Satisfactory	0	0	0
Unsatisfactory	0	0	0

Analyzing the aforementioned, we may conclude that application of the cosmetic product as acne monotherapy or within a combined therapy in combination with adapalene and benzoyl peroxide is highly effective and may be widely used by pediatricians and dermatologists as one of the therapy schemes for mild and moderate acne.

Thus, on the basis of the conducted studies, we have confirmed that application of topical antiseptic Kvotlan has a pronounced therapeutic effect on all acne forms in children, especially in the patients with mild acne; this is confirmed by the reduction in DAI and the average C.H. Cook et al. scale rate and life quality improvement (according to the DLQI). Simultaneous local application of a topical antiseptic and the traditional drugs improves therapeutic effect and considerably reduces the number of side effects occurring after the local combined therapy. A topical antiseptic may be used during the disease remission and as a supportive drug in between the drug therapy. The proposed method of treatment is available for and acceptable by the patients with acne of the age groups under study; it reduces the amount of rashes and effectively reduces frequency and number of exacerbations.

CONCLUSION

The drug under study is a highly effective cosmetic product, a topical antiseptic with a wide action spectrum. It may be considered the drug of choice for local acne therapy in children (from 8 years of age): as monotherapy at mild acne and within a combined therapy with local drugs, such as adapalene, benzoyl peroxide etc. – reducing intensity of their side effects (dryness, irritation); for mild and moderate acne therapy. This cosmetic product may be prescribed on the stage of the disease's remission in order to secure and support the drug's therapeutic effect; it does not have any aggressive impact on skin of children. The gel is convenient to use, characterized by good tolerance, safety, lack of side effects; it does not contain acids overdrying and irritating skin or alcohol causing exacerbation of the process; it may be prescribed to children with severe acute and chronic pathologies without any health hazard; this makes its use in pediatric practice convenient and possible.

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