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SEVERE ACNE: ANALYSIS OF SOME MODERN METHODS OF TREATMENT

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Annotation:
The article provides an updated review of the data on severe acne and the treatment of this dermatosis using systemic isotretinoin. The mechanisms of action, starting and course doses, as well as issues of bioavailability of isotretinoin are discussed. The analysis of infor- mation about isotretinoin, manufactured by Lidose technology, is presented.

Keywords: isotretinoin, isotretinoin Lidose, bioavailability.

Introduction:

Treatment of severe acne remains is a significant problem modern dermatology gii. Well known to specialists high prevalence of vulgaracne, a component, according to data a number of authors, up to 85% in adolescence populations. This dermatosis is very distributed not only among sub- sprouts: acne may persist after period of puberty, and more than 40% experience it for the first time after the end of puberty. Severe acne is common much less frequently than mild and moderate yellow Information has been accumulated according to which the frequency of severe acne in sub- sprouts is 20–35% and about 20% – in adults . Nega- positive impact of this disease on indicators of quality of life, comparison Visible with that for asthma, diabetes diabetes, arthritis, epilepsy and others life-threatening conditions. Currently the focus of interest is According to researchers, there is a problem \MA search for factors associated with severe acne. By now Genes have now been discovered encoding P450-1A1 and steroid-21- hydrolase, there are clear instructions for cases of acne in the family. High frequency of acne in close relatives patients with severe cases of this dermatosis was also identified in large large-scale study conducted nom in Russia: 83% of more than 1000 the patients examined had a sick mother and/or father. Also discussed severity of acne in different racial and ethnic groups. In recent years are paying more and more attention associations of excess body weight and severe acne, especially in the popular tions of adult women.

Recently were formulated prognostic Chinese acne severity factors that include those preceding in childhood acne at a young age, early onsetion of centrofacially located comedones, early and severe seborrhea in children before the onset of period puberty, beginning of menstruation after the appearance of acne. In accordance with Federal clinical guidelines for treatment of severe acne with the drug choice is a systemic isotret- noin. It is indicated for nodular severe/conglobate acne, and with severe papulopustular/ moderate nodular acne severity. It is recommended to take into account also the possibility of choosing isotret- noina for patients with acne, not suitable given to other types of therapy, with acne in combination with pronounced psycho-emotional disorders regarding the disease and tendency to healing with scar formation. High recommendatory power of iso-tretinoin is supported by a mass of con- controlled studies. More than over the 30-year period of existence market of this drug on the world market dermatologists have accumulated convincing information about its advantages. High effectiveness of isotrenium application noina in comparative studies with placebo, tetracycline and mino- cyclin. Comparable effect on deep inflammatory elements identified when comparing iso- tretinoin with minocycline in combination ni with 20% azelaic acid and with systemic tetracycline in combination tania with 0.1% adapalene, and mono- Isotretinoin therapy turned out to be as effective as therapy isotretinoin together with topical Sky clindamycin and adapalene. It is well known that this systemnal retinoid most effective affects the known links of the patho- acne genesis due to highly selective binding to nuclear receptors retinoic acid tori (RAR) retinoid acid receptor) and their activation. Has unique evidence - new database of numerous long-term studies demonstrating influencing its influence on all pathogenic links in the development of acne. For In recent years, additied detailed information about new mechanisms actions that explain the clinical effect of the drug. In particular, there was Isotretinoin has been shown to have local antiandrogenic effect eat due to competitive inhibition reduction of retinol dehydrogenase enzymes, responsible for the oxidation of andro- genes in sebocytes. Besides, long-lasting effect detected isotretinoin on congenital factors immunity and inflammation, in particular decrease in the expression of toll- similar receptors-2 (TLR-2 – toll- like receptors-2) on monocytes in patients ents with severe acne. Authors studies have demonstrated also prolonged positive

effect on this factor of innate immunity for 6 months after cessation of systemic therapy, which explains clinical recovery or persistent improvement in such pain-

nykh. It has also been proven that noin reduces the activity of matrix metalloproteinases-1, -3, -13 (MMP-1, -3, -13 – matrix metalloproteinases-1, -3, -13), responsible for the formation scars, and increases tissue activity new inhibitors of these MMPs. This work explains a lot positive effect of this retino- yes regarding scar changes, repeatedly registered in clinical studies.

The issue of dosage of systemic iso- tretinoin for varying severity acne is very important for daily clinical practice. Currently time to treat severe acne

Russia is recommended to have systemic iso- tretinoin at a dose of 0.5 mg/kg body weight, and its cumulative dose is in the range from 120 mg to 150 mg/kg body weight, with the duration of treatment should depend on the severity of the process and over- drug portability. Exactly this dose, according to the majority experts, allows you to achieve the needs good balance between efficiency and safety of treatment. This information set out in the latest European recommendations for the management of patients with acne, published in 2016 The regression rates were analyzed Ca rashes depending on the dose. So, in the domestic large-scale nom research on the effectiveness and safety of isotretinoin, in which 1349 patients were under observation entov, 90% regression of rashes was noted by the 30th week of treatment in persons receiving less than 0.5 mg/kg, and to 28 weeks in patients taking 0.5–0.89 mg/kg. There is a constant debate in the literature The starting dose of isotretinoin is changed. For decades of drug existence reported uses from 0.1 up to 1 mg/kg. It has been demonstrated that starting treatment using low doses of the drug (0.1–0.2 mg/kg body weight per day) followed by progressively increasing the dose to a high may reduce the risk and severity of complications strenuous acne upon initiation of therapy. In contrast to these data. It has been shown that high doses isotretinoin, especially when severe nodular/conglobate acne, associated with lower frequency relapses. That is why in latest recommendations, proposed by the American Academy of Dermato- logy, higher doses of pre- parata, which, however, can cause create more side effects. For the treatment of severe acne they suggest prescribing a starting dose 0.5 mg/kg for the first month treatment, and subsequently increase it up to 1 mg/kg body weight depending on patient tolerance. As for the total cumulative dose, then a significantly lower

What is the frequency of relapse noted in individuals receiving 120 mg/kg, compared with those who received less than 120 mg/kg. In all the latest recommendations documents included so-called dose-dependent my therapeutic effect plateau, component 120–150 mg/kg weight Bodies. At the same time, in one of the recent of these publications, the authors managed to pro- demonstrate that the total cumulative

latative dose (220 mg/kg) in 116 patients is interconnected with even less relapse rate. It should be emphasize the importance of further research progress in this direction. Data have also been accumulated on the effectiveness activity of low doses (0.1–0.3 mg/kg, regardless of body weight) with an average severe acne, demonstrate minimum number of side effects Effects. This does not require set of total cumulative dose, and treatment is stopped after reaching for a stable clinical result. For patients receiving low dosage of isotretinoin, course of treatment may be long lasting. Important control standard laboratory tory indicators, as well as the level creatine phosphokinase in individuals with high physical activity. Despite to low doses of isotretinoin, pre- precautions for such patients about pregnancy retain their full relevance. Appropriate emphasize also that the appointment low doses in severe cases acne is extremely undesirable due to high risk of relapse acne. Information has emerged about the combined using isotretinoin with deslo-ratadine. Showing faster anti-inflammatory effect and optimal tolerability compared to disagreement with isotretinoin monotherapy. The basis for such a combination is niya was the fact that mast cells actively participate in inflammatory acne reactions. Of interest is the modern vision of the pathogenesis of acne exacerbation at the start of therapy. It is known that isotretinoin causes not only to a decrease in skin production sebum and thinning of the stratum corneum, but and temporary irregularities in the composition a number of lipids (squalene, wax esters, cholesterol and its esters) in the latter. It is the violation of the barrier of skin properties induces re- scorching reaction through production of interleukin 1-α (IL-1a) and the appearance of fresh elements. Using products for gentle care that restores barrier properties of the skin, provides preventive tion of exacerbation. Dose adjustment isotretinoin and low doses of systemic of glucocorticosteroids prescribed. They are rare Gentle skin care using dermocosmetics, intended for patients, semi- those who rely on retinoids are considered important prevention factor is often encountered - existing side effects in the form dry skin, retinoid dermatitis that, eczematous rashes and others phenomena. Since isotretinoin is Xia derivatives of fat-soluble vitamin A, it is recommended to take it mother after a dense and fatty meal in order to improve bioavailability. The reason for this is the fact that the suction is standard different forms of isotretinoin by 60% in persons taking drugs outside and after meals. However, some authors claim know that patient adherence treatment in this case may be low. Inconsistent food habits that are very characteristic of sub-

sprouts and youth, can lead, according to J. Tan, to irregular dosing and significant variation of plasma isotretinoin levels both in the same patient and in different patients. Features of bioavailability of iso- tretinoin in a certain way limit reduction programs currently significant body weights time for acne. This way So, there was a need to create giving isotretinoin drugs, less dependent on food intake with with the aim of reducing their potential suboptimal absorption and sub- therapeutic plasma levels blood. An attempt was made creating a micronized ver- this original isotretinoin on (Accutane NF – new formulation, Hoffman-La Roche Pharmaceuticals Inc.). Manufacturers have reduced Shen active particle size substances, which led to an increase its bioavailability. In double blind randomized clinical clinical study of 600 patients with severe nodular acne was pro- demonstrated a similar general the effectiveness of the new drug compared to the standard one. However the new formula showed a tendency towards less effective in relation to proportion of persons achieving 90% reduction in the number of nodular elements cops by the end of treatment, reduction in the number of nodes, papulo- pustules, total number of inflammatory elements and dynamics of indicators global assessment of the effect. Marked slightly lower risk of developing side effects from the skin and mucous membranes, as well as hyper- triglyceridemia when used micronized isotretinoin.

Due to the lack of clear benefits micronized formula in relation to the standard in relation to research on the balance of effectiveness and side effects it was decided about the absence of grounds for the mark- ting of both formulas. Attempts to increase bioavailability isotretinoin continued, and in 2010 Russian specialists were able to whether to gain experience using a new drug - isotretinoin, manufactured using modern technology nology Lidose (drug Acnecutan, "SMB Technology S.A.", Belgium, issuing quality control property - the company "Jadran-Galenski Laboratories j.s.c., Croatia). He was created to reduce the risk of development of systemic side effects retinoids. The difference between this teacher is rate from standard isotretinoin is its increased bioavailability - ness. This innovative technology Logic of isotretinoin production also helps reduce dependence its absorption from food intake. It means encapsulation lipophilic drugs together with lipid agents, which creates more optimal conditions for them absorption. The proposed company her SMB Laboratories delivery system medicinal substance called Lidose consists of a solid desire- mud capsule, including two fractions of isotretinoin – dissolved known in fatty fillers and undissolved. This technology is already successfully used to create bioavailable fenofiber formula one intended for

treatment hyperlipidemia (LipofenTM Cipher Pharmaceuticals Inc.). New form has a higher rate of dis- creation of the active substance and as a consequence – increased quality of the dissolved drug, available for absorption in water environment of the digestive tract, which determines the increase in bioavailability isotretinoin toxicity when taken orally and achieving equivalent plasma low level of active substance quality at a lower one-time dose. Acnecutane release- Available in capsules of 8 and 16 mg. At this 8 mg of this drug corresponds to There are 10 mg of regular isotretinoin, and 16 mg – 20 mg. The benefits of isotretinoin, made using Lidose technology, compared to regular isotretinoin better tolerability with less significant irritation of the mucous membrane lobes of the gastrointestinal tract, rapid absorption and protection of the drug from oxidation. The drug is approved FDA (Food and Drug Administration) for use in the USA in 2012 for treatment of severe nodular and/or inflammation tile acne, conglobate acne, as well as acne resistant to therapy. Similar indications have been approved and in Canada. Pharmacokinetic study of the new drug compared to regular isotretinoin at 60 healthy subjects demonstrated them pharmacokinetic bioequivalent difficulty when taken after standard food (modified high-quality high-calorie breakfast fat reduction and reduced content lack of vitamin A). At the same time there was demonstrated significantly greater absorption of isotretinoin and its metabolites among persons receiving Isotretinoin using Lidose technology outside of meals. It was revealed that plasma isotretinoin levels reached 67% when taking the drug using Lidose technology on an empty stomach from level that was obtained under the condition when taking the drug with food. And in in the case of conventional isotretinoin level of isotretinoin in blood plasma on an empty stomach reached only a level of 40% relative to the level that was obtained under the condition of taking the drug the one with food. Significant differences in no incidence of side effects was identified Russian specialists have already have had considerable experience in using of Aknekutan. In domestic literature published data on treatment of about 1000 patients, auto- ry noted good therapeutic effect of isotretinoin, manufactured using Lidose technology.

Overall, the total cumulative the dose of the drug ranged from 100 to 120 mg/kg body weight. For evaluation treatment results were used like standard indexes and counting inflammatory elements and methods of dermatoscopy and echogra- skin diseases. Frequency of such side effects like cheilitis, dry skin, etc., was compared vima with isotretinoin or lower. The safety of the drug has been confirmed on biochemical research blood. It should be emphasized that when prescribing

isotretinoin, made using Lidose technology, all contraindications should be taken into account research and conduct standard research indications indicated upon admission isotretinoin. Thus, isotretinoin still remains a drug choice when treating patients with severe slow progression of acne. Available specialists, a new pre-paratha with increased bioavailability stu – isotretinoin, manufactured using Lidose technology. Important again emphasize the importance of comprehensive and analytical approach when conducting patients with severe acne.

References

1. Leyden J. A review of the use of combination therapies for the treatment of acne vulgaris. J. Am. Acad. Dermatol. 2003;49:200–10.
2. Nast A., Dreno B., Bettoli V., Bukvic Mokos Z., Degitz K., Dressler C., Finlay A.Y., Haedersdal M., Lambert J., Layton A., Lomholt H.B., López- Estebaranz J.L., Ochsendorf F., Oprica C., Rosumeck S., Simonart T., Werner R.N., Gollnick H. European Evidence-based (S3) Guidelines for the Treatment of Acne. J. Eur. Acad. Dermatol. Venenreol. 2016;30(8):1261–68.
3. Poli F., Dreno B., Verschoore M. An epi- demiological study of acne in female adults: results of a survey conducted in France. J. Eur. Acad. Dermatol. Venereol. 200;15(6):541–45.
4. Amado J.M., Matos M.E., Abreu A.M., Loureiro L., Oliveira J., Verde A., Massa A. The prevalence of acne in the north of Portugal. J. Eur. Acad. Dermatol. Venereol. 2006;20:1287–95.
5. Nijsten T., Rombouts S., Lambert J. Acne is prevalent but use of its treatments is infrequent among adolescents from the general population. J. Eur. Acad. Dermatol. Venereol. 2007; 21:163–68.
6. Smithard A., Glazebrook C., Williams H.C. Acne prevalence, knowledge about acne and psychological morbidity in mid-adolescence: a community-based study. Br. J. Dermatol. 2001;145(2): 274–79.
7. Mallon E., Newton J.N., Klassen A., Stewart- Brown S.L., Ryan T.J., Finlay A.Y. The quality of life in acne: a comparison with general medical conditions using generic questionnaires. Br. J. Dermatol. 1999;140(4):672–76.
8. Tan J.K. Psychosocial impact of acne vulgaris: evaluating the evidence. Skin Therapy Lett. 2004;9(7):1–3, 9.
9. Dreno B., Poli F. Epidemiology of acne. Dermatology. 2003;206(1):7–10.
10. Herane M.I., Ando I. Acne in infancy and acne genetics. Dermatology. 2003;206(1):24–8.

11. Кубанова А.А., Аравийская Е.Р., Соколов-ский Е.В., Дворова Е.К., Фадеева Е.И. Системное лечение тяжелых форм акне: опыт использования изотретиноина в Российской Федерации. Вестн. дерматол. и венерол. 2013;5:102–14.
12. Perkins A., Cheng C.E., Hillebrand G.G., Miyamoto K., Kimball A.B. Comparison of the epidemiology of acne vulgaris among Caucasian, Asian, Continental Indian and African American women. J. Eur. Acad. Dermatol. Venereol. 2010;25(9):1054–60.
13. Smith R.N., Mann N.J., Braue A., Mäkeläinen H., Varigos G.A. A low-glycemic-load diet improves symptoms in acne vulgaris patients: a randomized controlled trial. Am. J. Clin. Nutr. 2007;86(1):107–15.
14. Федеральные клинические рекомендации по ведению больных акне. М., 2013. 20 с.
15. Peck G.L., Olsen T.G., Butkus D., Pandya M., Arnaud-Battandier J., Gross E.G., Windhorst D.B., Cheripko J. Isotretinoin versus placebo in the treatment of cystic acne. A randomized double- blind study. J. Am. Acad. Dermatol. 1982;6(Pt. 4, Suppl. 2):735–45.
16. Pigatto P.D., Finzi A.F., Altomare G.F., Polen- ghi M.M., Vergani C., Vigotti G. Isotretinoin versus minocycline in cystic acne: a study of lipid metabolism. Dermatologica. 1986; 172(3):154–59.
17. Lester R.S., Schachter G.D., Light M.J. Isotretinoin and tetracycline in the management of severe nodulocystic acne. Int. J. Dermatol. 1985;24(4):252–57.
18. Gollnick H.P., Graupe K., Zaumseil R.P. Comparison of combined azelaic acid cream plus oral minocycline with oral isotretinoin in severe acne. Eur J Dermatol 2001; 11(6): 538–544.
19. Oprica C., Emtestam L., Hagströmer L., Nord C.E.Clinical and microbiological comparisons of isotretinoin vs. tetracycline in acne vulgaris. Acta. Derm. Venereol. 2007;87(3):246–54.
20. Dhir R., Gehi N.P., Agarwal R., More Y.E. Oral isotretinoin is as effective as a combination of oral isotretinoin and topical anti-acne agents in nodulocystic acne. Indian J. Dermatol. Venereol.Leprol. 2008;74(2):187.
21. Karlsson T., Vahlquist A., Kedishvili N., Törmä H. 13-cis-retinoic acid competitively inhibits 3 alpha-hydroxysteroid oxidation by retinol dehydrogenase RoDH-4: a mechanism for its anti-androgenic effects in sebaceous glands? Biochem. Biophys. Res. Comm. 2003;303(1):273–78.

22. Dispenza M., Wolpert E.B., Gilliland K.L., Dai J.P., Cong Z., Nelson A.M., Thiboutot D.M. Systemic isotretinoin therapy normalizes exaggerated TLR-2-mediated innate immune responses in acne patients. J. Invest. Dermatol. 2012;132(9):2198–205.

23. PapaconstantinouE.,AletrasA.J.,GlassE.,TsogasP., Dionyssopoulos A., Adjaye J., Fimmel S., Gouvousis P., Herwig R., Lehrach H., Zoubou-lis C.C., Karakiulakis G. Matrix metalloproteinases of epithelial origin in facial sebum of patients with acne and their regulation by isotretinoin. J.Invest. Dermatol. 2005;125(4):673–84.

24. Lee J.W., Yoo K.H., Park K.Y., Han T.Y., Li K., Seo S.J., Hong C.K. Effectiveness of conventional, low- dose and intermittent oral isotretinoin in the treatment of acne: a randomized, controlled comparative study. Br. J. Dermatol. 2011;164; 369–75.

25. Cyrulnik A.A., Viola K.V., Gewirtzman A.J., Co- hen S.R. High-dose isotretinoin in acne vulgaris: improved treatment outcomes and quality of life. Int. J. Dermatol. 2012;51;1123–30.

26. Goldsmith L.A, Bolognia J.L., Callen J.P., et al. American Academy of Dermatology Consensus Conference on the safe and optimal use of isotretinoin: summary and recommendations. J. Am. Acad. Dermatol. 2004;50:900–906.

27. Zaenglein A.L., Pathy A.L., Schlosser B.J., et al. Guidelines of care for the management of acne vulgaris. J. Am. Acad. Dermatol. 2016;74(5):945–73.

28. Blasiak R.C., Stamey C.R., Burkhart C.N., et al. High-dose isotretinoin treatment and the rate of retrial, relapse, and adverse effects in patients with acne vulgaris. JAMA. Dermatol. 2013;149:1392–98.

29. Mandekou-Lefaki I., Delli F., Teknetzis A., Euthimiadou R., Karakatsanis G. Low-dose schema of isotretinoin in acne vulgaris. J. Int. Clin. Pharmacol. Res. 2003;23:41–6.

30. Nau H. Teratogenicity of isotretinoin revisited: species variation and the role of all-trans- retinoic acid. J. Am. Acad. Dermatol. 2001; 45(5):183–87.

31. LeeH.E.,ChangI.K.,LeeY.,KimC.D.,SeoY.J.,LeeJ.H.,Im M. Effect of antihistamine as an adjuvant treatment of isotretinoin in acne: a randomized, controlled comparative study. J. Eur. Acad. Dermatol. Venereol. 2014;28(12):1654–60.

32. Stewart M.E., Benoit A.M., Downing D.T., Strauss J.S. Suppression of sebum secretion with 13-cis-retinoic acid: effect on individual skin surface lipids and implications for their anatomic origin. J. Invest. Dermatol. 1984;82:74–8.

33. King R., Jones D.H., Daltrey D.C., Cunliffe W.J. A double-blind study of the effects of 13-cis- retinoic acid on acne, sebum excretion rate and microbial population. Brit. J. Dermatol. 1982;107:583–90.
34. Jeremy A., Holland D.B., Roberts S.G., Thom- son K.F., Cunliffe W.J. Inflammatory events are involved in acne lesions initiation J. Invest. Dermatol. 2003;121: 20–7.
35. Araviiskaia E., Dréno B. The role of topical dermocosmetics in acne vulgaris. J. Eur. Acad. Dermatol. Venereol. 2016;30(6):926–35.
36. Colburn W.A., Gibson D.M., Wiens R.E., Hanigan J.J. Food increases the bioavailability of isotretinoin. J Clin Pharmacol. 1983;23(11– 12):534–39.
37. Tan J., Knezevic S. Improving Bioavailability with a Novel Isotretinoin Formulation (Isotretinoin- Lidose). Skin Therapy letter. 2013;18(6).
38. HLR Technology Corporation (Hoffman- La Roche), Nutley, NJ. NDA 21-177: New formulation isotretinoin [Executive Summary]. Summary date: August 9, 2000. backgrd/3639b1d_01. doc. Accessed July 29, 2013.
39. Webster G.F., Leyden J.J., Gross J.A. Comparative pharmacokinetic profiles of a novel isotretinoin formulation (isotretinoin-Lidose) and the innovator isotretinoin formulation: a randomized, 4-treatment, crossover study. J. Am. Acad. Dermatol. 2013. [Epub ahead of print].
40. Волкова Е.Н., Есимбиева М.Л., Ландышева К.А., Лебедева С.В., Елистратова И.В. Инновация ведения больных с акне: предварительные результаты лечения. Клин. дерматол. и вене- рол. 2011;1:59–63.
41. Самцов А.В., Стаценко А.В., Волкова С.В., Горбунов Ю.Г., Хайрутдинов В.Р. Вопросы эффективности и безопасности применения акнекутана в терапии акне. Вестн. дерматол. и венерол. 2011;2:58–62.
42. Сафонова Т.Г., Владимиров В.В., Сирмайс Н.С. Системные ретиноиды в терапии тяжелых и резистентных форм акне. Клин. дерматол. и венерол. 2013;3:60–2.
43. Кунгуров Н.Н., Кохан М.М., Шабардина О.В. Опыт терапии больных среднетяжелыми и тяжелыми акне препаратом изотрети- ноин. Вестн. дерматол. и венерол. 2013;1:56– 62.
44. Масюкова С.А., Мордовцева В.В., Кахишви- ли Н.Н. Лечение акне низкими дозами изо- третиноина. Клин дерматол. и венерол. 2012;2:79–85.
45. Сергеева И.Г., Криницына Ю.М., Онипчен- ко В.В., Гвоздарева М.А., Дягилева А.А. Клинико-морфологическая характеристика состояния кожи пациентов с акне в динамике терапии изотретиноином в форме LIDOSE.