# PHARMACEUTICAL SCIENCES

## COMBINATION THERAPY OF ACNE (ACNE VULGARIS) IN PATIENTS OF DIFFERENT AGE GROUPS

***Bushueva I.***
*Doctor of Pharmacy, Professor Department of Clinical Pharmacy, Pharmacotherapy and Management and Economics of Pharmacy Zaporizhzhya State Medical University, Zaporizhzhia, Ukraine*
***Kileeva O.***
*Applicant of the Department of Clinical Pharmacy, Pharmacotherapy and Management and Economics of Pharmacy Zaporizhzhya State Medical University, Zaporizhzhia, Ukraine*

**Abstract**

Acne takes the lead among all skin diseases. According to epidemiological studies conducted in industrialized Western governments, the prevalence of acne development among adolescents ranges from 50% to 95%, depending on kind of defeat. Acne is a disease that is most common in adolescents. First it appears in childhood after the start of the production of androgenic hormones by the sex glands and adrenal glands, and, stops usually after the period of adulting. However, it can continue to manifest in a significant part of adults, especially it is widespread by women [1, 10].

Acne is an androgen-dependent disease of hair follicles (or sebaceous hair formations). There are four main pathogenetic factors, the interaction of which contributes to the development of acne disease: the production of sebum by the sebaceous gland, changes in the process of keratinization, colonization of the follicles of *Propionibacterium acnes*, and the release of inflammatory mediators.

Precise molecular level understanding of the acne development proves that acne is a disease that includes both innate and adaptive immune responses and inflammation.

**Keywords:** acne, severity of acne, benzoyl peroxide, retinoids, antibacterial drugs.

**Experimental (Materials and methods).** During the study process the following methods were used: information search, content analysis, analytical and comparison approach, descriptive and graphic method, generalizations.

**Results and its discussion.** According to the International Statistical Classification of Diseases and Related Disabilities (eleventh edition), acne (acne) refers to L70. ICD-10 version 2016 classifies it as follows: **Acne** keloid (L73.0); **L70.0 Acne vulgaris; L70.1 Acne conglobata; L70.2 Acne varioliformis;** Acne necrotica miliaris; **L70.3 Acne tropica; L70.4 Infantile acne; L70.5 Acné excoriée;** Acné excoriée des jeunes filles; **L70.8 Other acne; L70.9Acne, unspecified.**

According to MeSH (Medical Subject Heading - Descriptor Data 2019, Medical Subject Headings) and the US National Library of Medicine National Institutes of Health, the following classification system exists:

Skin and Connective Tissue Diseases [C17]

- Skin Diseases [C17.800]
- Acneiform Eruptions [C17.800.030]
- Acne Keloid [C17.800.030.030]
- **Acne Vulgaris [C17.800.030.150]**
- Acne Conglobata [C17.800.030.150.500]
- Chloracne [C17.800.030.575]

Skin and Connective Tissue Diseases [C17]

- Skin Diseases [C17.800]
- Sebaceous Gland Diseases [C17.800.794]
- **Acne Vulgaris [C17.800.794.111]**
- Acne Conglobata [C17.800.794.111.500]
- Dermatitis, Seborrheic [C17.800.794.230]
- Mucinosis, Follicular [C17.800.794.550]
- Rhinophyma [C17.800.794.650]
- Sebaceous Gland Neoplasms [C17.800.794.712]

In practice, you can find many signs of this disease. Determination of the disease severity are given in Table 1. [2].

Table 1

Determining the severity of acne development (Self-design project adopted from the Unified Clinical Protocol of primary, secondary (specialized), tertiary (highly specialized) medical care Acne

| CLASSIFYING the ACNE SEVERITY | | | | | |
|---|---|---|---|---|---|
| ACNE Severity / PRESENCE AND NUMBER OF DAMAGING ELEMENTS | | | | | |
| ***Comedone*** | ***Papules / pustules*** | ***Knots (less than 1 cm)*** | ***Knots / cysts / fistulas*** | ***Inflammation*** | ***Scarring*** |
| **EASY (CAMEDON ACNE)** | | | | | |
| <20 | <10 | absent | absent - | absent | absent |
| **MODERATE ACNE (PAPULOPUSTULAR ACNE)** | | | | | |
| >20 | 10-20 | <10 | absent - | present | absent |
| **SEVERE ACNE (NODULAR ACNE)** | | | | | |
| >20 | >20 | 10-20 | - or <5 | evident | present |
| **VERY SEVERE ACNE (CONGLOBATE SPECIAL FORM ACNE)** | | | | | |
| numerous | >20 | >20 | >5 | evident, deep | present |

Diagnosis and medical care of the disease presented in Fig. 1 depends on many factors. The most common of them are: nutrition, smoking, adverse reactions to drugs, hormonal imbalance, weakened immunity, hyperkeratosis, excessive work of the sebaceous glands, digestive diseases, inadequate care, stress, mechanical damage, sun, moisture, the so-called “fixation on cleanliness " and so on. [3, 4].

There are some differences in the pathogenesis of acne by men and women, and this disease is also common among children and adolescents. The high frequency of acne in adolescents can quite naturally be associated with changes in the hormonal balance in the body, because the secretion of androgen adrenal glands has age-related features. By puberty, the mesh zone of the adrenal cortex is poorly developed and poorly identified. But at the age of 5 to 10 years, its activation occurs, is called “adrenarche”. Throughout the entire period of puberty, the secretion of hormones in the net zone of the adrenal cortex gradually increases, reaching a maximum at the end of puberty. Therefore, it is precisely in the late puberty that a physiologically determined precedent for a relative excess of androgens is created. Fig. 2 presents the differential diagnosis of acne in young children and adolescents. Based on this analysis, it becomes clear that, despite the age of the child (adolescent), there is a large number of cases of this disease (clinical picture) [5, 6].

The medical treatment of children with skin disease differs significantly: light form (Fig. 3), moderate severity (Fig. 4) or strong severity (Fig. 5) includes different treatment regimens, and individually available fixed combinations for local use and subsequent monitoring by Dermatovenerologist.

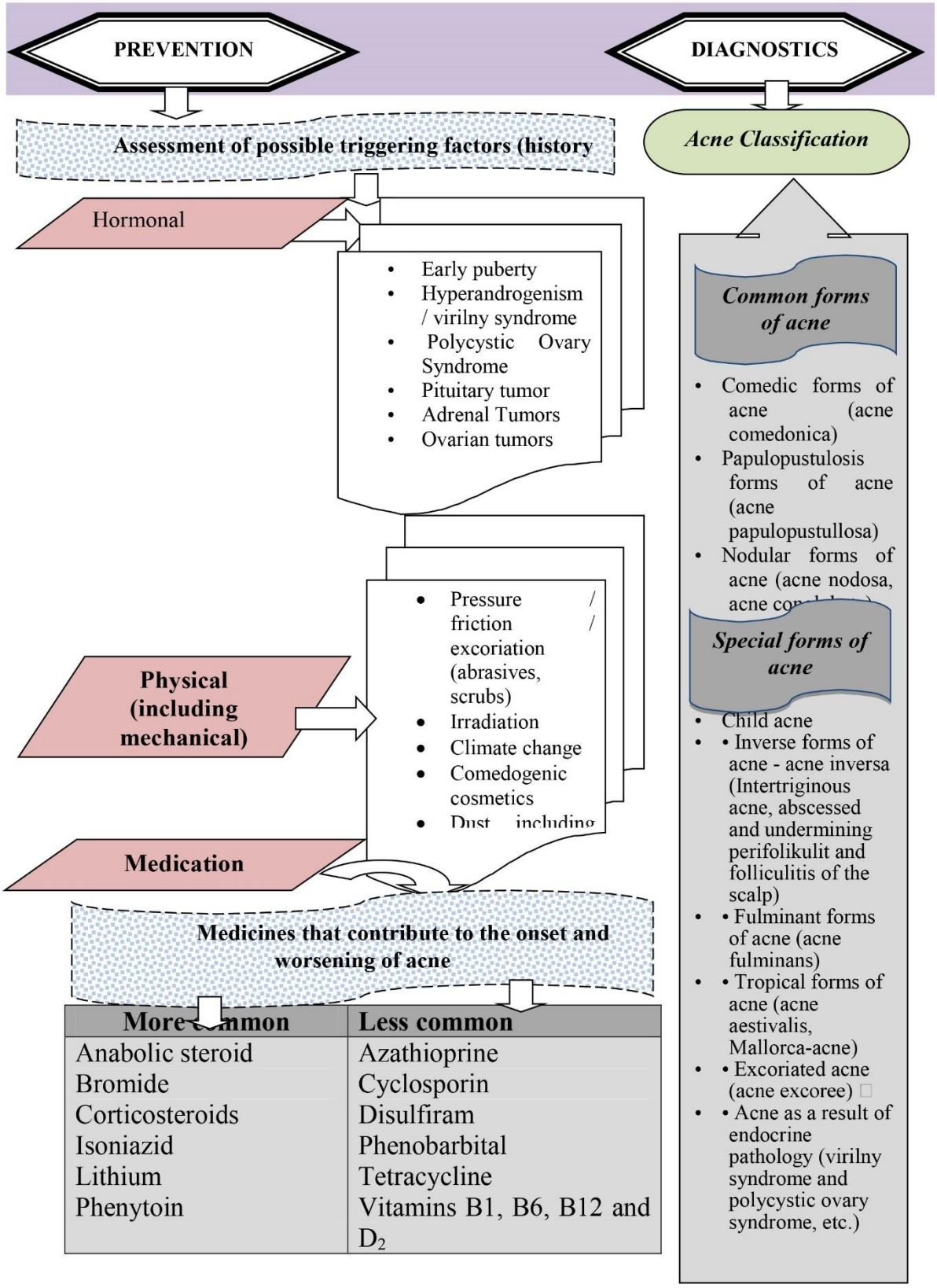


*Fig. 1. Diagnosis and medical acne treatment*

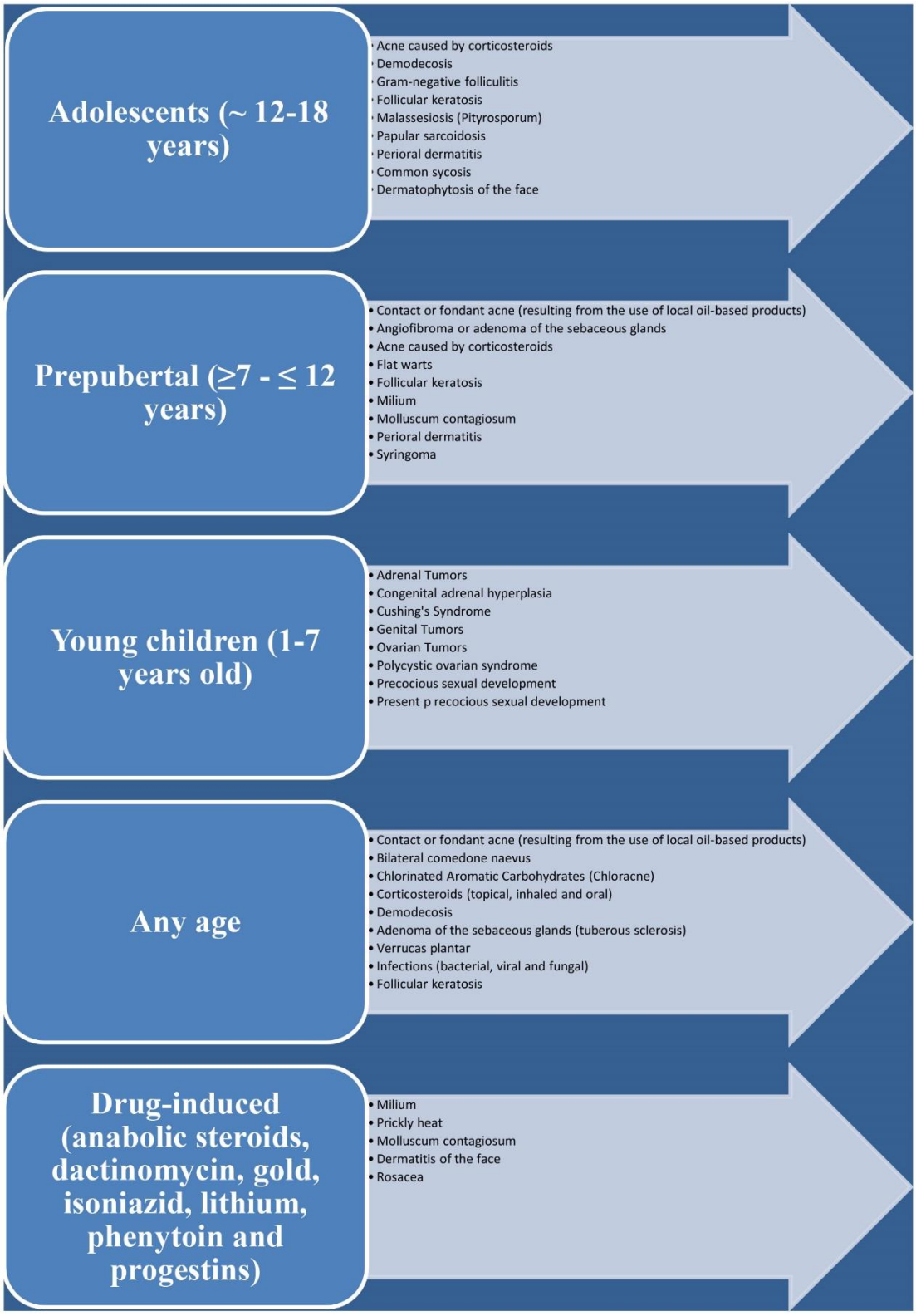


*Fig. 2. Differential diagnosis of acne in young children and adolescents*

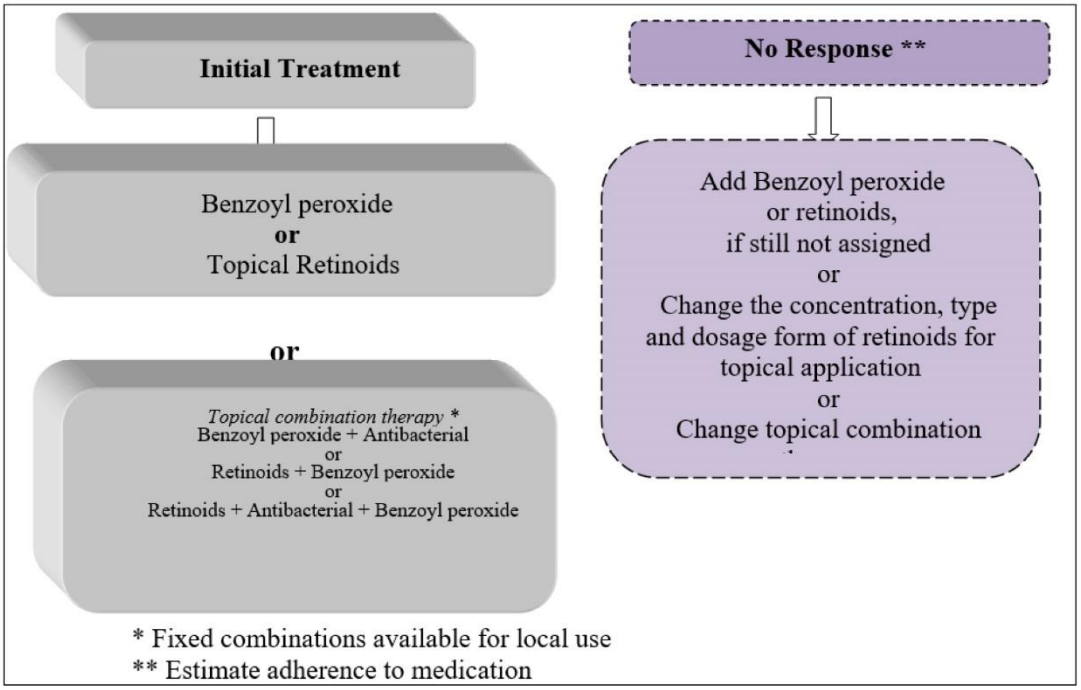


*Fig. 3. Recommendations for the treatment of mild acne children*

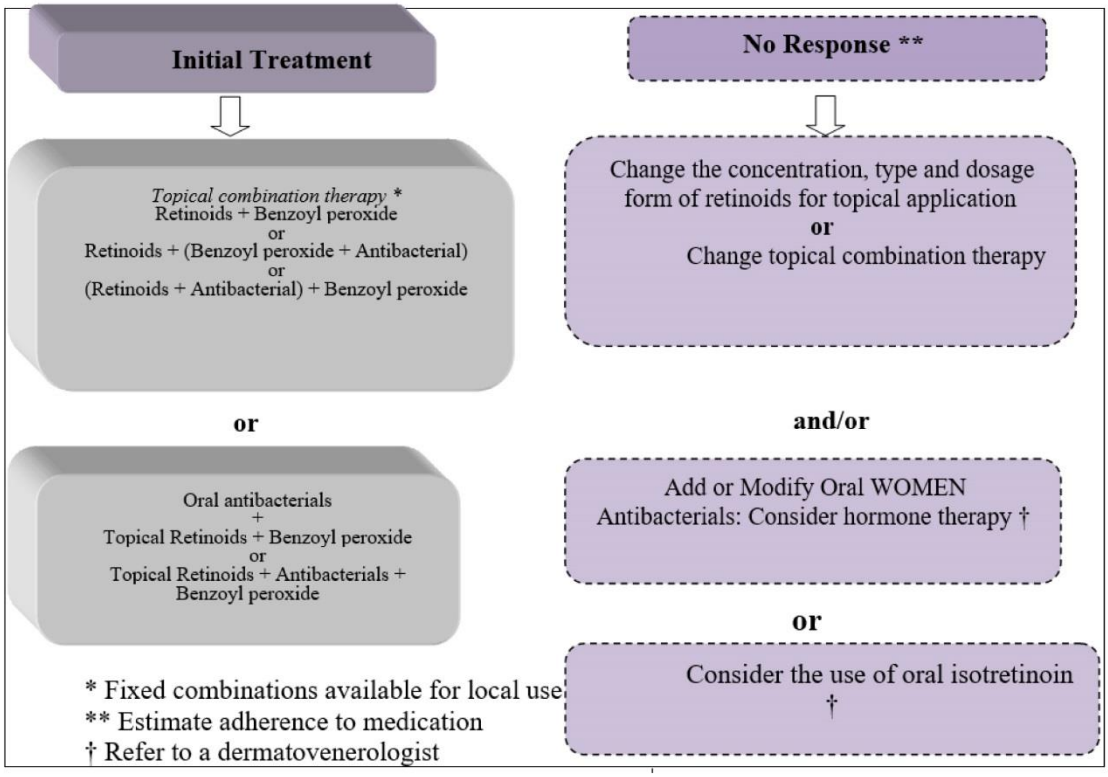


*Fig. 4. Recommendations for the treatment of moderate acne in children*

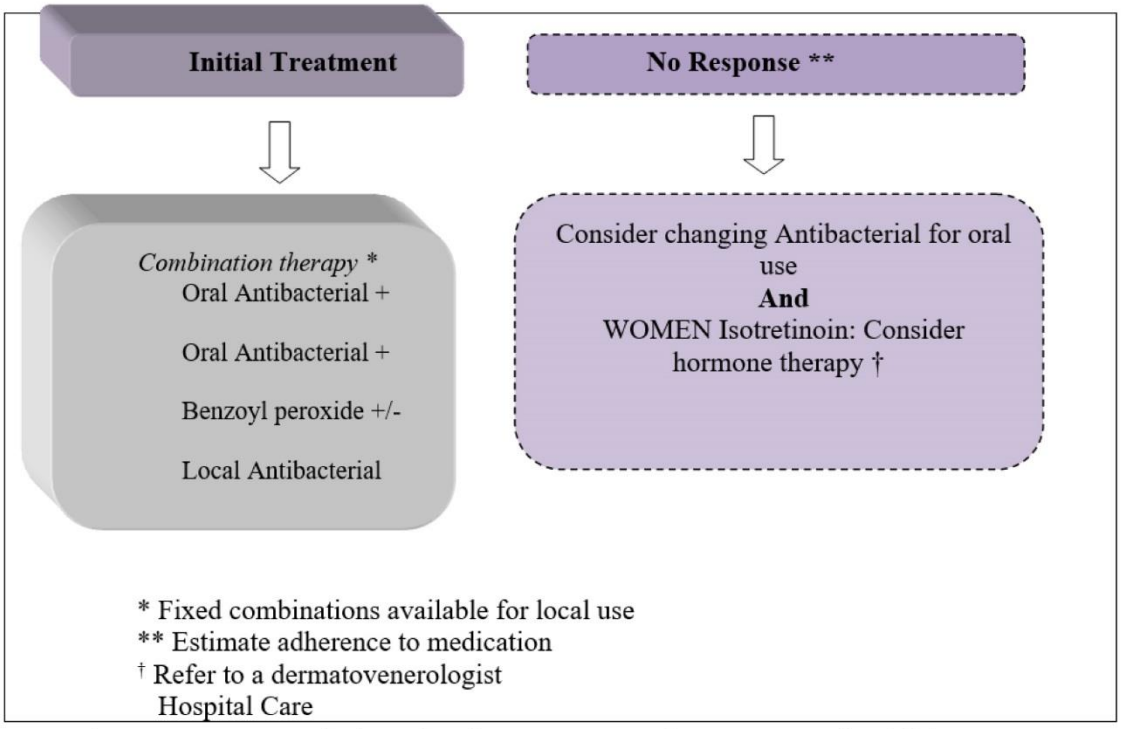


*Fig. 5. Recommendations for the treatment of severe acne in children*

There are some peculiarities at prescribing systemic retinoids also for men and women. The recommended dose is 0.4-0.8 mg of isotretinoin per kg of body weight per day. The cumulative dose of isotretinoin is 100-120 per kg of patient weight.

If the patient is male: due to the possibility of side effects such as dry lips, it is recommended to prescribe skin care products to prevent it. (Vichy Mineral 89 moisturizer for skin care, La Roche-Posay Hydraphase moisturizer for combination skin care , Lumene Voima Men moisturizer for skin care, etc.) It is also recommended to warn the patient for the following period of treatment with isotretinoin, to avoid using contact lens, work less at the computer, and if the patient has a dry eye - to use fluids such as a "Theratears"; to warn about the possibility of a short-term exacerbation of the disease in the second week of therapy with subsequent regression of symptoms; explain to the patient that the recommended dosage of isotretinoin is taken once or twice a day with food for more effective absorption of the drug, to warn the patient about the need to exclude alcohol during isotretinoin therapy, to limit foods rich in vitamin A (carrots, liver, eggs, etc.); do not eat excessively fatty foods, do not use multivitamins and food additives; to warn the patient about the need to limit the action of solar insolation and UV therapy. If necessary, use a sunscreen with a high value of the protective factor of at least 15 SPF; explain to the patient that he cannot be a blood donor during the period of treatment with isotretinoin and within next 30 days after the end of therapy, explain to the patient that therapy with isotretinoin is the most effective treatment for acne, but for stable remission, a cumulative dose of isotretinoin must be maintained 100-120 mg / kg body; patient, who started such treatment has to remember about the importance of completing the entire course; remind the patient that in case of any ailment, possibly related to taking the drug, he should immediately inform the doctor. If the patient feels the symptoms of depression or a state of depression, it is also necessary to inform the doctor about dose adjustment, to explain to the patient that isotretinoin is a strictly individual drug and the possibility of taking the drug by others has to be excluded [7, 8].

If the patient is female: it is imperative to use effective contraceptives (a double method of contraception is recommended) during isotretinoin therapy, a month before the planned therapy and within a month after isotretinoin therapy (to remove 99% of the drug from the body, a time equal to 7 half-lives is required, which for the main the metabolite of isotretinoin - 4-oxoisotretinoin - is about 15 days) to take a receipt from the patient that she has been warned and agrees to follow contraceptive recommendations throughout the period therapy with isotretinoin and 5 weeks after therapy (hereinafter all recommendations, as with therapy in men) [9].

In keeping with the rules, the course of treatment usually lasts 6-8 months. The final result of treatment should be evaluated no earlier than 8 weeks later. For most patients, one course of treatment is enough to get rid of acne. If it is necessary to conduct a second course of treatment, the drug is prescribed in accordance with the above recommendations.

According to the Global Alliance (2016) dedicated to improving outcomes in patients of different ages with acne, acne treatment is also different. Table 2 presents acne treatment regimens, depending on the severity of the disease in adult patients.

Table 2

Acne treatment, Global Alliance, Improving the Acne Treatment of Adult Patients (2016) (based on Unified Clinical Pathway of Medical Care) [11]

| **Mild Acne** | | **Moderate Acne** | | **Severe Acne** |
|---|---|---|---|---|
| Comedonal | Papulopustular (Up to 10 elements) | Papulopustular (More than 10 elements) | Nodal (Knots over 0.5-1 cm) | Nodular conglobate |
| **First Line Drugs** | | | | |
| Topical Retinoids | + Topical Antibiotics | Systemic Antibiotics + Topical Retinoids +/- Benzoyl Peroxide | Systemic Antibiotics + Topical Retinoids +/- Benzoyl Peroxide | Systemic Isotretinoin |
| **Alternative Drugs** | | | | |
| Alternative topical retinoids or Azelaic Acid / Salicylic Acid | Alternative Topical Antibacterials + Alternative Topical Retinoids or Azelaic Acid | Alternative Systemic Antibiotics + Alternative Topical Retinoids +/- Benzoyl Peroxide | Systemic Isotretinoin or Alternative Systemic Antibiotics + Alternative Topical Retinoids +/- Benzoyl Peroxide / Azelaic Acid | High doses of Systemic Antibiotics + Topical Retinoids + Benzoyl Peroxide |
| **For women * (excluding periods of pregnancy and lactation)** | | | | |
| First-line drugs | First-line drugs | Systemic antiandrogens + Topical retinoids / azelaic acid +/- Topical antibiotics | Systemic antiandrogens + Topical retinoids +/- Systemic antibiotics +/- Alternative antibacterial drugs | High doses of systemic antiandrogens + Topical retinoids +/- Alternative topical antibacterial drugs |
| **Maintenance Therapy** | | | | |
| Topical Retinoids | | Topical Retinoids +/- Benzoyl Peroxide | | |

As can be seen from the table, Treatment of acne, first-line drugs and alternative drugs belong to the same pharmacotherapeutic groups, namely: Topical Retinoids, Alternative Topical Retinoids, Systemic Antibiotics and Alternative Systemic Antibiotics, Benzoyl Peroxide / Azelaic Acid. Despite the fact that dermatologists pay attention and prescribe cosmetic medicines to patients with acne, the Global Alliance, Improving the Acne Treatment of Adult Patients (2016) (based on Unified Clinical Pathway of Medical Care) does not include it.

**Conclusion.**

1. Treatment of mild acne in children is carried out locally by drugs which include benzoyl peroxide or topical retinoids. Local combination therapy includes drugs which include benzoyl peroxide and antibacterial drugs; benzoyl peroxide and topical retinoids or preparations in combination with benzoyl peroxide, topical retinoids and antibacterial drugs.

2. The treatment of moderate acne in children is provided by using combined local therapy (benzoyl peroxide, topical retinoids and antibacterial drugs), but antibacterial drugs are prescribed inside, or topical retinoids together with benzoyl peroxide or complex benzoyl peroxide, topical retinoids and antibacterial drugs.

3. Treatment of severe acne in children is provided orally, using antibacterial drugs; locally doctors can prescribe benzoyl peroxide with antibacterial drugs.

4. There are some peculiarities by prescribing systemic retinoids for men and women - strictly individual drugs.

5. Acne treatment regimens, depending on the severity, in accordance with the Global Alliance (2016) Improving the Acne Treatment of Adult Patients, does not include cosmetic medicines.

**References**

1. Kalyuzhnaya LD, Slabky G.O., Gorbenko O.V. European recommendations for treatment of atopic dermatitis in 2011: analysis of modern technologies of topical therapy // Ukrainian Journal of Dermatology, Venereology, Cosmetology. - 2012. - No. 2 (45). - S. 52-60.

2. Unified clinical protocol of primary, secondary (specialized), tertiary (highly specialized) medical aid (acne).

3. Bowe W. et al. Body dysmorphic disorder symptoms among patients with acne vulgaris // J. Am. Acad. Dermatol. — 2017. — Vol. 57. — P.222–230.

4. Capitanio B., Sinagra J.L., Ottaviani M. et al. Acne and smoking // Dermatoendocrinol. — 2017. — Vol. 1. — P.129–135.

5. Isard O., Knol A.C., Aries M.F. et al. Proprionibacterium acnes activates the IGF–1 / IGF–1R system in the epidermis and induces keratinocytes proliferation // J. Invest. Dermatol. — 2011. — Vol. 131. — P. 59–66.

6. Melnik B.C., Schmitz G. Role of insulin, insulin–like growth factor–1, hyperglycaemic food and milk consumption in the pathogenesis of acne vulgaris // Exp. Dermatol. — 2014. — Vol. 18(10). — P. 833–841.

7. Preneau S., Dreno B. Female acne – a different subtype of teenager acne? // JEADV, 2011.Rivera R., Guerra A. Management of acne in women over 25 years of age // Actas Dermosifiliogr. — 2009. — Vol. 100. — P. 33–37.

8. Seirafi H., Farnaghi F., Vasheghani–Farahani A. et al. Assessment of androgens in women with adult–onset acne // Int. J. Dermatol. — 2007. — Vol. 46. — P.1188–1191.

9. Tan J.K. et al. Divergence of demographic factors associated with clinical severity compared with quality of life impact in acne // J. Cutan. Med. Surg. — 2015. — Vol. 12(5). — P. 235–242.

10. Veith W.B., Silverberg N.B. The association of acne vulgaris with diet // Cutis. — 2011. — Vol. 88(2). — P.84–91.

11. Kileeva, O.P. The Use of Medicinal Cosmetics in the Complex Treatment of Rosacea / O.P Kileeva, IV. Bushueva // Topical Issues in Pharmaceutical and Medical Science and Practice. - 2018. - Vol. 11, No. 1. - P. 91-96.

## ДОСЛІДЖЕННЯ СТРУКТУРНО-МЕХАНІЧНИХ ВЛАСТИВОСТЕЙ СУПОЗИТОРІЇВ З ОЛИВОЮ ЖУРАВЛИНИ

***Олійник І.М.***
*асистент кафедри фармації Державного вищого навчального закладу*
*« Івано-Франківський національний медичний університет»*
***Федоровська М.І.***
*доцент кафедри організації, економіки фармації і технології ліків*
*Державного вищого навчального закладу*
*«Івано-Франківський національний медичний університет»*
*кандидат фармацевтичних наук*
***Лисянська А.П.***
*доцент кафедри технології ліків*
*Запорізького державного медичного університету,*
*кандидат фармацевтичних наук*
***Гладишева С.А.***
*асистент кафедри фармакогнозії, фармхімії і технології ліків*
*Запорізького державного медичного університету,*
*кандидат фармацевтичних наук*

## STUDY OF STRUCTURAL AND MECHANICAL CHARACTERISTICS OF SUPPOSITORIES WITH CRANBERRY OIL

***Oliynyk I.***
*Assistant of department of pharmacy, Ivano-Frankivsk National Medical University*
***Fedorovska M.***
*Associate professor of department of organization and Economics in Pharmacy and Technology*
*Department, Ivano-Frankivsk National Medical University*
*Candidate of pharmaceutical sciences*
***Lisianskaia A.***
*Associate professor of department of technology of medications of the*
*Zaporizhzhya state medical university, candidate of pharmaceutical sciences*
***Gladysheva S.***
*Assistant of department of technology of medications of the*
*Zaporizhzhya state medical university, candidate of pharmaceutical sciences*

**Анотація**

Зараз серйозною медико-соціальною проблемою є лікування геморою, комбінованого з тріщинами прямої кишки, пов'язаною з широким поширенням і значним впливом на якість життя людини. Олива журавлини є досить перспективною сполукою для використання в м'яких проктологічних лікарських формах,