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Topical treatment of acne using a compounded medication based on clindamycin

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ABSTRACT

Clindamycin, a lincosamide antibiotic, is widely used in the treatment of bacterial infections. It acts by inhibiting protein synthesis in bacteria, primarily targeting the peptidyl transferase centre in the bacterial ribosome. It exhibits bacteriostatic activity, inhibiting bacterial growth, and at higher doses, it can be bactericidal. In the treatment of acne vulgaris, clindamycin not only exerts direct antibacterial effects but also possesses anti-inflammatory and immunomodulatory properties. It reduces the growth of *Cutibacterium* acnes and inhibits the production of proteins and lipases, which contribute to skin inflammation. Clindamycin also enhances bacterial opsonization and phagocytosis and reduces neutrophil chemotaxis. Combination therapy with benzoyl peroxide can help minimize antibiotic resistance. Topical clindamycin, often in combination with benzoyl peroxide or retinoids, is recommended in treatment for mild to moderate papulopustular acne. In *hidradenitis suppurativa* clindamycin improves disease control and reduces cutaneous lesions, particularly superficial ones like papules and pustules. Various topical preparations containing clindamycin are available commercially, including gels, lotions, and combination products with tretinoin or benzoyl peroxide. Additionally, the registration of clindamycin as a pharmaceutical raw material allows for compounding personalized formulations, providing a cost-effective alternative. Compounded medications can be tailored to individual patient needs and increase treatment effectiveness.

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Keywords: clindamycin, acne vulgaris, acne inversa, *hidradenitis suppurativa*, treatment

INTRODUCTION

Clindamycin is an antibiotic that belongs to the lincosamide group. It is a semi-synthetic derivative of lincomycin, a natural antibiotic produced by the actinomycete Streptomyces lincolnensis. Lincomycin was discovered in 1952 and has been used in medicine to treat various bacterial infections [1].

Clindamycin was first synthesized and introduced for use in the 1960s. It was developed to enhance the effectiveness of lincomycin and improve its pharmacokinetic properties [1].

Clindamycin works on bacteria by blocking protein synthesis. The mechanism of action of clindamycin involves the inhibition of the peptidyl transferase centre within the 50S subunit of the bacterial ribosome. Peptidyl transferase is an enzyme involved in the elongation process of the polypeptide chain during protein synthesis in bacterial cells. By blocking this activity, clindamycin inhibits the further growth of bacteria and prevents their multiplication [1].

At typical doses, clindamycin primarily exhibits bacteriostatic activity, which means it inhibits the growth and multiplication of bacteria but does not cause their immediate death. However, at higher doses, clindamycin may also demonstrate bactericidal activity, meaning it directly kills bacteria [1].

The spectrum of activity of clindamycin mainly includes gram-positive cocci, such as *Staphylococcus aureus* and *Streptococcus pyogenes*, as well as anaerobic bacteria, including *Cutibacterium* acnes and *Actinomyces israelii*, while most gram-negative bacteria are resistant to lincosamide antibiotics, including clindamycin [2].

In Poland, topical preparations containing clindamycin are registered for the treatment of common acne, but its positive effects are also well-documented in the therapy of acne inversa.

ACNE VULGARIS

Clindamycin, used in the treatment of common acne, exhibits a multifaceted action. In addition to its direct antibacterial effect on *C. acnes*, it also demonstrates

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anti-inflammatory and immunomodulatory properties, contributing to the reduction of skin inflammation. Clindamycin acts directly on *C. acnes*, reducing their growth, as well as the production of proteins and lipases. Lipases as hydrolytic enzymes, break down triglycerides present in sebum into free fatty acids (FFAs). FFAs on the skin surface can have irritant and pro-inflammatory effects, as well as increase perifollicular keratinization. By reducing the number of *C. acnes*, the concentration of FFAs is decreased, favouring esters, which in turn reduces inflammation and the risk of developing comedones [3]. Clindamycin also exhibits immunomodulatory effects by inducing bacterial opsonization, increasing their susceptibility to phagocytosis, and reducing neutrophil chemotaxis [4]. Its anti-inflammatory action is manifested by reducing the release of free radicals and the production of inflammatory cytokines such as IL-1β, IL-6, INF-γ, TNF-α, and GM-CSF [5].

The treatment of acne is a complex and multifaceted process, and the choice of appropriate treatment depends on various factors such as the type of acne, its severity, the patient's skin condition, and overall health. In the management of acne lesions, multiple methods are employed, but one of the main approaches is topical treatment, which is usually sufficient for approximately 60% of patients [6].

Topical antibiotics are commonly used in acne treatment due to their good patient tolerance and rare, mild side effects. They demonstrate a rapid onset of action, particularly in papulopustular acne, but their impact on non-inflammatory lesions and comedones is less pronounced.

Two antibiotics, clindamycin and erythromycin, are registered for the treatment of acne. However, reports of increasing antibiotic resistance and declining efficacy of antibiotics raise concerns about the continued use of these preparations. The prevalence of strains resistant to at least one antibiotic in the European population ranged from 51% in Hungary to 94% in Spain, reflecting local trends in antibiotic prescribing [7]. It is important to note that due to the shared target site of action among macrolides, lincosamides, and streptogramins, cross-resistance often occurs between these drugs (MLSB resistance). In a study by Simonart et al. [8], an analysis of 75 studies conducted between 1974 and 2003 regarding the efficacy of 1–2% clindamycin and 1.5–4% erythromycin in acne treatment was performed. The analysis showed that in treatments lasting more than 12 weeks, the efficacy of erythromycin in reducing inflammatory and non-inflammatory lesions decreased by 2.1% and 2% per year, respectively. In contrast, the efficacy of clindamycin remained unchanged during the studied period. This means that over time, erythromycin became less effective in treating skin lesions, while clindamycin maintained its efficacy at a constant level [8]. These findings reflect changing trends in the prescription of topical antibiotics, with a significant decrease in the prescription of erythromycin and an increase in the prescription of clindamycin in the United States [9].

One way to reduce antibiotic resistance is by combining antibiotics with benzoyl peroxide, which exhibits synergistic bactericidal effects and has not shown any resistance to it [10]. The use of benzoyl peroxide in combination with erythromycin [11], clindamycin [12], or adapalene [13] has led to a decrease in the number of antibiotic-resistant strains of *C. acnes*. A similar effect was achieved by once-daily facial washing with a cleanser containing 6% benzoyl peroxide [14].

To limit the development of bacterial antibiotic resistance during treatment, the following principles should be followed [6]:

— Use antibiotics according to indications, for the necessary period to resolve inflammatory lesions, but not longer than 12 weeks.
— Avoid using antibiotics as monotherapy and instead prefer combination therapy with benzoyl peroxide or a retinoid (in a fixed combination or at different times of the day), which further enhances treatment efficacy, shortens its duration, and limits adverse effects.
— Do not combine topical antibiotics with systemic antibiotics, as it does not improve treatment effectiveness and increases the risk of developing antibiotic resistance.

According to the guidelines of the Polish Dermatological Society, topical antibiotics are used in the treatment of mild to moderate papulopustular acne in combination with benzoyl peroxide (preferred treatment) or topical retinoid (alternative treatment) [6]. Similar recommendations are presented in European guidelines, which recommend the use of topical antibiotics in the treatment of mild to moderate papulopustular acne in combination with benzoyl peroxide (strong recommendation) or tretinoin (moderate recommendation). However, the use of antibiotics in the treatment of comedonal acne and as monotherapy is not recommended [15].

HIDRADENITIS SUPPURATIVA

The effectiveness of clindamycin has also been demonstrated in the treatment of hidradenitis suppurativa. In a double-blind study involving 27 patients with hidradenitis suppurativa, 1% clindamycin or placebo was applied for 3 months. The clindamycin group showed improvement in disease control according to the participants' assessment and a reduction in cutaneous lesions, particularly superficial ones such as papules, pustules, and folliculitis. The effect was less pronounced for deeper lesions such as nodules and abscesses [16]. In another study, the efficacy of topical 1% clindamycin was compared to oral tetracycline (500 mg twice daily) in a group of 34 patients with *hidradenitis suppurativa*. During the first 3 months of treatment, improvement

Figure 1. Celugel® hydrogel base (**A**); Clindamycin powder (**B**); Clindamycin hydrogel (**C**)

Table 1. Examples of formulations in the form of solutions

Rp.	Rp.	Rp.
Clindamycini hydrochloridi 1.0	Clindamycini hydrochloridi 1.0	Clindamycini hydrochloridi 1.0
Glyceroli 10.0	Glyceroli 10.0	Glyceroli 5.0
Ethanoli 60% 25.0	Acidi citrici 0.07	Celugeli* 60.0
Aquae purificatae ad 100.0	Aquae purificatae ad 100.0	Acidi citric 0.07
M.f. solutio	M.f. solutio	Aquae purificatae ad 100.0
Use: two times a day	Use: two times a day	M.f. solutio
		Use: two times a day

*Ready-made hydrogel compounding base based on hydroxyethyl cellulose; M.f. — mix and make; Rp. — presciption

in overall disease assessment by both the patients and the investigator, as well as a reduction in the number of abscesses, were noted. After 3 months of therapy, a decrease in the number of nodules was also observed [17]. In a study involving 60 patients with mild to moderate *hidradenitis suppurativa*, the efficacy of topical clindamycin was compared to systemic antibiotic therapy using clindamycin and rifampicin. Although both treatment methods provided similar improvements in the IHS4 (International Hidradenitis Suppurativa Severity Score System) score and a reduction in the number of nodules and abscesses, the group using topical clindamycin showed greater improvement in the DLQI (Dermatology Life Quality Index) score, VAS (Visual Analogue Scale) score, and number of fistulas [18].

European guidelines for the treatment of *hidradenitis suppurativa* recommend the use of clindamycin in Hurley stage 1 or mild forms of Hurley stage 2 [19].

PREPARATIONS

In Poland, there are various commercially available topical preparations containing clindamycin, such as 1% gel (Clindacne®, Dalacin T®, Klindacin T®, Normaclin®), 1% lotion (Dalacin T®), as well as combination products in the form of a gel containing 1% clindamycin with 0.25% tretinoin (Acnetac®) and with 3% or 5% benzoyl peroxide (Duac®).

Thanks to the registration of the hydrogel base Celugel® as a pharmaceutical raw material in 2019, it became possible to formulate gel preparations. In March 2023, clindamycin was also registered as a pharmaceutical raw material, enabling prescriptions for compounding preparations containing clindamycin with a refund, providing a cheaper alternative to fully-paid finished medicines (Fig. 1). In addition to ready-made gel and lotion preparations, compounding formulations also allow for the creation of creams and solutions that are not available in Poland. The use of compounded medications can bring many benefits to patients. Preparing a formulation involves not only using the appropriate dosage of the active substance but also selecting other ingredients that affect the effectiveness of the medication and its tolerability by the body. Patients can receive a medication tailored to their individual needs, which increases treatment effectiveness. This way, it is possible to avoid situations where commercially available preparations are not suitable for a particular patient, for example, due to allergens they may contain. Below are several examples of compounding formulations using clindamycin in the form of gel, cream, lotion, and solutions (Tab. 1, 2) [20].

CONCLUSIONS

Topical antibiotic therapy can be an attractive treatment option for patients with common acne and acne inversa due to its quick and effective action and good tolerability. It is important to adhere to principles of antibiotic use, such as dosing frequency, duration of therapy, and combination therapy, in order to minimize the risk of bacterial resistance to the medications.

Table 2. Examples of formulations in the form of gel, cream, and lotion

Rp.	Rp.	Rp.
Clindamycini hydrochloridi 1.0	Clindamycini hydrochloridi 1.0	Clindamycini hydrochloridi 1.0
Aquae purificatae 10.0	Aquae purificatae 10.0	Lekobazae 20.0
Celugeli ad 100.0	Lekobazae ad 100.0	Aquae purificatae ad 100.0
M.f. gelatum	M.f. cremor	M.f. lotion
Use: two times a day	Use: two times a day	Use: two times a day

M.f. — mix and make; Rp. — presciption

Article information and declarations

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Mikołaj Łanocha — wrote the paper; Beata Bergler-Czop — editorial supervision over the work

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Conflict of interest

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Supplementary material

None.

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