Taurine bromamine: a new therapeutic option in inflammatory skin diseases

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ABSTRACT
Acne vulgaris is a multifactorial inflammatory skin disease. One of the pathogenic factors in acne is Propionibacterium acnes (P. acnes). Traditional treatment of acne lesions involves topical application of antibiotics with anti-bacterial and anti-inflammatory properties. However, a failure of this therapy is widely associated with emergence of resistant bacteria. Therefore, a search for alternative topical anti-acne drugs is necessary.

Taurine bromamine (TauBr), the physiological product of hypobromous acid reaction with taurine, shows antioxidant, anti-inflammatory, and anti-bacterial properties. Importantly, P. acnes, a potential pathogenic agent for acne vulgaris, is extremely sensitive to TauBr. In addition, TauBr inhibits the generation of H2O2 by activated neutrophils, which seems to be crucial for reducing the number and severity of inflammatory acne lesions. All these data strongly support the concept of using TauBr for topical anti-acne therapy. In our pilot clinical study, we have compared the efficacy of TauBr cream with clindamycin gel, one of the most common topical agents used in the treatment of acne. After 6 weeks, both treatments produced comparable, beneficial results. More than 90% of patients improved clinically with similar reductions in a number of acne lesions (~65%). Therefore, the results from clinical studies are consistent with previous in vitro data and strongly suggest that TauBr could be considered a new therapeutic option in inflammatory acne.
that exogenous TauCl exerts microbial activity at concentrations well tolerated by human tissue but higher than that achieved by endogenous TauCl. Importantly, a number of clinical studies have confirmed that TauCl might be useful in treating various topical infections due to its combined microbicidal and anti-inflammatory properties. Much less is known on potential therapeutic application of TauBr. Recently, we have reported that TauBr shows strong anti-bacterial activity at physiological non-cytotoxic concentrations. Interestingly, in vitro, at the same concentrations TauBr killed tested bacteria (Escherichia coli, Propionibacterium acnes [P. acnes], Staphylococcus epidermidis) and reduced ROS generation by neutrophils. Because bacterial infections and ROS generation are closely associated with the pathogenesis of many inflammatory skin diseases, these data suggest that TauBr may be a good candidate for topical therapy in dermatology.

**Perspectives for TauBr application in dermatology**

Is TauBr a good candidate in acne topical therapy? In dermatology, medications containing a mixture of anti-inflammatory agents (steroids) and antibiotics are widely used. Therapies which allow to achieve the same result without side effect of steroids seem to be the future in the treatment of various inflammatory skin diseases, including acne vulgaris. Acne is a multifactorial inflammatory skin disease affecting pilosebaceous follicles. Acne is not an infectious disease, although the role of P. acnes is outlined in many studies. P. acnes and S. epidermidis belong to bacterial flora of the skin, but only P. acnes is considered to be involved in the pathogenesis of chronic skin inflammation in acne. During proliferation P. acnes secretes various inflammatory mediators that initiate and perpetuate the local inflammatory response.

A variety of agents for the treatment of acne vulgaris are available today. Current clinical strategy in the case of mild to moderate inflammatory acne involves combination with typical topical antibiotics, retinoid, and benzoyl peroxide to achieve a simultaneous anti-bacterial, anti-oxidant, and anti-inflammatory therapeutic effect. During the last few years, clindamycin and benzoyl peroxide have become the most widely prescribed topical drugs for acne. However, resistance of P. acnes to anti-acne antibiotics is considered a therapeutic failure of topical treatment. These findings indicate the need to develop strategies to minimize the use of antibiotics in acne therapy.

Based on our knowledge on the biological properties and functions of taurine halomines, we have decided to examine clinical efficacy of TauBr in the treatment of acne. We suggest that TauBr may be a good candidate for topical therapy, without the risk of inducing bacterial resistance, the major problem of topical antibiotic therapy in acne. From a clinical point of view, it is interesting that susceptibility of P. acnes to TauBr appeared to be significantly higher than that of S. epidermidis, as we have shown recently. Therefore, due to its ability to selectively kill P. acnes, TauBr seems to be a promising candidate as a topical agent in acne therapy.

In our double blind study, the efficacy and safety of 0.5% TauBr in a cream formulation was compared with 1% clindamycin gel, one of the most common topical agents in the treatment of acne vulgaris. Forty patients with mild to moderate inflammatory facial acne vulgaris were randomly treated with either TauBr or clindamycin for 6 weeks, twice a day. More than 90% of patients improved after both treatments. No adverse effects were observed. Both TauBr and clindamycin produced significant reduction of inflammatory skin lesion counts (papules/pustules). After 6 weeks, comparable reduction in acne lesions have been observed in the TauBr and clindamycin groups – 65% and 68%, respectively.

**Conclusions**

Our in vitro studies and a pilot clinical investigation suggest that TauBr can be used in monotherapy or in a combination with other drugs as a topical agent in the treatment of acne vulgaris. TauBr at non-cytotoxic concentrations demonstrates bactericidal activity in vitro, being significantly stronger than that of TauCl. P. acnes, a potential pathogenic agent in acne, is more susceptible to TauBr than S. epidermidis, which supports the concept of using TauBr as a selective topical disinfectant in the treatment of acne vulgaris. Moreover, TauBr showed the capacity to reduce generation of ROS by neutrophils, which seems to be crucial for reduction of the number and severity of inflammatory acne lesions. Finally, TauBr may be a desirable alternative treatment for acne vulgaris, especially in patients who have already developed antibiotic resistance (Patent No. EP 1 663 195). We also suggest that TauBr and TauCl, because of their ability to stimulate heme oxygenase-1 expression, may be used as novel players in cutaneous wound repair and psoriasis.

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Bromamina tauryny – nowa strategia w leczeniu chorób skóry o podłożu zapalnym

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**STRESZCZENIE**

Trądzik pospolity (*Acne vulgaris*) jest chorobą zapalną skóry, powodowaną przez wiele czynników. Jednym z nich jest *Propionibacterium acnes* (*P. acnes*). Klasyczne leczenie polega na miejscowym podawaniu antybiotyków wykazujących właściwości bakteriobójcze i przeciwpalenne. Jednakże częste niepowodzenia takiej terapii są związane z narastającą antybiotykoopornością bakterii skórnych. Istnieje zatem konieczność poszukiwania alternatywnych leków.

Bromamina tauryny (TauBr), fizjologiczny produkt reakcji HOBBr z tauryną, wykazuje właściwości przeciwbakteryjne, przeciwpalne i antyoksydacyjne. Co ważne, *P. acnes*, potencjalny czynnik patogenny trądziku jest wysoce wrażliwy na TauBr. Wykazano ponadto, że TauBr hamuje produkcję H2O2 przez zaaktywowane neutrofile, co wydaje się być kluczowe dla redukcji ilości i natężenia zapalnych zmian trądzikowych. Powyższe dane potwierdzają, że TauBr jest dobrym kandydatem do miejscowego leczenia trądziku pospolitego. W naszych pilotowych badaniach klinicznych porównywalny efekt leczniczy, który można zauważyć już w 6–tygodniowym okresie, wykazywał podobny efekt terapeutyczny w obu badanych grupach. Poprawę zaobserwowano u > 90% pacjentów, z podobną redukcją ilości zmian skórnych wynoszącą ~65%. Badania kliniczne potwierdziły zatem wyniki poprzednich badań *in vitro* nad właściwościami TauBr i sugerują wyraźnie, że TauBr powinna być rozpatrywana jako nowa opcja terapeutyczna w leczeniu zapalnego trądziku.