Buspirone Inhibits Contact Hypersensitivity in the Mouse

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Key Words

Buspirone
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Immunomodulation

Abstract

We have observed that 8-4-[4-2-pyrimidyl]-1-piperazinyl]butyl]-8-azaspiro [4.5]decane-7.9-dione, an agent commonly known as buspirone HCl, possesses immunosuppressive activity when administered either topically or systemically, as assessed in a mouse model of contact hypersensitivity. Topical or systemic administration of buspirone significantly reduced the tissue swelling and leukocyte infiltration associated with the elicitation phase of contact hypersensitivity. Buspirone is a safe, widely used drug which has a history of use in humans throughout the world. These data demonstrate a previously unknown pharmacologic activity of buspirone.

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Methods

Contact hypersensitivity reactions were elicited in female BALB/c mice (Charles River Laboratories, Wilmington, Mass., USA) by applying a hapten oxazolone (Sigma) in 4:1 (vol/vol) acetone:olive oil topically to one or both ears, after prior ep-icutaneous sensitization with a 4% (wt/wt) solution of oxazolone. Each treatment group contained five mice. Immediately before and 24 h after topical challenge with oxazolone, ear thickness was measured with an engineer's micrometer. The change in ear thickness (Δ) was calculated as the 24-hour value minus the baseline (prechallenge) value and was expressed in units of μ inches. Statistical analysis was performed using the two-tailed Student's t test. All data are

Results

| Left Ear, oxazolone, no treatment | | Right Ear, oxazolone, buspirone
100 mg/ml 10 mg/ml 1 mg/ml 0.5 mg/ml 0.25 mg/ml Vehicle-N Buspirone Buspirone Buspirone
Buspirone Buspirone Solution Solution Solution Solution Solution

As illustrated in figure 1, a dose-dependent response was observed upon topical application of buspirone to the right ears, 4 h after elicitation of the response. The left ears were challenged at the same time as the right but were not treated with buspirone, so that possible systemic effects of the drug could be observed. Additionally, doses of 50 or 500 mg/kg,

Fig. 1. Buspirone diminished the inflammation caused by challenge with the hapten oxazolone. Buspirone (in solutions of 0.25-100 mg/ml), when applied topically to the right ear, 4 h after elicitation of the response, significantly reduced the swelling of the right ear, but had little or no effect on the swelling of the untreated, but oxazolone-challenged, contralateral (left) ear.

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administered subcutaneously, 1 h after elicitation of the contact hypersensitivity response, significantly reduced the ear-swelling response (data not shown).

In a comparison of the potential immunosuppressive activities of buspirone HCl versus other serotonin or dopa-mine antagonists, only buspirone suppressed the inflammation caused by the contact hypersensitivity response (fig. 2). In this experiment, 50 mg/kg of one of the test agents was administered via intraperitoneal injection to female BALB/c mice 2 h after elicitation of the response. The serotonin receptor antagonists trazodone or mianserin or the do-pamine receptor antagonist haloperidol were not effective in reducing either the tissue swelling or inflammatory cell infiltration (data not shown) associated with an immune response. At this dose, however, buspirone HCl significantly reduced the response.

Mianserin HCl

Vehicle

Trazodone Haloperidol BuspironeHCl HCl

Fig. 2. Effects of buspirone HCl versus other serotonin and dopa-mine receptor antagonists (administered systemically) on 24-hour ear swelling associated with a contact hypersensitivity response.

Discussion

We report here the previously unknown immunosuppressive activity of the safe, widely used drug buspirone HCl (BuSpar®, a Mead Johnson product). Systemic administration of this drug resulted in significant reduction in both the swelling and inflammatory cell infiltration (data not shown) associated with the immune response. Additionally, topical administration resulted in the localized reduction of both of these characteristics of the immune response, without observable systemic side effects.

The role of serotonin (5-hydroxytryptamine, 5-HT) has been investigated in cell-mediated immunity, including contact hypersensitivity [reviewed in ref. 1]. However, the data presented here suggest that buspirone HCl, although documented to have an affinity for serotonin receptors,

probably acts as an immunosuppressant in contact hypersensitivity via another mechanism.

Buspirone is a safe drug with a long history of use in humans for the treatment of anxiety. Our results suggest that buspirone may represent an effective treatment for undesirable immunological responses in the skin and perhaps other sites. Moreover, by applying buspirone topically, it may be possible to induce local immunosuppression without systemic side effects. Systemic administration of buspirone might be useful for a variety of immunological disorders, including atopic dermatitis and related conditions that affect large areas of the skin.

Reference

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