

Mechanisms and Treatments of Dry Skin Induced itch

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ABSTRACT

Pruritus (itch) is an unpleasant sensation of the skin that causes a scratching impulse. Itch sensation is produced by binding itch-inducing substances (pruritogens) on peripheral sensory afferents, especially C-fibers, to their cognate receptors (pruriceptors). The evoked action potential is transmitted to the somatosensory cortex via the ascending sensory pathway, resulting in itch perception. Since histamine is a well-known pruritogen, the first line of treatment against itch is antihistamines (histamine H1 receptor antagonists). However, in some dermatological conditions, such as xerosis, atopic dermatitis (AD) and psoriasis, and systemic diseases such as chronic renal failure and chronic cholestasis, which are characterized by dry skin, antihistamines are not fully effective. Hence, dry skin is thought to be an essential antihistamine-resistant (histamine-independent) itch feature.

The skin is the body's largest organ which covers the body and provides the outer environment with the first physiological barrier. Skin not only prevents damage caused by adverse external factors, acting as an external barrier to the inside, but also loss of moisture and nutrients, acting as an external barrier within. Loss of integrity of the skin barrier thus causes vital internal water to evaporate from the skin, contributing to dryness of the skin. Disruption of the skin barrier by tape stripping or treatment with acetone, diethyl ether and water (AEW) has been found to improve dry skin characteristics including increased transepidermal water loss (TEWL) and decreased stratum corneum hydration (SC). Specific forms of pruritogens and pruritogen-associated factors fluctuate in cutaneous cells following induction of dry skin. Notably, in contrast with animal models involving acute barrier destruction by tape stripping or single acetone treatment, animals receiving continuous AEW treatment demonstrated increased scratching activity induction, with the latter depending on the number of treatments. This AEW model is often characterized by irregular itch sensations, called alloknesis (itch caused by non-itchy stimuli) and hyperknesis (enhanced itch caused by itchy stimuli).

The binding of itch-inducing compounds (pruritogens) to their cognate receptors (pruriceptors) on peripheral

sensory afferents induces the sense of itch. Because histamine is a well-known pruritogen, antihistamines are the most often used class of agents for the treatment of itch. In some dermatological and systemic diseases characterized by dry skin, however, antihistamines are not fully effective, suggesting dry skin is an important feature of antihistamine-resistant itch. Recent studies have identified various pruritogens and pruriceptors involved in a dry-skin patient, such as xerosis, and a mouse model of dry skin-induced itch involving continuous acetone, diethyl ether, and water (AEW). Continuous AEW treatment in contrast with single acetone treatment showed increased induction of scratching activity, with the latter depending on the number of treatments. The result, that increased scratching activity needed repeated AEW care, suggested that itch induced by dry skin was not only caused by disruption of the skin barriers. Additionally, this mouse model displays irregular itch symptoms, including alloknesis (itch induced by non-itchy stimuli) and hyperknesis (enhanced itch induced by itchy stimuli) that may result from neural sensitization (i.e. reduction of neural thresholds for stimuli). Dry skin-induced itch can be caused not only by concentrations of pruritogens and pruriceptors, or by nerve fiber distributions, but also by functional changes in neurons. To date, dry skin-induced itch has not provided widely approved therapy. Moisturizers enhance the working of the membranes and help relieve pruritus. Following a decline in skin barrier function, neural sensitization and itch-scratch-itch process may cause varying conditions in dry skin. Thus treatment can involve the vicious cycle of itch-scratch-itch prevention and rapid disruption.

Keywords: Dry skin; Neural sensitization; Epidermal nerve fibers; Moisturizer; Itch; Pruritogen