Role of cutaneous prostaglandin D$_2$ level in the itch-scratch reaction in mice

Iwao Arai, Yuki Hashimoto, Masanori Sugimoto, Norikazu Takano, Nobuko Futaki, Akiko Takaoka, Tomoyuki Inoue and Shiro Nakaike
(Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd.)

Itching, which elicits the reaction of scratching, is considered to be a physiological phenomenon to eliminate foreign matter from the skin surface. In addition, however, scratching can also be a skin disrupting behavior. It is, therefore, presumed that there may be some strict regulatory mechanism to suppress excessive skin disruption and maintain cutaneous homeostasis. We examined the effects of various substances in NC/Nga mice, a known animal model of atopic dermatitis, using prolonged scratching as an indicator of itching. The results revealed that while indomethacin aggravated the scratching, and prostaglandin D$_2$ (PGD$_2$) significantly suppressed it. These results suggest that PGD$_2$ plays a physiological inhibitory role against pruritus in the NC/Nga mice. Therefore, we investigated the relationship between scratching and the cutaneous PGD$_2$ production level using the mechanical scratching test. Mechanical scratching increased the skin damage and cutaneous PGD$_2$ levels in a scratch-count-dependent manner, suggesting the existence of a regulatory mechanism for itching, in which scratching increases the cutaneous PGD$_2$ production, and PGD$_2$, in turn, suppresses the pruritus. To investigate the relationship between scratching and the cutaneous PGD$_2$ levels in NC/Nga mice, the cutaneous PGD$_2$ levels were compared between NC/Nga mice without dermatitis and NC/Nga mice with dermatitis. The results revealed that aggravation of the scratching in the spontaneous dermatitis model was caused by a defect in the ability to produce PGD$_2$, which has a physiological inhibitory role against pruritus, resulting in the development of dermatitis.