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Local administration of genistein as a local anesthetic agent inhibits the trigeminal nociceptive neuronal activity in rats

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ABSTRACT

A modulatory role has been reported for the isoflavone, genistein, on voltage-gated Na⁺ channels in the trigeminal ganglion *in vitro*. However, the acute effects of genistein *in vivo*, particularly on nociceptive transmission in the trigeminal system, remain to be determined. The aim of the present study was to examine whether acute local genistein administration to rats attenuates the excitability of wide-dynamic range (WDR) spinal trigeminal nucleus caudalis (SpVc) neurons in response to nociceptive and non-nociceptive mechanical stimulation *in vivo*.

Extracellular single unit recordings were made from SpVc WDR neurons in response to orofacial non-noxious and noxious mechanical stimulation of pentobarbital-anesthetized rats. The effects of local administration of genistein, lidocaine, and lidocaine with genistein to the receptive field on the discharge frequency of SpVc neurons were evaluated. The mean firing frequency of SpVc WDR neurons in response to both non-noxious and noxious mechanical stimuli was significantly and dose-dependently (0.1–10 mM) inhibited by genistein, and maximum inhibition of the discharge frequency of both non-noxious and noxious mechanical stimuli was seen within 10 min. The inhibitory effect of genistein lasted for 20 min and was reversible. No significant difference was seen between the relative magnitude of inhibition by genistein on the SpVc WDR neuronal discharge frequency for noxious and non-noxious stimulation. The mean magnitude of inhibition by genistein (10 mM) on SpVc neuronal discharge frequency was almost equal to that of the local anesthetic, 1% lidocaine (37 mM). Local injection of half-dose of lidocaine replaced the half-dose of genistein. These results suggest that local injection of genistein into the peripheral receptive field suppresses the excitability of SpVc neurons, possibly via inhibition of voltage-gated Na⁺ channels in the nociceptive nerve terminals of trigeminal ganglion. Therefore, administration of genistein as a local anesthetic may provide relief from trigeminal nociceptive pain without side effects, thus contributing to the area of complementary and alternative medicines.

ハイライト: これまでに大豆に含まれるイソフラボンの一つ「ゲニステイン」は *in vitro*の実験では電位依存性Naチャンネルを修飾することで一次感覚ニューロンの興奮性を変調させることは判明しておりましたが、*in vivo*での効果は不明でした。今回我々は二次感覚ニューロンの細胞外記録法を用いて「ケルセチン」が既存の局所麻酔酔薬と同等の効果を発揮することを明らかとして補完代替医療に応用できる可能性を指摘致しました。