THE MECHANISM OF PAIN RELIEF IN EXTRACORPOREAL SHOCK-WAVE THERAPY

INTRODUCTION: There have been many reports on the use of extracorporeal shock-waves for the treatment of chronic plantar fasciitis. However, the mechanism of pain relief from this therapy has not yet been clarified. Although shock-wave treatment was applied repeatedly (usually three times) for pain relief in past reports, there is no scientific basis for such protocols. To investigate the analgesic properties of shock-wave application, we examined whether it produced morphologic changes in cutaneous nerve fibers from the plantar skin (experiment 1) or dorsal root ganglia (DRGs) (experiment 2) in rats and compared the effect of a single shock-wave application on cutaneous nerve fibers from the plantar skin with that after two shock-wave applications (experiment 3).

METHODS and RESULTS: [Experiment 1] Low-energy shock-waves were applied to the planter skin of fifteen rats. The planter skin of the rat hind paws was then resected. Skin sections were processed immunohistochemically using antibodies to PGP 9.5 and CGRP. PGP 9.5 is a marker present in all types of nerve fibers, and CGRP is a marker of sensory fibers typically involved in pain perception. Result 1: The number of PGP 9.5-immunoreactive (IR) or CGRP-IR nerve fibers on days 2, 4, and 7 were significantly less than in non-treated skin. However, on days 14 and 21, no significant differences in these values were observed between shock-wave treated and non-treated rats. (Fig1)(1) [Experiment 2] In twelve rats, DRG neurons innervating foot pad were labeled by using Fluorogold crystals (FG) as a neurotracer. Low-energy shock-waves were applied to the foot pads of 6 rats (shock-wave group). Immunohistochemistry with antibody to CGRP was performed on DRG sections. Result 2: In the untreated control group, FG-labeled CGRP-IR DRG neurons comprised 61% of the FG-labeled DRG neurons, but in the shock-wave group only 18% of FG-labeled DRG neurons were CGRP-IR. The percentage of FG-labeled CGRP-IR DRG neurons in the shock-wave group was significantly less than that in the control group. [Experiment 3]: Shock-waves were applied to the foot pads of 36 rats. After 14 days, 18 rats received a second, identical shock-wave application. After immunohistochemistry for PGP 9.5 and CGRP, cutaneous nerve fibers were counted. Result 3: In single and double application shock-wave groups, the numbers of PGP 9.5 and CGRP-IR nerve fibers were significantly less than those of the control groups during 4-week period after the final application of shock-waves. However, the number of these nerve fibers at day 42 in single treatment group was significantly more than in the repeated treatment group.

DISCUSSION: Shock-wave application may lead to the release of CGRP in free nerve endings or the destruction of the nerves labeled by CGRP and PGP 9.5. We concluded that the decrease of CGRP in nerve endings following shock-wave application induced a depression in CGRP levels in DRG neurons and in the spinal dorsal horn. Reinnervation of the epidermis commenced during the 2 to 3-week period after the application of shock-waves. Shock-waves have been applied two or three times, at weekly intervals, because one application was thought to be insufficient. The observation that reinnervation of the epidermis by CGRP-IR nerve fibers after two shock-wave exposures is less and that two shock-wave exposures more effectively causes degeneration of nerves labeled by CGRP and PGP 9.5 may explain the clinical analgesic effect of repeated extracorporeal shock-wave therapy.

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Fig 1: The number of PGP9.5-IR or CGRP-IR sensory nerve fibers over time.

Fig 2: In non-treated rat skin, PGP 9.5 –IR nerve fibers are abundant in the epidermis.

Fig 3: On day 7 after second shock-wave application, PGP 9.5 –IR nerve fibers are rarely observed.

Reference