Capsaicin restores cutaneous microcirculation in diabetes: a capillaroscopic study

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Summary

Background. Capsaicin (8-methyl-N-vanillyl-6-nonenamide), the active component of the chilli peppers, is able to induce receptor desensitization and defunctionalisation of peripheral nociceptors. It can induce also vascular responses by different mechanisms.

Objectives. Hypothesis that skin application of capsaicin could have beneficial effects on cutaneous microcirculatory dysfunction associated with diabetes.

Materials and methods. Videocapillaroscopic examination of periangual vascular pattern before and after application of topical capsaicin in diabetic patients.

Results. Skin application of 15% capsaicin oleoresin caused a local improvement in microvascular function in diabetic patients.

Conclusions. Topical capsaicin application may be beneficial for the management of microvascular complications in diabetic patients.

KEY WORDS: capsaicin; diabetes; TRPV1; cutaneous microcirculation; videocapillaroscopy; microangiopathy.
Each patient was examined while in sitting posture after an acclimatisation of 30 minutes at a room temperature of 20-26°C. Videocapillaroscopy at 50x and 200x magnification was performed on the nailfold of the fourth finger of the left hand (Figure 1). The following parameters were evaluated: number of vessels (increased, decreased, normal), distribution, morphology, length, presence of volutes and tortuosities and flow rate. To increase initial transparency during morphological videocapillaroscopic examination, a drop of immersion oil was placed on the nailfold.

After the initial videocapillaroscopic evaluation, AISPES Capsaicin oleoresin 15% (2ml) was applied topically on the nailfold and the same parameters were examined at 5 and 15 minutes from application. 15% Capsaicin oleoresin was applied to all patients once a day during 7 days with a dropper, directly on the nailfold of the fourth finger of the left hand. In order to verify the vasoactive effect of a one week application of topical Capsaicin, all patients were examined by Lunedei’s Test and CO₂ Cryotest after 7 days of capsaicin oleoresin application. Lunedei’s Test is performed by applying a tourniquet above the elbow and waiting 2 minutes at 5mmHg above the patients systolic pressure, then 5 minutes at 5 mmHg below patient’s systolic pressure. The tourniquet is then removed and the presence of ecchymoses using videocapillaroscopy is examined, cronometering and recording the time taken for normal microcirculation to appear. CO₂ Cryotest consisted in application of a balloon filled with cold water (12 or 15°C) to the left hand, until the skin temperature of 26°C was reached. The cold water balloon was subsequently removed and the reactive vasodilatation was observed. The time taken for the vasodilatation to disappear was then cronometered and recorded.

Results

In the 10 diabetic patients evaluated at time 0, the following morpho-functional aspects were found by capillaroscopic evaluation (Table 1): (i) decrease in capillary number, (ii) dilatation and tortuosities of capillaries in all nailfolds, (iii) decreased flow rate, and (iv) several volutes in capillary morphology. At 5 min from the application of 2 ml of 15% capsaicin oleoresin, we observed a reduction of capillary calibre and disappearance of venous stasis because of reduced vessel diameter. Finally, a 7-day treatment...
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Table 1 - Patient characteristics and capillaroscopic features.

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Legend: - decrease; + no modification; ++ increase; +++ marked increase.

with capsaicin caused an almost complete disappearance of the abnormal vascular response to the Lunedei's test and normalized the recovery time to CO₂ cryotest.

Discussion

Capsaicin is widely studied for its role in pain transmission and in mechanisms of nociceptive sensitization. However, a large body of evidence suggests that TRPV1 receptors, the molecular targets of capsaicin, are expressed not only in neurons but also in non-neuronal cells, such as smooth muscle cells and endothelial cells of blood vessels (9). Capsaicin causes vascular responses, which result from neurogenic mechanism (vasodilation, increase in vascular permeability) (5), as well as from a direct action of capsaicin on TRPV1 receptors expressed by the endothelium (vasodilation) or smooth muscle cells (vasoconstriction) (10).

We have shown here that skin application of 15% capsaicin oleoresin caused a local improvement in microvascular function in diabetic patients. The precise mechanisms underlying this beneficial effect of capsaicin in diabetic patients remain to be determined. Diabetic neuropathy is known to be associated with a reduced production of CGRP, a vasoactive molecule that is under the control of TRPV1 receptors in nerve terminals, and causes neurogenic vasodilation (11). Activation of TRPV1 by capsaicin may cause an increased CGRP release, thereby restoring the blood vessel response to stimulation of sensory nerve endings (12). However, this mechanism cannot explain the beneficial effect seen after 7-day treatment with capsaicin, which should result into TRPV1 desensitization and a lower secretion of CGRP and other vasoactive compounds from nerve terminals. It is possible that TRPV1 receptors expressed on endothelial cells are refractory to capsaicin-induced desensitization (for example, because of a high receptor reserve), and their activation stimulates nitric oxide formation (with resultant vasodilation and vasoprotection) during the 7-day treatment with capsaicin. This hypothesis warrants further investigation on isolated capillary vessels or cultured endothelial cells obtained from control or diabetic patients.

This study may be biased for the absence of a group control of patients. Further studies are needed to better clarify the pathogenetic mechanism that correlate the topical capsaicin in the management of microvascular complications in diabetic patients.

Further studies are needed to establish whether, and to what extent, this particular approach can be applied to the treatment of diabetes complications.

Disclosure. The Authors declare no conflict of interests.
References