A critical evaluation of iontophoresis as used in physiotherapy

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Introduction

In physiotherapy iontophoresis is used to enhance the penetration of drugs in the topical treatment of muscles, tendons and joints (Gudeman et al., 1997). In practice the drug is applied under a wet cellulose sponge which covers the electrode. The used current intensity is rather limited: up to maximum 0.5 mA/cm² during 20 minutes. When screening the literature on iontophoretic delivery as used in physiotherapy, we observed that in most human in vivo studies, some basic principles of percutaneous penetration were not always taken into account. Indeed the iontophoretic delivery is seldom evaluated versus passive diffusion. Iontophoretic delivery is usually compared with a placebo without active ingredient. Since the passive penetration can be substantial during the delivery, it is important to include this control to estimate the enhancement factor. In this study we investigated the bioavailability of iontophoretically delivered diclofenac with the methylnicotinate (MN) test. The inhibition of an erythema provoked by MN is proportional with the bioavailability of diclofenac in the skin. It was our aim to use this procedure in the determination of the contribution of respectively the passive diffusion, the occlusion and the electrically assisted delivery during an iontophoretic procedure as used in physiotherapy.

Methods

A total of 6 application sites was marked on the volar forearm of each volunteer (n=12), for the following treatment and/or control modes: A= Cathodal iontophoresis of 12mg/cm² Voltaren Emulgel® (Diethylammonii diclofenac 1%) during 20 minutes; B=passive diffusion under a contact sponge; C=passive diffusion without any covering; D=current alone; E=standard MN response and F=blanco site. Tristimulus surface colorimetry and Laser Doppler flowmetry were used to measure respectively the skin color (a* parameter) and the perfusion of the microcirculation. Bioavailability was assessed by quantification of a MN induced erythema under the different conditions. Areas under the response curve were compared using an ANOVA procedure followed by the Sheffé’s test. Significance level was set at 5%.

Results

A significant reduction of the MN induced erythema was observed with the Chromameter and Laser Doppler measurements for the following treatment modalities: (1) electrically assisted delivery: respectively 65 and 100%, (2) application under the contact sponge: 66 and 97%, (3) passive diffusion without occlusion: 32 and 65%. A significant reduction was equally observed for the site treated with the current alone: 19 and 42%. There was no significant difference between the response after iontophoretically delivered diclofenac (Mode A) and application of diclofenac under the contact sponge (Mode B).

Fig. 1: Colorimetric evaluation of the microcirculation: response to a MN application; comparison of the different application modes expressed in percentage of the standard MN response. a* = dimensionless color units. Data presented as total kinetic response (area under the curve) corrected for blanc values. *= p<0.05, **= p<0.001, compared with standard MN response

Conclusion

The used procedure enabled us to evaluate the bioavailability of a non-steroidal anti inflammatory drug in the skin. Under the used conditions we did not find an increased bioavailability after electrically assisted delivery of diclofenac compared with the passive percutaneous penetration under the contact sponge. This may be an indication that the occlusion and not the current is the enhancing factor during iontophoresis as used in physiotherapy.

Reference