Topical versus systemic Diclofenac in the treatment of temporomandibular joint dysfunction symptoms

**Confronto Diclofenac topico versus sistemico nel trattamento dei sintomi da disfunzione dell’articolazione temporomandibolare**

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**Summary**

The most frequent symptom of cranio-mandibular dysfunction is pain in the preauricular area or in the temporomandibular joint, usually localized at the level of the masti- catory musculature. Patients sometimes also complain of reflect otalgia, headaches and facial pain. Osteoarthrosis is a frequent degenerative debilitating chronic disorder that can affect the temporomandibular joint. It causes pain and articular rigidity, a reduction in mobility, and radiological alterations are visible in stratigraphy. The aim of this study was to compare the efficacy of a topically applied non-steroid anti-inflammatory drug that has recently become commercially available (diclofenac sodium in a patented carrier containing dimethyl sulfoxide, that favours transcutaneous absorption) which is commonly used to alleviate pain in knee or elbow joints, versus oral diclofenac, in the treatment of symptoms of temporomandibular joint dysfunction. Dysfunction of the temporomandibular joint was diagnosed in 36 adult patients. The patients were randomized in two age- and gender-matched groups. Group A (18 patients) received oral diclofenac sodium administered after a meal in 50-mg tablets twice a day for 14 days. Group B (18 patients) received 16 mg/ml topical diclofenac (diclofenac topical solution, 10 drops 4 times a day for 14 days). All patients completed a questionnaire at the start and end of therapy. Patients were asked to quantify on a graded visual analogue scale and to reply to questions about the pain and tenderness of the temporomandibular joint and the functional limitation of mouth opening. Patients were also requested to report side-effects of the treatment. All patients showed relief from pain after treatment: the difference between the two groups was not significant (p>0.05). Post-treatment, 16 patients of group A had epigastralgic symptoms. Three patients treated with topical diclofenac showed a modest irritation of the temporomandibular joint region, and disappeared spontaneously. Our results demonstrate that topically applied diclofenac and oral diclofenac are equally effective in the treatment of temporomandibular joint dysfunction symptoms. Topical diclofenac has the advantage that it does not have adverse systemic effects, whereas oral diclofenac had untoward effects on the gastric apparatus. The efficacy of diclofenac topically applied on the temporomandibular

**Key words**

Temporomandibular joint • Dysfunction • Arthrosis • Treatment • Diclofenac

**Parole chiave**

Articolazione temporo-mandibolare • Disfunzione • Artrosi • Trattamento • Diclofenaco

**Riassunto**

Il sintomo più frequente delle disfunzioni cranio-mandibolari è il dolore della regione dell’articolazione temporomandibolare. Talvolta i pazienti lamentano anche otalgia riflessa, cefalea e dolore facciale. L’osteoarthrosi è una frequente patologia degenerativa debilitante cronica che può colpire anche l’articolazione temporomandibolare e che causa dolore e rigidità articolari con riduzione della mobilità, con alterazioni radiologiche ben riconoscibili alla stratigrafia.

Abbiamo confrontato l’efficacia di un farmaco anti-infiammatorio non stereideo topico di recente immissione sul mercato (Diclofenac sodico con un veiculante brevettato brevettato dimetilsolfossido in grado di favorire l’assorbimento transcutaneo), comunemente usato per alleviare il dolore nell’articolazione del ginocchio o del gomito contro un farmaco anti-infiammatorio non stereideo orale (Diclofenac) nel trattamento dei sintomi da disfunzione dell’articolazione temporomandibolare. 36 pazienti adulti con disfunzione dell’articolazione temporomandibolare sono stati randomizzati in due gruppi omogenei (A e B) per sesso ed età. Il gruppo A di 18 pazienti è stato trattato con diclofenac sodico per via orale assunto a stomaco pieno in compresse da 50 mg per 2 somministrazioni al di per 14 giorni, il gruppo B di 18 pazienti con diclofenaco per uso topico 16 mg/ml (diclofenaco soluzione topica 10 gocce 4 volte al di per 14 giorni). Tutti i pazienti all’inizio ed al termine della terapia hanno compilato un questionario con particolare riguardo ai singoli sintomi dolore e dolorabilità dell’articolazione temporomandibolare e limitazione funzionale dell’apertura della bocca, quantificati dal paziente con una scala analogica visiva graduata e con questionari dedicati. È stato richiesto inoltre specificamente di indicare eventuali effetti collaterali legati al trattamento. Tutti i 36 pazienti hanno manifestato sensibile miglioramento della sintomatologia dolorosa dopo il trattamento senza differenze significative tra i due gruppi (p>0.05). L’88,8% (16 pazienti) dei 18 pazienti trattati con farmaco anti-infiammatorio non stereideo orale al termine della terapia hanno manifestato sintomi esofago-gastrico. Tre pazienti trattati con diclofenaco topico hanno mostrato solo una modesta irritazione e sensazione di calore sulla regione cutanea trattata, risoltasi spontaneamente. I nostri risultati dimostrano la stessa efficacia del diclofenaco topico rispetto alla terapia con diclofenaco sistemico nel trattamento dei sintomi della disfunzione dell’articolazione temporomandibolare. Il vantaggio dell’impiego del diclofe-
Introduction

Craniomandibular dysfunctions (CMD) constitute a group of disorders often associated with painful signs and symptoms that can affect one or more components of the masticatory apparatus, i.e., the temporomandibular joint (TMJ), mastication muscles, and teeth and their support structures. It is noteworthy that dimethyl-sulfoxide favours transcutaneous absorption when used in a multi-dose regime as in our study with 4 doses a day. Thus, single, “as required”, applications should be avoided because this practice results in scarce absorption of diclofenac.

Materials and methods

Sixty-four patients with pain in the ear and mandibular region were evaluated by ENT examination, audiometric test and impedenzometry, a dedicated flow-chart (Fig. 1) and, if necessary, stratigraphy of the TMJ, which is a low-cost procedure that provides information about mandibular joint movements (Fig. 2). Twenty-eight patients were excluded from the study because they were affected by inflammation of the middle ear. Dysfunction of the TMJ was diagnosed in 36 patients (34-61 years, median 43 years, 19 female and 17 male). The patients were randomized in two age- and sex-matched groups. Group A (18 patients) received oral diclofenac sodium administered after a meal in 50 mg tablets twice a day for 14 days. Group B (18 patients) received 16 mg/ml topical diclofenac (diclofenac topical solution, 10 drops 4 times a day for 14 days). Forty drops correspond to 1 ml of topical solution and thus contain 16 mg of diclofenac sodium in a carrier containing DMSO. All patients were requested to complete a questionnaire at the start and end of therapy. In particular, patients were asked to quantify on a graded VAS (0 min; 10 max) and to reply to questions about the pain and tenderness of the TMJ and the functional limitation of mouth opening (Fig. 3). Patients were also requested to report side-effects of the treatment.
Results

All patients showed relief from pain after treatment (Table I); the difference between the two groups was not significant (p > 0.05). Post-treatment, 16 patients of group A had epigastralgia at the end of therapy, 12 epigastric burning and 7 retrosternal burning (Table II). No significant differences were found in functional limitation of mouth opening between the two groups (p>0.05) (Table III). Three patients treated with topical diclofenac showed a modest irritation and heat sensation on the cutaneous region treated. This was due to friction during application of the drops, and disappeared spontaneously.

Conclusions

NSAIDs are effective for the control of symptoms of TMJ dysfunction. Our results demonstrate that topically applied diclofenac and oral diclofenac are equally effective in the treatment of TMJ dysfunction symptoms. Topical diclofenac has the advantage that it does not have adverse systemic effects,
whereas oral diclofenac had untoward effects on the gastric apparatus. Given the high incidence of dental and malocclusion disorders especially in the adult and elderly population, an effective treatment without undesirable effects is particularly important also because these patients often undergo multiple treat-
ment with drugs that may exert gastric effects. None of our patients had relevant limitations in mouth opening; hence it is not possible to establish significant differences between the two groups. The efficacy of diclofenac topically applied on the TMJ region observed in group B may be explained by the association of diclofenac with DMSO, which enables a rapid effective penetration into the joint tissues. Moreover, studies with radio-markers demonstrated that topical diclofenac is not metabolized in the skin during transdermic absorption, and is thus able to act effectively and safely without being metabolized.

In fact, sequential time analyses of blood and urine samples to determine the pharmacokinetics, bioavailability and metabolism of topical diclofenac, showed that the drug was excreted in urine in the form of hydroxyl conjugated metabolites. This suggests a continuous delivery of diclofenac sodium from the lotion into and through skin which only ceased when the dosing site was washed.

It is noteworthy that DMSO favours transcutaneous absorption when used in a multi-dose regime as in our study with 4 doses a day. Thus, single, “as required”, applications should be avoided because this practice results in scarce absorption of diclofenac. In fact, an in vitro study of human skin and topical radiolabelled diclofenac lotion demonstrated that transcutaneous absorption of topical diclofenac increased remarkably in relation to the number of applications, and absorption continued to increase up to 48 hours.

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### Table III. Mean VAS scores for mandibular opening in the two groups before and after treatment.

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<th>Functional mandibular limitation (Mean VAS)</th>
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<td></td>
<td>Pre-treatment</td>
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<td>Therapy with topical NSAID (group B)</td>
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**References**


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