Topical versus systemic Diclofenac in the treatment of temporo-mandibular joint dysfunction symptoms

Confronto Diclofenac topico versus sistemico nel trattamento dei sintomi da disfunzione dell'articolazione temporo-mandibolare

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Key words

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Parole chiave

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

Summary

The most frequent symptom of craniomandibular dysfunction is pain in the preauricular area or in the temporomandibular joint, usually localized at the level of the masticatory 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

Riassunto

Il sintomo più frequente delle disfunzioni cranio-mandibolari è il dolore della regione dell'articolazione temporo-mandibolare. Talvolta i pazienti lamentano anche otalgia riflessa, cefalea e dolore facciale. L'osteoartrosi è una frequente patologia degenerativa debilitante cronica che può colpire anche l'articolazione temporo-mandibolare 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 steroideo topico di recente immissione sul mercato (Diclofenac sodico con un veicolante brevettato brevettato dimetilsolfossido in grado di favorire l'assorbimentotranscutaneo), comunemente usato per alleviare il dolore nell'articolazione del ginocchio o del gomito contro un farmaco anti-infiammatorio non steroideo orale (Diclofenac) nel trattamento dei sintomi da disfunzione dell'articolazione temporo-mandibolare. 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 dì per 14 giorni, il gruppo B di 18 pazienti con diclofenac per uso topico 16 mg/ml (diclofenac soluzione topica 10 gocce 4 volte al dì 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 temporo-mandibolare 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 steroideo orale al termine della terapia hanno manifestato sintomi esofago-gastrico. Tre pazienti trattati con diclofenac 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 diclofenac topico rispetto alla terpia con diclofenac sistemico nel trattamento dei sintomi della disfunzione dell'articolazione temporo-mandibolare. Il vantaggio dell'impiego del diclofe-

joint region observed in group B is explained by the association of diclofenac with dimethyl-sulfoxide, which enables a rapid effective penetration into the joint tissues. It is noteworthy that dimethyl-sulfoxide favours transuctaneous 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.

nac topico è la completa assenza di effetti avversi sistemici, in particolare sull'apparato gastrico. La validità da noi osservata del trattamento con diclofenac per uso topico nella regione dell'articolazione temporo-mandibolare trova motivo nella vantaggiosa associazione con il dimetilsolfossido che consente una rapida ed efficace penetrazione nei tessuti articolari. È importante ricordare che il dimetilsolfossido migliora l'assorbimento transcutaneo quando usato in regime multi-dose, come somministrato nel nostro studio con posologia di 4 volte al giorno, e sono pertanto da evitare singole applicazioni di diclofenac "al bisogno" in quanto caratterizzate da scarso assorbimento.

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 [1-3].
Epidemiological studies show a 33% prevalence of CMD with at least one symptom of facial or TMJ pain. The prevalence reaches 75% of the population if joint signs are included, namely, movement abnormalities, noises, and pain upon palpation [3 4].
The most frequent symptom of CMD is pain in the preauricular area or in the TMJ, usually localized at the level of the masticatory musculature. Patients sometimes also complain of reflect otalgia, headaches and facial pain [3 5]. Pain is usually increased by mastication or by mandibular functions, but it is often present also at rest (in the case of oral parafunctions or in the case of inflammation, such as synovitis, capsulitis, polyarthritis and acute osteoarthritis) [6 7]. Osteoarthrosis is a frequent degenerative debilitating chronic disorder that can affect the TMJ. It causes pain and articular rigidity, a reduction in mobility, and radiological alterations are visible in stratigraphy [3 7].
At present, there is no standard test with which to identify and characterize TMJ disorders. In about 90% of cases, these disorders can be diagnosed from the symptoms and the patient's history, and an accurate physical examination. The latter should include examination of the patient's mouth, palpation of the masticatory muscles, auscultation of joint noises, and mandibular function appraisal (i.e., opening and laterality movements of the jaw bone). Pain is quantified by the patient on a graded scale, e.g., a visual analogue scale (VAS) that measures functionality and pain intensity. These data can also serve to evaluate the effectiveness of therapy.
Oral non steroidal anti-inflammatory drugs (NSAID) are the most commonly used drugs in osteoarthrosis treatment, but their long-term use causes gastro-intestinal disorders such as gastritis and ulcer. Differently, topically applied NSAID do not induce adverse gastro-intestinal effects because, being scarcely absorbed systemically and reaching very low serum levels, they have a low toxicity [8].
The aim of this study was to compare the efficacy of a topically applied NSAID that has recently become commercially available (diclofenac sodium in a patented carrier containing dimethyl sulfoxide [DMSO], 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 TMJ dysfunction.

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.

Fig. 1. Physical examination for the evaluation of craniomandibular dysfunction.

Extra-oral examination

Facial asymmetry	Yes___	No___	Short lower third	Yes___	No___
Ligamentous hyperlaxity	Yes___	No___	Anomalous labial posture	Yes___	No___
Deep chin fold	Yes___	No___	Flat labial profile	Yes___	No___
Cervical torticollis	Yes___	No___	Forward head posture	Yes___	No___
Long lower third	Yes___	No___	Speech anomalies	Yes___	No___

Examination of the TMJ and of the emergences of the cranial nerves

Painful zones at palpation (values from 0 to 5). Examination date _____

	right	left
Palpation of the lateral condyle polus		
(at rest)	_____	_____
(with clenched teeth)	_____	_____
(at maximum opening)	_____	_____
Palpation of the posterior condyle polus (digito-auricular examination)		
(at rest)	_____	_____
(with clenched teeth)	_____	_____
(at maximum opening)	_____	_____
Palpation of the coronoid process	_____	_____
Palpation of the emergences of the III branch of the trigeminal nerve	_____	_____
Palpation of the emergences of the II branch of the trigeminal nerve	_____	_____
Palpation of the emergences of the I branch of the trigeminal nerve	_____	_____

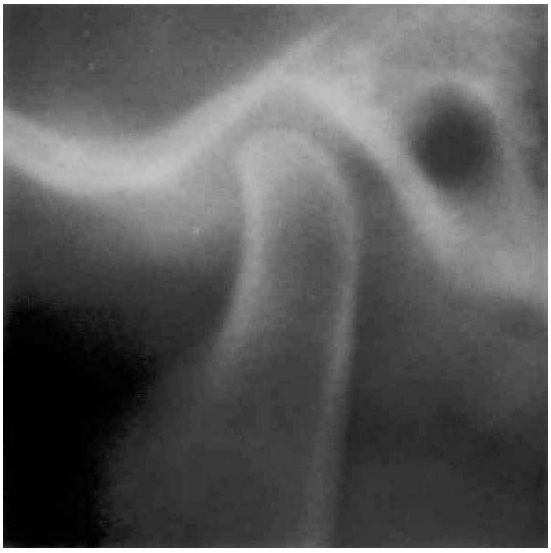

Fig. 2. Temporomandibular stratigraphy showing mandibular condyl hypoplasia in a patient with craniomandibular dysfunction.

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,

Fig. 3. Questionnaire to evaluate symptoms of temporomandibular dysfunction.

Onset of joint pain

Morning afternoon evening night

Degree of pain (0 absence of pain; 10 maximum pain)

1 2 3 4 5 6 7 8 9 10

Degree of tenderness (0 absence of tenderness; 10 maximum tenderness)

1 2 3 4 5 6 7 8 9 10

Functional limitation of mandibular movements (0 difficulty in opening mouth; 5 maximum opening)

1 2 3 4 5

Joint noises? yes no

Localization: right left bilateral

Presents following symptoms:

1. burning sensation in the stomach yes no
2. sensation of retrosternal oppression yes no
3. epigastric pain yes no

Table I. Average VAS scores for pain and tenderness before and after treatment with oral or topical NSAID.

	PAIN (Mean VAS)		TENDERNESS (Mean VAS)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Therapy with oral NSAID (group A)	7.2	1.1	9.2	1.9
Therapy with topical NSAID (group B)	7.1	1.2	8.9	1.5

Table II. Side effects of oral versus topical NSAID.

	Number of patients treated with oral NSAID (group A)	Number of patients treated with topical NSAID (group B)
Epigastric burning	12	0
Retrosternal oppression sensation	7	5
Epigastralgia	16	1

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-

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

	Functional mandibular limitation (Mean VAS)	
	Pre-treatment	Post-treatment
Therapy with oral NSAID (group A)	4.1	4.8
Therapy with topical NSAID (group B)	3.9	4.9

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 [9] [10]. 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 [9].
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 [11].

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