J Maxillofac Oral Surg 8(2):167–172

CLINICAL STUDY

A comparitive study of diclofenac transdermal patch against oral diclofenac for pain control following removal of mandibular impacted third molars

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Received: 03 July 2009 / Accepted: 04 July 2009

Abstract
Objective The objectives of this study was to evaluate subjectively the analgesic efficacy of Oral Diclofenac Sodium against Diclofenac Sodium Transdermal patch in the management of postoperative pain following surgical removal of impacted mandibular third molars.
Materials and methods Twenty healthy subjects belonging to both the sexes in the age group of 18–40 years with bilateral mesioangular impactions of mandibular third molar teeth underwent surgical removal under local anaesthesia by administering an inferior alveolar nerve block on two different occasions with a minimum interval of 1 week in-between the procedures. The postoperative pain was recorded on visual analog scale, a verbal rating scale, a pain relief scale and a pain intensity scale. Readings were taken at 2 hours, 4 hours, 8 hours, 12 hours and 24 hours postoperatively, taking the time at which the surgery was completed as a reference. On the second and third days, the repeat medication was administered at that reference time and recordings taken at the same intervals for a total of 3 days. Patients received the study medication i.e. Diclofenac Sodium 100mg once a day for 3 days after performing surgery on one side and the same patients were given Diclofenac Sodium Transdermal Patch 100mg once a day for 3 days after performing surgery on the contralateral side.
Results and observations Both the statistical analysis and clinical observation showed that on the first postoperative day diclofenac sodium administered orally has slightly more significant efficacy when compared to the drug administered transdermally. However, on the second and third postoperative days there was no statistical or clinical difference in the pain control by either route of administration.
Conclusions The study concludes that transdermal diclofenac sodium can be used as an alternative form of pain control following removal of impacted mandibular third molars, however considering that the analgesic potency might be lesser in the immediate postoperative period, it might be prudent to use oral diclofenac sodium for immediate postoperative pain relief, following which transdermal route can be used for pain control.

Keywords Diclofenac sodium · Oral · Transdermal

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Introduction

Pain is one of the most commonly experienced symptoms in surgery and as such is a major concern to the surgeon. It is often spoken of as a protective mechanism, since it is usually manifested when an environmental change occurs that causes injury to responsive tissue [1].

One of the most important aspects of the practice of dentistry is the control or elimination of pain. In the past, pain has been so closely associated with dentistry that the words pain and

dentistry have become almost synonyms [1].

The third molar surgical experiences are desirable pain models to evaluate the analgesic efficacy and tolerability of oral analgesics due to the following characteristics, the surgeries are elective; patients are young and healthy and ambulatory. The performed procedures are consistent and are generally completed within 25 minutes. Patients undergoing removal of third molars, are considered standardized mode for the evaluation of acute surgical pain and especially those who present with bilaterally similar impacted lower third molars provide an opportunity to carry out two similar surgical procedures on separate occasions such patients act as their own controls in cross over trials. An estimated 63.5% of patients experience severe pain at sometime during the first day for this reason oral analgesic is provided as standard care for postoperative time periods for atleast 24 hours. Non steroidal antiinflammatory drugs work well to relieve mild to moderate intense postoperative pain caused by 3rd molar surgery [2].

Analgesic drugs can be administered in a variety of routes, including oral, parentral, inhalation as well as transdermal. Oral route carries the risk of first pass metabolism and loss of substantial quantities of the drug before it is absorbed systemically. Parentral administration of drugs can be extremely painful and sudden increase in drug concentration in the plasma could lead to certain adverse effects.

Transdermal administration has the advantages of being a very easy, simple route of administration without the disadvantages of the routes mentioned above and also comparatively fewer side effects and complications.

This study attempts to compare two different drug delivery systems in the management of postoperative pain following surgical removal of impacted mandibular third molars using diclofenac sodium as a standard drug which was administered in two different routes, oral and transdermal.

Table 1 Age and sex distribution of patients

Age and sex distribution	
Age in years; Mean ± SD	23.90 ±7.46
Sex; Male: Female	13:7

Table 2 Comparison of VAS score in oral and patch

VAS	Oral		Patch		P value
	Mean	SD	Mean	SD	
DAY 1					
2 hour	4.7	2.7	5.5	2.7	0.178
4 hour	4.4	2.8	4.9	3.1	0.502
8 hour	3.5	2.9	4.3	3.3	0.284
12 hour	2.8	2.7	4.1	3.2	0.058
24 hour	2.4	2.2	3.1	3.2	0.256
DAY 2					
2 hour	2.8	2.4	2.9	3.0	0.838
4 hour	2.3	2.4	2.6	2.8	0.679
8 hour	2.1	2.3	2.4	2.6	0.699
12 hour	1.8	1.9	2.3	2.4	0.325
24 hour	1.6	1.5	2.0	1.9	0.322
DAY 3					
2 hour	1.5	1.9	1.3	1.7	0.519
4 hour	1.2	1.8	1.3	1.7	0.804
8 hour	1.2	1.8	1.3	1.6	0.725
12 hour	1.3	1.8	1.3	1.6	1.000
24 hour	1.2	1.5	1.2	1.6	0.789

Materials and method

Twenty healthy subjects belonging to both the sexes in the age group of 18–40 years, without any systemic diseases or previous drug allergy, who presented with bilaterally impacted mesioangular mandibular third molars to the department of Oral and Maxillofacial Surgery, Krishnadevaraya College of Dental Sciences and Hospital, Bangalore were selected for the study. The patients were informed about the nature and purpose of the study and the likely adverse effects and complications from the drugs being investigated. A written informed consent was obtained from all patients. Preoperative radiographs and routine hematological investigations were also performed.

Analgesics and Antibiotics were administered postoperatively. Following removal of the impacted mandibular third molar on one side the patients were given oral Diclofenac (Voveran SR) 100mg once daily and when the same patients returned back for the surgery on the contralateral side the drug administered was Diclofenac sodium transdermal patch (Nu Patch) 100mg once daily. The study drugs were administered to the patients 30 minutes after the surgery and the sides and drugs were randomly chosen.

The teeth were either sectioned or removed in toto. Standardization was

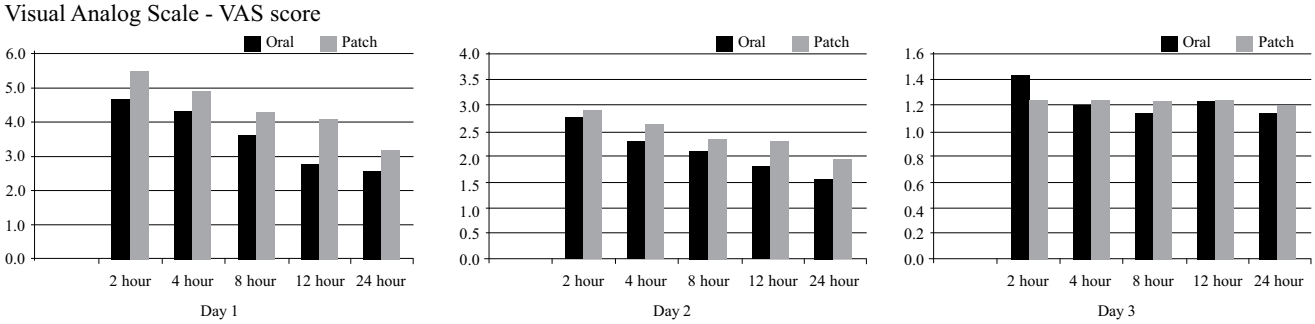


Table 3 Comparison of VRS score in oral and patch

VRS	Oral		Patch		P value
	Mean	SD	Mean	SD	
DAY 1					
2 hour	1.45	0.94	2.00	1.03	0.053
4 hour	1.25	0.97	1.70	1.03	0.107
8 hour	1.00	1.03	1.40	1.10	0.202
12 hour	0.85	0.88	1.20	0.95	0.090
24 hour	0.80	0.70	1.10	0.97	0.110
DAY 2					
2 hour	1.00	0.65	1.10	0.91	0.577
4 hour	0.90	0.72	1.00	0.86	0.577
8 hour	0.80	0.70	0.90	0.85	0.577
12 hour	0.70	0.73	0.85	0.75	0.419
24 hour	0.65	0.59	0.75	0.55	0.330
DAY 3					
2 hour	0.35	0.67	0.25	0.55	0.163
4 hour	0.25	0.55	0.20	0.52	0.330
8 hour	0.25	0.55	0.25	0.55	1.000
12 hour	0.30	0.57	0.30	0.57	1.000
24 hour	0.25	0.55	0.25	0.55	1.000

maintained by either removing both the teeth in the same patient in toto or both the teeth were sectioned and removed. Of the twenty cases in this study, in ten cases, the teeth were sectioned and removed and in ten cases the teeth were removed in toto.

The Transdermal diclofenac patch (Nu Patch) is one of the few drugs, which can be administered via the skin. It is used to relieve mild to moderate postoperative pain. It is applied once for duration of 24hrs and produces rapid pain relief with minimal or no side effects. The patch is to be applied on the skin, preferably in an area devoid of any hair. It comes in 2 strengths of 100mg and 200mg. this particular patch is a product of Zydus Cadila. The 100mg patch is 50 square cm in size and 200mg is 75 square cm in size. It is a flat and transparent device and is packaged in hermetically sealed, foil-lined packets. The patch achieves plasma levels ranging between 20 and 50ng/ml, which is lesser when compared to the oral route, but these levels are sustained for a longer time.

Oral formulation of diclofenac sodium (Voveran SR) was used in the dosage of 100mg and was administered once daily for a period of three days.

Four subjective scales were used to record the pain postoperatively. The Visual Analog Scale (VAS) and three other four point scales. A simple category scale, such as the four point 'none, mild, moderate and severe' scale is acceptable for recording pain magnitude, but need numbers to be assigned to each level (0,1,2,3) to quantify the data.

The four point scales used were a Verbal Rating Scale (VRS) [3], a Pain Relief Scale (PRS) [2] and a Pain Intensity Scale (PIS) [2]. Further a scale to record any adverse effects was also used.

The patients had to assign scores for each parameter at intervals of 2hrs, 4hrs, 8hrs, 12hrs and 24 hrs postoperatively. Further the patients were asked to assign scores for a total of 72 postoperatively.

Statistical methods

Descriptive analysis has been carried out with mean and Standard deviations were computed. Wilcoxons signed rank test has been used to find the significance of VAS, VRS, PRS an PIS between two drug delivery techniques namely, ORAL and PATCH

1. Significant figures

+ Suggestive significance $0.05<P<0.10$

* Moderately significant $0.01<P\leq0.05$

** Strongly significant $P\leq0.01$

Statistical software: The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Statistical analysis

Four scales were used to collect the data for this study. The Visual Analog Scale, The Verbal Rating Scale, The Pain Relief Scale and The Pain Intensity Scale.

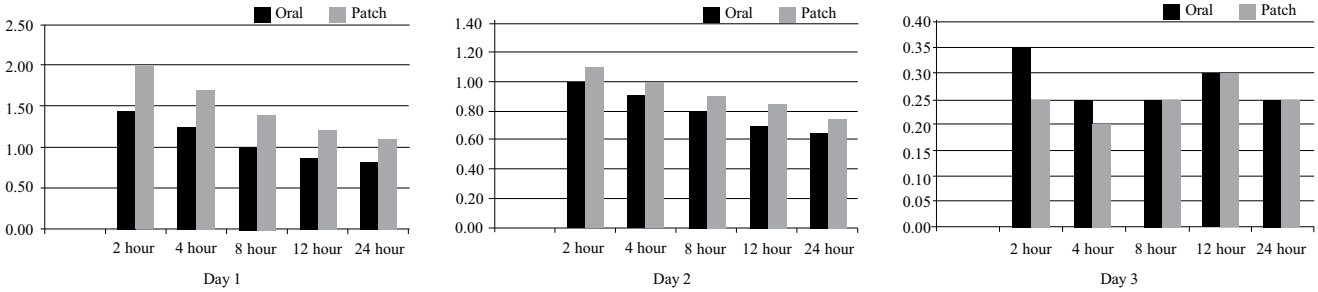
The VAS provides a simple, efficient, and non invasive measure of pain intensity that has been used widely in clinical and research settings where a quick index of pain is required and to which a numerical value can be assigned. The VAS consists of a l0 cm horizontal or vertical line with the two endpoints labeled 'no pain' and 'worst pain ever.' The patient is required to mark the l0 cm line at a point that corresponds to the level of pain intensity he or she presently feels, The distance in centimeters from the low end of the VAS and the patient's mark is used as a numerical index of the severity of pain.

Based on the statistical data, for the visual analog scale, the P value suggested significantly better pain relief on oral administration compared to transdermal at the 12 hour interval. The p values obtained suggested no difference in the efficacy of either route of administration over the subsequent two days of administration.

The Verbal Rating Scale is a four point scale with values assigned ranging from 0–3.

Comfortable, Mild, Moderate and Severe were the corresponding interpretation for the above scores.

Verbal Rating Scale - VRS score



Based on the statistical data, for the verbal rating scale, the P value suggested significantly better pain relief on oral administration compared to transdermal at 2 hours as well as the 12 hour interval. The p values obtained suggested no difference in the pain control of either route of administration over the subsequent two days of administration.

The Pain Relief Scale is also a four point scale, again with values from 0–3. In this scale, the interpretation for the values was complete relief for a score of 0 and no relief for a score of 3.

Based on the statistical data, for the pain relief scale, the P value suggested significantly better pain relief on oral administration compared to transdermal at the 2 hour interval. There was no statistical difference in p values obtained in the efficacy of either route of administration over the subsequent two days of administration.

The Pain Intensity Scale is a scale which is similar to the Verbal Rating Scale. In this scale, the interpretation for the values was 'none, mild, moderate and severe' for corresponding scores between 0–3.

Based on the statistical data, for the pain intensity scale, the P value indicated moderately significant pain relief on oral administration compared to transdermal at the 2nd, 4th, 8th and 24 hour intervals. There was no statistical difference in p values obtained in the efficacy of either route of administration over the subsequent two days of administration.

On the whole, evidence points to the fact that diclofenac sodium administered orally is slightly more effective compared to diclofenac sodium administered transdermally over the first twenty four hours. However, on the second and third days, there is no significant statistical difference in the pain control by either mode of delivery. No adverse effects were reported by the patients following any of the procedures performed.

Table 4 Comparison of PRS score in oral and patch

PRS	Oral		Patch		P value
	Mean	SD	Mean	SD	
DAY 1					
2 hour	1.50	0.89	2.10	0.79	0.014
4 hour	1.35	0.88	1.70	0.98	0.185
8 hour	1.10	0.91	1.45	1.05	0.217
12 hour	1.00	0.79	1.20	0.95	0.359
24 hour	0.85	0.67	1.05	0.94	0.258
DAY 2					
2 hour	1.00	0.65	1.15	0.93	0.453
4 hour	0.90	0.72	1.00	0.86	0.577
8 hour	0.80	0.70	0.95	0.83	0.419
12 hour	0.70	0.73	0.90	0.72	0.297
24 hour	0.70	0.57	0.70	0.57	1.000
DAY 3					
2 hour	0.25	0.55	0.25	0.55	1.000
4 hour	0.25	0.55	0.20	0.52	0.330
8 hour	0.30	0.57	0.25	0.55	0.577
12 hour	0.25	0.55	0.30	0.57	0.577
24 hour	0.25	0.55	0.25	0.55	1.000

Statistical analysis and results

Twenty healthy patients in the age group 18–40, with a mean age of about 23 were considered in the study undertaken. Thirteen of them were male and the remaining female.

Descriptive analysis was carried out with mean and Standard deviations were computed. Wilcoxon signed rank test was used to find the significance of VAS, VRS, PRS and PIS between two drug delivery routes.

Four scales were used to collect the data for this study. The Visual Analog Scale, The Verbal Rating Scale, The Pain Relief Scale and The Pain Intensity Scale.

Based on the statistical data, for the visual analog scale, the P value suggested significantly better pain relief on oral administration compared to transdermal at the 12 hour interval. The p values obtained suggested no difference in the efficacy of either route of administration over the subsequent two days of administration.

Based on the statistical data, for the verbal rating scale, the P value suggested significantly better pain relief on oral administration compared to transdermal at 2 hours as well as the 12 hour interval. The p values obtained suggested no difference in the pain control of either route of administration over the subsequent two days of administration.

Based on the statistical data, for the pain relief scale, the P value suggested significantly better pain relief on oral administration compared to transdermal at the 2 hour interval. There was no statistical difference in p values obtained in the efficacy of either route of administration over the subsequent two days of administration.

Based on the statistical data, for the pain intensity scale, the P value indicated moderately significant pain relief on oral administration compared to transdermal at the 2nd, 4th, 8th and 24 hour intervals. There was no statistical difference in p values obtained in the efficacy of either route of administration over the subsequent two days of administration.

Pain Relief Scale - PRS score

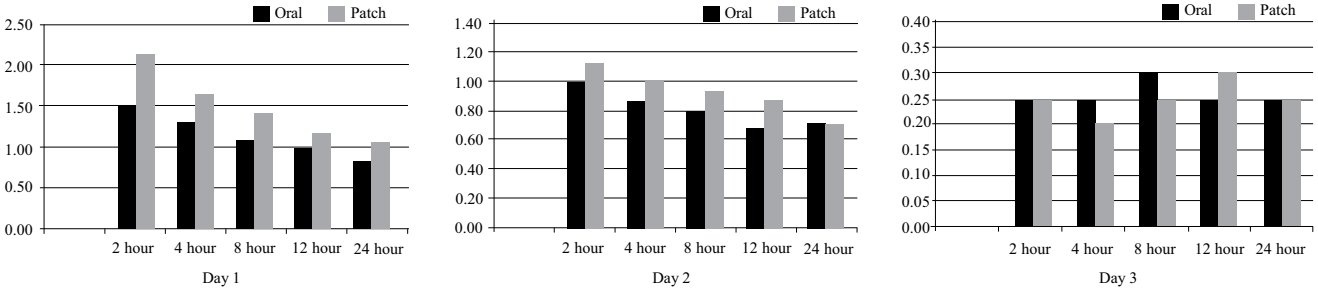


Table 5 Comparison of PIS score in oral and patch

PIS	Oral		Patch		P value
	Mean	SD	Mean	SD	
DAY 1					
2 hour	1.40	0.99	2.05	0.94	0.019
4 hour	1.25	1.02	1.75	0.97	0.076
8 hour	0.95	0.89	1.45	1.05	0.096
12 hour	0.90	0.85	1.25	0.91	0.110
24 hour	0.75	0.72	1.15	0.93	0.028
DAY 2					
2 hour	1.00	0.65	1.15	0.93	0.453
4 hour	0.90	0.72	1.00	0.86	0.577
8 hour	0.80	0.70	0.95	0.83	0.419
12 hour	0.70	0.73	0.90	0.72	0.297
24 hour	0.65	0.59	0.70	0.57	0.666
DAY 3					
2 hour	0.35	0.67	0.25	0.55	0.163
4 hour	0.25	0.55	0.20	0.52	0.330
8 hour	0.25	0.55	0.25	0.55	1.000
12 hour	0.30	0.57	0.30	0.57	1.000
24 hour	0.25	0.55	0.25	0.55	1.000

On the whole, evidence points to the fact that diclofenac sodium administered orally is slightly more effective compared to diclofenac sodium administered transdermally over the first twenty four hours. However, on the second and third days, there is no significant statistical difference in the pain control by either mode of delivery. No adverse effects were reported by the patients following any of the procedures performed.

Discussion

Patients typically associate dental care with pain and an experience of poorly managed pain related to dental treatment can lead patients to avoid or postpone treatment, as well as make them more difficult to treat [4].

Third molar removal represents a major part of oral and maxillofacial surgical practice. It is essential that anaesthesia be obtained during removal, but effective postoperative analgesia is equally important for good patient care [5].

Impaction of third molar teeth is a common disorder which often necessitates their removal [6]. Surgical removal of an impacted third molar is a model used commonly to test the efficacy of analgesics for acute dental pain [4].

It is well documented that pain after removal of third molars is of short duration and reaches its maximum intensity in the early postoperative period [6]. Most young, healthy adults may expect to experience some symptoms and limitation of activity for 5 days or less after third molar surgery. Interference with routine activities and work and school may be expected to be restricted to the first 3 days after surgery, with pain decreasing steadily over the first 5 days [7].

Bilaterally symmetrical impacted mandibular third molars are a useful mode of comparison because the surgical procedures for both the sides remain the same, the individuals who will be studied are the same, the depth and degree of impaction will be the same, the pain perception also remains the same, since the parameters assessed will be the same bilaterally symmetrical impacted mandibular third molars provide an opportunity to carry out two similar surgical procedures on two different occasions.

In the present study two drug delivery routes - oral against transdermal were compared using the drug, diclofenac sodium, 100 mg as a standard and the comparative analgesic efficacy trail was done on 20 patients undergoing surgical removal of bilateral mesioangularly impacted mandibular third molars.

The statistical analysis and the clinical observation indicate that diclofenac sodium administered per orally provides slightly better analgesia than when administered transdermally, on the immediate postoperative day. However, on the second and third postoperative days, there was neither clinical nor any statistical difference observed.

Conclusions

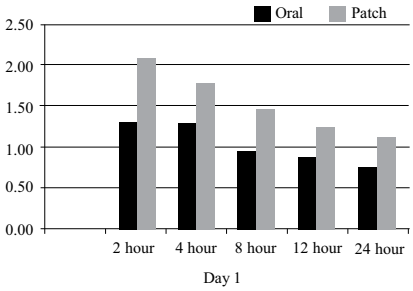
The results of the study, both statistically and clinically showed that diclofenac sodium when administered orally showed slightly better pain control in the first 24 hours when compared to the transdermal form. However, over the next two postoperative days, there was no difference was observed in either form of administration.

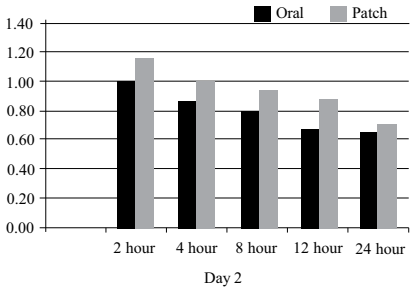
Transdermal administration has its role in pain control following minor surgical procedures, especially in patients who are susceptible to gastritis and in whom compliance is a problem. Considering the small size of the sample, it would need a larger study to validate the above findings

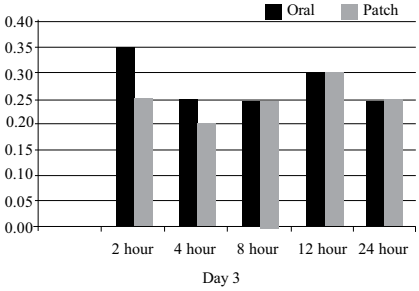
References

1. Monheim's local anaesthesia and pain control in dental practice, 7th edition
2. Zuniga JR, Phillips CL, Shugars D, Lyon JA, Peroutka SJ, Swarbrick J, Bon

Pain Intensity Scale - PIS score







C (2004) Analgesic Safety and Efficacy of Diclofenac Sodium Softgels on Postoperative Third Molar Extraction Pain. J Oral and Maxillofac Surg 62(7): 806–815

3. Joshi A, Parara E, Macfarlane TV (2004) A double- blind randomized controlled clinical trial of the effect of preoperative ibuprofen, diclofenac, paracetamol with codeine and placebo tablet for relief of postoperative pain after removal of impacted third molars. Br J Oral Maxillofac Surg 42(4): 299–306
4. Pozos-Guillen A, Martinez-Rider R, Aguirre-Banuelos P, Perez-Urizar J (2007) Pre-Emptive Analgesic Effect of Tramadol After Mandibular Third Molar Extraction: A Pilot Study. J Oral Maxillofac Surg 65(7) 1315–1320
5. Bailey BM, Zaki G, Rotman H, Woodwards RT (1993) A double-blind comparitive study of soluble aspirin and diclofenac dispersible in the control of postextraction pain after removal of impacted third molars. Int J Oral Maxillofac Surg 22(4): 238–241
6. Meechan JG, Seymour RA (1993) The use of third molar in clinical pharmacology. Br J Oral Maxillofac Surg 31(6): 360–365
7. Shugars DA, Benson K, White RP Jr, Simpson KN, Bader JD (1996) Developing a Measure of Patient Perceptions of Short- Term Outcomes of Third Molar Surgery. J Oral Maxillofac Surg 54(12): 1402–1408

Source of Support: Nil, **Conflict of interest:** None declared.