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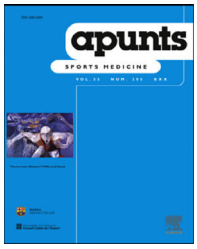

REVIEW

Use of analgesics in professional soccer players: A systematic review

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Abstract
Objective: Use of painkillers appears to have become a widespread issue in the sporting environment as athletes pursue successful pain relief during competitions. We conducted a systematic review on the prevalence of analgesics use in soccer, using literature from January 1980 to July 2021.
Methods: The systematic review followed PRISMA guidelines. Studies were obtained from the Cochrane Library, PubMed, Scopus, and Web of Science (WOS) databases. In total, 213 articles were found where 14 were selected. The risk of bias was assessed using the NIH scale for prevalence studies and the PEDro quality scale for randomized control trials (RCTs).
Results: Less than 3% of the literature were randomized studies (n=10 observational; n=4 double-blind trials) and only 2 studies included females. At least 54% of the research subjects consumed analgesic drugs during the course of their tournaments, and nearly half of them (39-67%) did so before each match, mostly in the form of non-steroidal anti-inflammatory drugs (NSAIDs) (15% of daily use).
Conclusion: Given that short-term observational studies indicated high consumption of analgesics despite limited evidence of their pain control effectiveness, the question is raised whether

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this potential drug abuse affects the sexes at the same rates and in the same ways. Further investigation into these specific cohorts is needed.

Introduction

Analgesics are widely used in sport to treat pain and inflammation associated with injury.[1,2] However, there is growing evidence that some athletes might be taking these substances in an attempt to enhance performance.[3,4] Although the pharmacologic mechanisms of analgesics and their utility in treating pain, either with or without anti-inflammatory effects, are well established, their effect on sport performance is debated.[1,4–7]

Soccer is a popular team sport and highly demanding activity that requires high effort, especially among professional players.[8–10] For that reason, the use of medication in international football has been monitored since the 2002 FIFA World Cup.[11] Data at the time was alarming because up to 69% of adult male players reported use of analgesics, mostly in the form of non-steroidal anti-inflammatory drugs (NSAIDs). Besides their well-documented analgesic effects, NSAIDs also interfere with bone healing and callus formation and may cause impairing bending stiffness,[12] as well as cause gastrointestinal bleeding, cardiovascular and renal effects.[13] To date, all the alerts published about risks associated with their consumption seem to have not been effective, with data collected during the FIFA Women's World Cup indicating that the mean intake of medication was significantly higher among females whereas the use of NSAIDs was similar.[11] Moreover, in an anonymous survey given to 211 U.S. college soccer players before the season, 96% reported current or previous use of NSAIDs. Half of these reported having first used NSAIDs in junior high school or high school, with 3-fold higher consumption after games than before games (33% vs 11%, p=0.002).[14]

This reported incidence is alarming, more so because it is most probably underestimated, since self-medication by the players or treatments previously prescribed by club physicians are usually not included in the published reports. Furthermore, the reports reviewed usually did not show gender-disaggregated data, and thus we cannot infer that the same evidence found in men applies to women. What's more, a recent review that investigated 226,256 athletes showed that risk factors associated with opioid analgesic use (e.g.: Caucasian, postretirement unemployment, and undiagnosed concussion) also included participation in contact sports (hockey, football, and wrestling). Again, results were not analyzed by sex.[15]

The objective of this our study was to perform a systematic review of literature to determine the prevalence of analgesic use in professional soccer players. Patterns of other drug or substance use, potential side effects and the motivation for consumption (e.g.: reducing pain vs. performance enhancement), were also taken into consideration.

Materials and methods

We conducted a systematic review on the use and the effects of analgesics in soccer using literature from January 1980 to July 2021. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were followed.[16] The systematic review was carried out in the PubMed, Scopus, and Web of Science (WOS) databases, the Cochrane Library, and by manual searching of reference lists from studies and reviews (without language restrictions applied).

The following key words were used in combination with Boolean operators AND or OR for the literature search: "analgesics" OR "opioids" OR "paracetamol" OR "acetaminophen" OR "painkillers" OR "NSAIDs" OR "nonsteroidal anti-inflammatory drugs" OR "glucocorticoids" OR "ibuprofen" OR "tramadol" OR "codeine" AND "football" OR "soccer" OR "football players" OR "soccer players" AND "exercise" OR "performance" OR "strength" OR "agility" OR "pain" OR "injuries" OR "resistance".

Inclusion and exclusion criteria for selected studies

The eligibility of publications was assessed on the basis of their abstracts. Where the abstract indicated that the study met the inclusion criteria, the entire article was read. Inclusion criteria were: 1) a) Randomized control trials (RCTs) and b) non-randomised control trials (non-RCTs), c) observational studies (cross-sectional, case-control and cohort studies) explored an intervention to manage pain; 2) Published as original research in a peer-reviewed journal; 3) Published as full-text: 4) Soccer players; 5) No restrictions regarding gender, ethnicity and follow-up duration (in the case of longitudinal studies); 7) Only human participants.

Exclusion criteria were: 1) Diseased populations (e.g., cancer) or animals; 2) Reviews, case series, case reports, editorials and abstracts.

Two authors (TZ and JJL) assessed all identified titles/abstracts regarding a possible inclusion. The same authors reviewed the full texts of the remaining studies against the inclusion criteria. The disagreements were settled by consensus. In cases where consensus was not achieved, the other two authors (ME, AMP) assessed each study in order to obtain a total agreement.

Study quality evaluation

We used the NIH Study Quality Assessment Tools (NIH).[17] This quality assessment tool includes fourteen criteria. For each criterion, a score of 1 was assigned if 'yes' was the response, whereas a score of 0 was assigned otherwise (i.e. for an answer of 'no', 'not applicable', 'not reported' or 'cannot determine'). A study's quality was rated as 0 for poor (0—4 out of 14 questions), i for fair (5—10 out of 14 questions), or ii for good (11—14 out of 14 questions). Disagreements were discussed between two authors (TZ and JJL) until a consensus was reached. Methodological quality was not evaluated for the purpose of including/excluding studies.

For clinical trial studies we used the Physiotherapy Evidence Database (PEDro, range 0-11 scores) to assess the methodological quality of the studies included. This scale scores 11 items: (1) eligibility criteria, (2) random allocation, (3) concealed allocation, (4) similarity at baseline, (5) subject blinding, (6) therapist blinding, (7) assessor blinding, (8) > 85% follow up for at least one key outcome, (9) intention-to-treat analysis, (10) between-group statistical comparison for at least one key outcome, and (11) point and variability measures for at least one key outcome. Items are scored as present (1) or absent (0).[18]

Data extraction

Fig. 1 summarizes the study selection process, in which a total of 213 articles were selected and 150 articles remained after discarding duplicates. While filtering according to the established exclusion criteria, we discarded 88 articles, resulting in 62 articles after review of abstracts. Confirmation of the initial inclusion criteria was also done once the abstracts had been reviewed. Following review of the complete articles, 48 more articles were discarded as they did not have the desired format, being reviews, only abstracts or case reports. Ultimately, the definitive number of studies included in the final review was fourteen.

Results

The data collected from 14 studies included in this review were divided into two groups: 1) epidemiological studies analyzing the prevalence of analgesics and other drugs' use (Table 1); and 2) clinical trials that studied the effects on performance after analgesic doses (Table 2).

Prevalence studies

Ten studies were epidemiological studies: n=2/10 cross-sectional,[19,20] n=5/10 retrospective descriptive epidemiology,[21–25] n=2/10 prospective studies design[26,27] and n=1/10 descriptive epidemiology.[28] The quality summary following NIH evaluation showed that all studies investigated

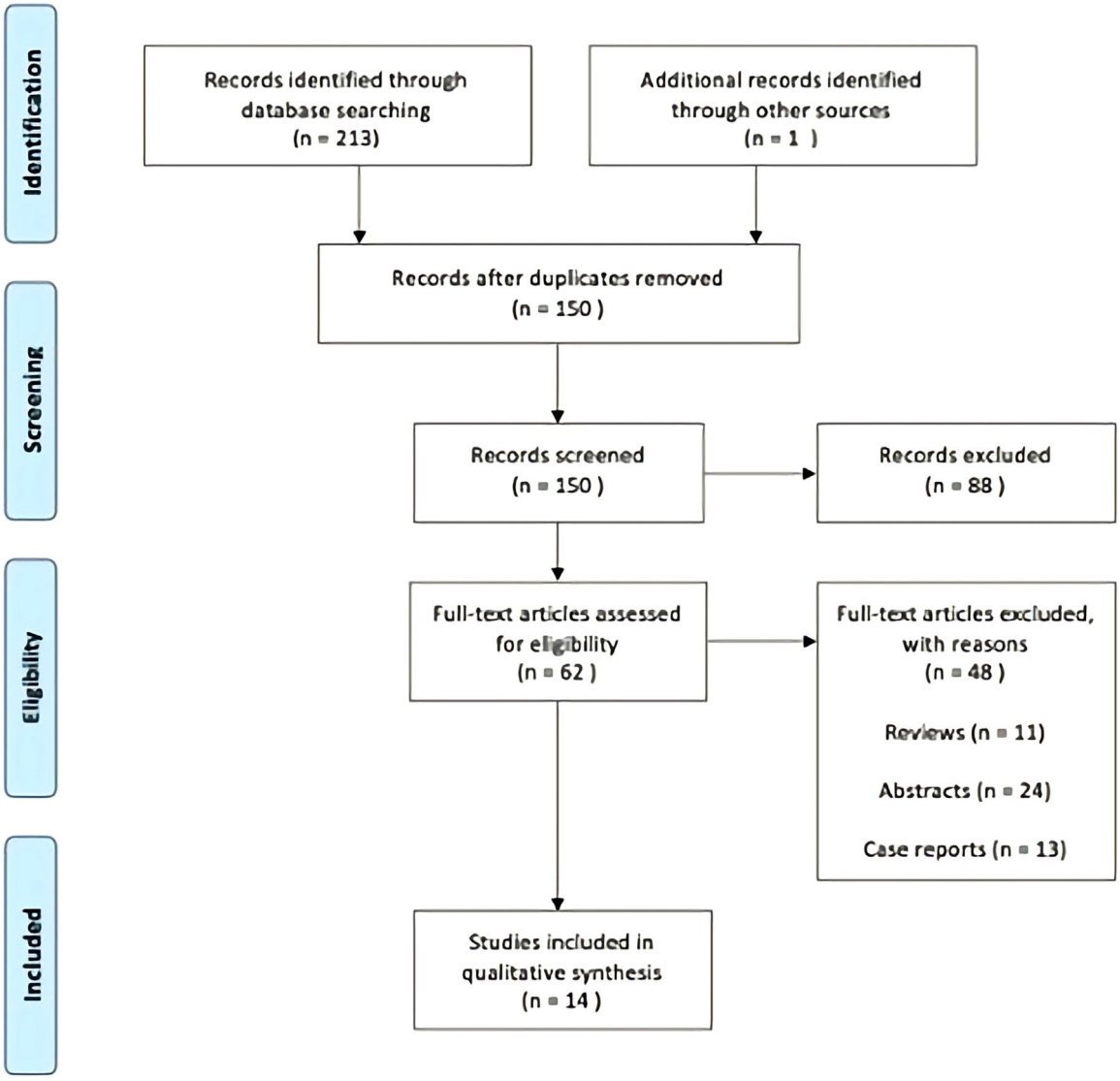

Fig. 1 PRISMA summary of the study selection process (n, number of studies).

Table 1 Prevalence study characteristics of the included studies.

Study (year) /	Study design	Participant characteristics		Summary of results
		N (Competitions)	Gender (%)	
Rossi et al. [19]	Observational cross-sectional	378 (Second league soccer players)	378 male (100%)	92% reported the use of NSAIDs in the previous year. 34% Other Analgesics 29% Intraarticular treatments
Oester et al. [21]	Retrospective	736 (2018 FIFA World Cup)	736 male (100%)	54% of the players took at least one medication during tournament 39% took at least one medication before each match: 39% NSAIDs 14% Other analgesics 13% Insomnia and anxiety prescription
Vaso et al. [22]	Retrospective	736 (2014 FIFA World Cup)	736 male (100%)	67% players took at least one medication during the tournament: 54 % NSAIDs 13% Other analgesics: paracetamol and metamizole 0,5% B2 agonist
Pedrinelli et al. [23]	Retrospective	1064 (2000,2004,2008,2012 FIFA Futsal World Cup)	1064 male (100%)	64% were using medications at least once during the tournament: 46 % NSAIDs. 18% Other analgesics. 8% Medication acting in respiratory tract. 52% Nutritional supplements.
Baume et al. [24]	Not Reported	779 urine samples (2014 FIFA World Cup)	100% male	0.5% urine samples showed traces of clenbuterol. 1% contained tramadol. 0.5% contained glucocorticoids.
Denham [20]	Not Reported	1663 (U.S. high school students)	799 male (48%) and 864 female (52%)	12% of males and 8% of females reported using analgesics at least once in the previous 12 months. Males: alcohol (13%), marijuana (5%) and pain killers (2%) near daily Females: alcohol (10%), marijuana (3%) and pain killers
Tscholl and Dvorak [25]	Not Reported	736 (2010 FIFA World Cup)	736 male (100%)	72% took medication: 49% NSAIDs 11% Other analgesics 4% muscle relaxants 2% local injections

Table 1 (*Continued*)

Study (year) /	Study design	Participant characteristics		Summary of results
		N (Competitions)	Gender (%)	
Tscholl et al. [28]	Descriptive epidemiology study.	2488 (FIFA Women's World Cup 2003 and 2007, and the FIFA U-17 and U-20 World Cup 2005 and 2007)	1832 adolescent male (74%) and 656 female (26%)	63% of the players took at least one painkilling agents during the tournament. Intake of medication per tournament: Females: 72%; Males: 57% in U-17s and 63% in U-20s 39% NSAIDs: Females: 31%: Males: 17% U-17 and 21% U-20 13% Medication acting in respiratory tract. Prescription B2 agonist: Females: 4%; Males: 1% U-17 and 1% U-20
Tscholl et al. [26]	Not Reported	1472 (2002, 2006 FIFA World Cup)	1472 male (100%)	10,384 substances were reported (2 substances/player/match). 57% Nutritional supplements and 43% medicinal: 20% NSAIDs 7% Corticosteroids 6% Other analgesic
Warner et al. [27]	Not Reported	604 (Not Reported)	604 male (100%)	75% reported the use NSAIDs in previous 3 months: 15% described as daily use. No significant differences in age, race, or insurance between users and nonusers.

were evaluated as fair (5—10 out of 14 questions) (See Table 1 in Supplementary File).

In a sample of 378 second league soccer players, 92% of them reported having used NSAIDs in the previous year, and 34% reported use of other analgesics.[19] Interesting to note is that of those using other analgesics, 54-67% took at least one medication during their tournaments, with 39-67% directly before the matches. Of those using mostly NSAIDs (46-54% of the total test population), 75% reported use during tournaments as being higher than at any time in the previous 3 months, with 15% reporting daily use.[19,27]

Other drugs such as tramadol, glucocorticoids, or muscle relaxants showed lower consumption rates.[25,26,28] Females consumed more pharmaceutical drugs, such as painkillers or NSAIDs, than men.[28]

Clinical trials studies

Four of the articles were clinical trials (n=1/4 controlled with placebo[29]) (Table 2).[29—32] The mean PEDro score of the RCTs included was 8 (range 6—10), corresponding to a high level of internal validity (see Table 2 in Supplementary File).[33] The criteria with the worst scores were those related to random allocation and concealed allocation (50%, 2/4) and assessor blinding (0%, 0/4).

Information from four clinical trials was gathered. All clinical trials were double-blind[29—32] and only two of them were comparative.[29,32] Their participant characteristics were: 24-60 professional soccer players with tissue injuries. Minimal impact of the analgesics on recovery was shown in these studies. No information related to tolerability was reported.

A double-blind study that compared Flurbiprofen (150 mg) and Aspirin (3600 mg) in soft tissue lesions in the lower limbs demonstrated that the period of return to competition was shortened by one day with Flurbiprofen.[30] A second study with a similar methodology compared the use of Ibuprofen (1200 mg) vs. Aspirin (3600 mg), showing that return to competition with Ibuprofen occurred 4 days more quickly.[31] In the third study, a double-blind comparison

Table 2 Study design and intervention characteristics of the included studies.

Study (year) /	Study design	Participant characteristics		Drug (dose administered, mg) / Control / Intake timing	Exercise testing / Moment	Summary of results
		N (Injuries)	Gender (%)			
Muckle [30] (Study I)	Double-blind trial	51 (soft tissue injures in the lower limb)	51 male (100%)	150 mg Flurbiprofen (F) 3600 mg Aspirin (A) Once per day for 6 days	Six days after injury	One day less to training and matching (F) 65% (F) vs 35% (A) were able to train 3 days after injury ($p<0.05$).
Muckle [31]	Double-blind trial	60 (soft-tissue injuries)	60 male (100%)	1200 mg of ibuprofen (I) 3600 mg of Aspirin (A) Divided doses between the afternoon of injury and bed time the same day	Three days after injury	Able to play after 6 days (I) vs 10 days (A) ($0.01>p>0.001$).
Santilli et al. [29]	Controlled, double-blind trial	30 (soft-tissue injuries)	30 male (100%)	Ibuprofen 300 mg/ (I) Placebo (lactose) (Pl) 3 times a day Piroxicam 20 mg (P) once plus placebo twice a day.	Treatment could not last more than 10 days	(I) did not reduce the functional damage period Days of treatment: 6 ± 1 (P), 5 ± 1 (I), and 5 ± 1 (Pl). (P) improved symptoms: Average value before/after: Induced pain: 9/3 (P) vs. 7/3 (I) ($p<0.01$) vs. 8/4 (Pl) ($p<0.01$). Passive functional disability: 7/2 (P) vs. 6/3 (I) ($p<0.01$) vs. 7/3 (Pl) ($p<0.01$)
Chiapuzzo [32]	Comparative, double-blind trial	24 (recent soft- tissue injuries)	24 male (100%)	Indomethacin 20 mg (I) Endoprofen 200 mg (E), 4 capsules/day	To assess the condition at the 3rd day	A reduction in pain on active movement ((E) vs. (I): 1 ± 0.2 vs. 0.3 ± 0.2, $p<0.05$) and swelling (0.9 ± 0.2 vs. 0.6 ± 0.2, $p<0.05$) was observed in the (E) group

Data are reported as mean (SD) unless otherwise state

between Ibuprofen (300mg), Piroxicam (20mg) and a Placebo (lactose) resulted in no significant decrease in the period of functional limitation.[29] In the fourth study, another double-blind study was carried out among soccer players with recent soft tissue injuries, with the result that both 80 mg of Indometacin and 800 mg of Endoprofen were able to achieve a reduction in inflammation and in pain during active movement.[32]

In relation to the presence of females in the studies (prevalence and clinical trials), the results showed that only 14% (n=2/14 papers) included female participants,[20,28] and only one analyzed data disaggregated by sex.[28]

Discussion

Our review gives evidence of concerning levels of use of analgesics for successful pain relief during soccer tournaments. Data was alarming because up to 69% of adult male players reported analgesic use, mostly in the form of non-steroidal anti-inflammatory (NSAIDs) drugs. This reported incidence is most probably underestimated, since self-medication by the players and treatments previously prescribed by club physicians are usually not included in published reports.

This systematic review indicated that consumption of analgesics, remains at a high level despite limited evidence of their effectiveness on exercise recovery or tolerability. The key finding of this systematic review is that there is a lack of evidence which support the current use of analgesics in soccer. Moreover, females are underrepresented in currently available data sets, which furthermore include few clinical studies on analgesics' effects on exercise and recovery performance. We believe this merits further investigation in these specific cohorts.

Existing empirical research does not provide a sufficient body of evidence to guide athletes and healthcare professionals in making analgesic medication treatment decisions. Due to the limitation evidences regarding the widespread use of NSAIDs, clinicians and policymakers should carefully assess their current recommendations for NSAIDs' use and establish a more unified consensus based strategy for multidisciplinary pain management in elite athletes.[1,5,7]

This is quite relevant in soccer because it is one of the disciplines within professional sports that has evolved the most in terms of physical demand.[8–10] Nowadays, match-related fatigue leads athletes to limit muscular effort in ways that put their bodies to the test, with hardly any time for full recovery.[1,34] After each game, there is significant muscle pain associated with play-induced performance demands, as well as with resulting injuries.[2,4] Furthermore, the short time available for the footballer's recovery exacerbates the frequent use of analgesic drugs, thus increasing potential risk of misuse and related harms.[11]

Related to drugs, paracetamol has been suggested to improve endurance and performance in repeated sprint exercises by reducing activation of the higher brain structures involved in pain and cognitive/affective processing.[35,36] NSAID drugs indeed affect both central and peripheral body systems, but research on their ergogenic effect on muscle strength development has provided equivocal results.[4] The therapeutic use of glucocorticoids is indubitable, but no clear evidence exists for performance-enhancing effects after short-term oral administration.[3] In contrast to the aforementioned analgesics, there is a paucity of research on the use of opioids such as tramadol on sporting performance. Based on the evidence presented in this review article, the ergogenic benefit of analgesics may warrant further evaluation by regulatory bodies.

Alternatively, infiltration is a therapeutic option used for the treatment of various diseases, consisting of injected administration of different substances into precise locations on the body. This procedure may have an analgesic and/or anti-inflammatory and healing effect, but it must be preceded by the appropriate diagnosis. Its use is common in the treatment of many soft tissue injuries, such as bursitis, synovitis, plantar fasciitis, sprains, muscle injuries, tendinopathies and chondral injuries. The most frequently used active substances are corticosteroids and local anesthetics that produce immediate pain relief, such as lidocaine and bupivacaine.[37] However, in our review, use of these drugs was scarcely reported, meaning that the risk of non-medical usage was probably lower than for other oral analgesics.

Despite a decreasing gender gap in exercise participation, a significant under-representation of women included in sport and exercise medicine research studies still remains.[38] In relation to the presence of females in the studies (prevalence and clinical trials), the results showed that only 14,3% (n=2/14 papers) included female participants. Here, any gender information was analyzed in the papers. Moreover, a recent scoping review on all aspects of competitive women's football found that the most-researched area was injuries. These were predominantly assessed in epidemiology studies that most frequently focused on the whole body, knee or head/face injuries.[39] In our review we confirmed that a lack of data on the women involved in these studies exists.

Some limitations within the studies reviewed must be taken into consideration. Most studies were observational and retrospective and as such included all types of bias that accompany such a design, especially a lack of generalizability. Hence, caution is advised when applying the results to the population as a whole. Another point of concern is that the trials included in this review only one was controlled with a placebo and thus imply that all observed effects were due to the drug's consumption and not due to a placebo-effect. Future randomized controlled studies should account for this factor. Another weakness is that the use of pain medication, including NSAIDs, was only documented using questionnaires that lacked information related to tolerability. A further limitation was the lack of information about sociodemographic variables that could have increased misuse or abuse risk profiles, such as any pressure exerted by sport clinicians.

This systematic review has some of its own limitations, too. Because of the heterogeneity of the scores used in the studies, no meta-analysis could be performed. In addition, the low number of studies included (only four randomized trials) could be considered to be a limitation that might have introduced a systematic bias. Further clinical studies are needed to more precisely characterize the targeted subgroup of athletes. In the future, we hope to see more rigorous, prospective studies of various pain management strategies in elite athletes, thus enabling a shift from

consensus-based recommendations to evidence-based recommendations.

At first glance, transversal or short-term observational studies showed high consumption levels of analgesics despite limited evidence of improved exercise recovery. The question of whether differences in potential analgesic abuse exist between the sexes thus remains open. We believe these merits further investigation in these specific cohorts.

Conclusions

Our review indicated that high consumption rates of analgesics appear to frequently be paired despite limited evidence of their effectiveness on improving exercise recovery or tolerability. The key finding of this systematic review is that there is a lack of evidence to support the current use levels of analgesics in soccer. Moreover, females are underrepresented in current data sets available, which include few clinical studies on the effects of analgesics on exercise performance and recovery. We believe further investigation in the abovementioned cohorts is needed.

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Conflicts of interest

The authors declare that they have no competing interests.

Confidentiality of data

The authors declare that no patient data appear in this article.

Supplementary materials

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