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Efficacy and tolerability of a new ibuprofen 200mg plaster in patients with acute sports-related traumatic blunt soft tissue injury/contusion

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ABSTRACT

Background: Ibuprofen is used for the treatment of non-serious pain. This study assessed the efficacy and safety of a new ibuprofen plaster for the treatment of pain associated with acute sports impact injuries/contusions.

Methods: In this randomised, double-blind, multi-centre, placebo controlled, parallel group study, adults (n = 130; 18–58 years of age) diagnosed with acute sports-related blunt soft tissue injury/contusion were randomized to receive either ibuprofen 200 mg plaster or placebo plaster. Plasters were administered once daily for five consecutive days. The primary assessment was area under the visual analogue scale (VAS) of pain on movement (POM) over 0 to three days (VAS $AUC_{0\text{-}3d}$). Other endpoints included algometry AUC from 0 to three days ($AUC_{0\text{-}3d}$) and 0 to five days ($AUC_{0\text{-}5d}$), to evaluate improvement of sensitivity at the injured site, and patient and investigator global assessment of efficacy. Safety was monitored throughout the study.

Results: The ibuprofen plaster resulted in superior reduction in $AUC_{0\text{-}3d}$ compared with placebo; the Least Squares (LS) mean difference was 662.82 mm*h in favour of the ibuprofen 200mg plaster (P = 0.0011). The greater improvement in VAS AUC of POM was also observed after 12 h, 24 h, and five days of therapy. Tenderness also significantly improved with the ibuprofen plaster compared with placebo; LS mean difference in algometry/tenderness $AUC_{0\text{-}3d}$ was 1.87 N/cm^2*d and $AUC_{0\text{-}5d}$ was 1.87 N/cm^2*d (P values ≤0.0004). At all study timepoints, a greater percentage of patients and investigators rated the effectiveness of the ibuprofen 200 mg plaster as good/excellent than the placebo plaster. Treatment-emergent adverse events for the ibuprofen plaster were few (≤1.5%) and were mild in severity.

Conclusions: The results of this study indicate 200 mg plaster is effective and safe for the treatment of pain due to acute sports-related traumatic blunt soft tissue injury/contusion in adults.

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Ibuprofen; pain; efficacy; safety; convenience; plaster; tenderness

Introduction

The use of medicated plasters for delivery of drugs across the skin to treat certain types of pain is gaining in acceptance and is increasingly being used over oral formulations [1]. The use of medicated plasters has several advantages over other forms of administration, including avoiding systemic effects and oscillation of blood levels of the drug; no first-pass metabolism occurs and metabolism in the skin is relatively low; medicated plasters are easily administrated compared with gels, which may improve compliance [2,3].

Varied pharmacological and non-pharmacological approaches are often used to manage musculoskeletal pain [4]. First-line therapy in Europe varies across countries, although nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used [4]. NSAIDs are known to be beneficial in the treatment of acute soft-tissue injuries, postoperative pain, and recurrent pain, and they have the advantage that they do not require a prescription [5–9].

Ibuprofen is a widely used NSAID to treat soft-tissue pain, postoperative pain, and chronic pain due to a number of diseases such as rheumatoid arthritis and ankylosing spondylitis [10,11]. Ibuprofen inhibits the cyclooxygenase enzyme system resulting in the reduction of the production of inflammatory prostaglandins, such as PGE2 [12]. Ibuprofen is most commonly administered orally and consequently acts systemically to reduce pain. Gel formulations of the drug are also commercially available and have been demonstrated to deliver drug to tissues and muscles for extended periods of time at levels sufficient for clinical benefit [13]. The over-the-counter oral dose of ibuprofen is 200–400 mg, and most commercially available gel formulations contain 5% ibuprofen [14,15]. The oral administration of ibuprofen is associated with a small dose-dependent risk of adverse effects, with the most common being related to the gastrointestinal tract, kidneys, and the coagulation system [16–18]. Gel formulations avoid the side effects associated with systemic administration of the drug, particularly GI-related toxicities, and are associated with fewer adverse events (AEs), most of which are mild skin reactions

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at the site of application [19–21]. However, gel formulations can be unwieldy to apply and require the gel to be reapplied up to three times per day. Moreover, due to variability in the application process, gel formulations do not deliver a specific drug dose.

An ibuprofen-medicated plaster has recently been developed for over-the-counter treatment of nonserious localized pain in adults. The ibuprofen plaster is applied once per day to the skin at the origin of pain and consists of an effective ibuprofen gel formulation supported on a flexible platform. The ibuprofen plaster may have the advantage over the gel formulation in that it may be effective in reducing pain, only requires once daily administration, and that it is easier to apply. The aim of this phase 3, randomized study was to assess the efficacy and safety of the ibuprofen plaster in patients with acute sports impact injuries/contusions.

Methods

The efficacy and tolerability of an ibuprofen 200-mg plaster was investigated in a phase 3, randomized, double-blind, multi-center, placebo controlled, parallel group study (EudraCT number: 2009-018018-21) in patients with acute sports-related traumatic blunt soft-tissue injury/contusion. The study involved four centers in Germany between July 2010 and December 2010. The study was conducted at four sites in Germany in accordance with ICH Good Clinical Practice and the ethical principles contained within the Declaration of Helsinki (South Africa, 1996) [22]. The study was approved by the appropriate Institutional Review Board and all patients gave their written informed consent. A patient could withdraw on their own accord at any time during the study. An investigator could withdraw a patient for several reasons including AEs that the investigator judged could cause severe or permanent harm, protocol violations, or poor compliance.

Study population

Eligible patients were 18–60 years of age and had a primary diagnosis of acute sports-related blunt soft-tissue injury/contusion that did not require hospitalization and that occurred within 3 h of enrolment. Patients had to have baseline algometric measurement values on the injured site of ≤50% of the respective value at the contralateral site and the pain on movement (POM) at baseline of ≥50 mm on a visual analog scale (VAS) (0–100 mm). The absolute sensitivity to pain on the contralateral site was at least 2.5 N/cm^2, while the size of trauma was between 25 and 150 cm^2.

Patients were excluded from the study if they had a history of blood coagulation disorders; a history of significant disease deemed by the investigator to render the patient unsuitable for inclusion; any significant ongoing painful condition other than that associated with the sports-related injury/contusion; any other treatment or medication, except RICE (rest, ice, compression, and elevation), that could interfere with the trial (e.g. corticosteroids) up to 3 days prior to the trial; and any ongoing condition that might interfere with the absorption, distribution, metabolism, or excretion of the study medication. Further exclusion criteria were as follows: any previous history of allergy or known intolerance to any of the drugs or formulation constituents which, in the investigator's opinion, might preclude use of an NSAID, including aspirin-sensitive asthma or a previous allergic response to a NSAID, including bronchospasm, urticaria, angioedema, and rhinitis; participation in a clinical trial in the previous 30 days; injured area was too hairy; current skin disorders in the area to be treated; open wounds to the area to be treated; suspected fractures; suspected torn ligaments; head injuries; or relevant consumption of alcohol 24 h prior to randomization.

Study design

Recruited patients were randomized in a double-blind fashion to treatment with the ibuprofen 200-mg plaster or placebo plaster according to a computer-generated randomization schedule with an allocation ratio of 1:1 to active and placebo treatments. On entry, patients were allocated a unique patient number in numerical sequence. Issue of the study drug in this sequence ensured randomization.

The study consisted of five clinic visits: Days 0, 1, 2, 3, and 5. Plasters were administered once every 24 h. The correct position of the plaster was marked with a water-resistant pen to ensure the plaster was applied at the same site. The investigator instructed patients how to use the plaster. At clinic visit on Days 1, 2, 3, and 5, the prior plaster was removed, algometric and POM assessments were performed, compliance was evaluated by the investigator, and a new plaster was applied. The first plaster application (Day 0) was performed by the staff. Subsequent removal of the prior plaster and application of a new plaster on Days 1–3 were performed in the clinic by the study staff and on Day 4 by the patient. Patients used a patient diary to record VAS on movement, AEs, rescue-medication use, and concomitant medications 1, 2, 4, 6, 12, and 96 (±1 h) after first plaster application. On Days 1, 3, and 5, the patient and the investigator gave a global assessment of the treatment efficacy and local tolerability. Global assessment of efficacy was classified using a 5-point Likert scale (0 = excellent, 1 = good, 2 = fair, 3 = poor, and 4 = none). Global assessment of local tolerability was evaluated using a 4-point scale (3 = excellent, 2 = good, 1 = fair, and 0 = poor). Baseline demographics and medical history were collected on the first visit (Day 0).

The algometry/tenderness was measured such that the greater the algometry value, the greater the pressure required to produce the first tenderness reaction. Therefore, greater algometry values indicated less pain at the site of interest.

The following treatments were not permitted during the study: analgesics or anti-inflammatory drugs within 24 h of study entry; psychotropic drugs, antidepressants, or sedative hypnotics taken within five times their elimination half-life prior to Day 0; physical therapy or other comfort measures, excluding RICE, or herbal preparations for bruises. Selective serotonin reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors could be used during the study if patients maintained a stable dose for at least 4 weeks prior to first study visit.

Outcomes

The primary end point was the area under the curve of VAS assessment of POM over a 3-day period (VAS $AUC_{0-3\ days}$). The $AUC_{0-3\ days}$ was chosen as the outcome of interest as it

included multiple VAS recordings offering a more meaningful end point over time, and because pain is self-limiting and may have diminished after the 3 days.

Secondary variables were AUC of VAS assessment of POM over 12 h (VAS $AUC_{0–12\ h}$) and over 24 h (VAS $AUC_{0–24\ h}$), VAS assessment of POM at hour 24, tenderness/algometry at hour 24, area under the tenderness/algometry assessment curve over Days 0–3 (algometry $AUC_{0–3\ days}$) and Days 0–5 (algometry $AUC_{0–5\ days}$), and the ratio of algometry injured/contralateral sites for $AUC_{0–3\ days}$ and $AUC_{0–5\ days}$. Other end points included time to resolution of pain and global assessment of treatment efficacy by patients and investigators. Global assessment of treatment efficacy by patients and investigators using a 5-point scale (0 = excellent, 1 = good, 2 = fair, 3 = poor, and 4 = none) were made on Days 1, 3, and 5 (final visit). Safety was evaluated throughout the study.

Statistical analysis

The sample size was estimated based on a difference of 13 points between the ibuprofen 200-mg plaster and the placebo plaster based on changes in POM (mm VAS). To achieve these differences, it was determined that 60 patients who completed study treatment in each treatment group would provide approximately 80% power to demonstrate that the topical ibuprofen gel provided significantly greater pain relief (superiority) in comparison with placebo at the 1% significance level.

The intention-to-treat population consisted of all patients who were randomized to the study and received at least one dose of study medication and had efficacy data for at least one post-baseline assessment. Any patients with treatment administration errors were analyzed according to the treatment to which they were randomized. This population was used for summaries of efficacy data and was the primary analysis population in this superiority trial. The safety population included all patients who were randomized to the study and received at least one dose of study medication.

The VAS assessments of POM at 12 and 24 h were compared between treatment groups using ANCOVA with terms in the model for treatment group, baseline tenderness/algometry assessment, total sum of RICE duration, and baseline VAS assessment of POM.

The area under the tenderness/algometry assessment curve over Days 0–3 ($AUC_{0–3\ days}$), Days 0–5 ($AUC_{0–5\ days}$), the tenderness/algometry assessment at 24 h, and the AUCs over Days 0–3 and Days 0–5 for the ratio of the tenderness/algometry assessments for $AUC_{0–3\ days}$ and $AUC_{0–5\ days}$ were compared between treatment groups using an ANCOVA model with terms in the model for treatment group, total sum of RICE duration, and the relevant baseline algometry assessment. For AUC analyses, missing values between two time points were linearly interpolated. If last values were missing, missing data were replaced using the last-observation-carried-forward (LOCF) approach. For all non-AUC analyses, missing efficacy data were replaced using the LOCF approach.

Patient and investigator global efficacy assessments were compared between treatment groups using ordinal logistic regression with terms in the model for the treatment group and baseline tenderness/algometry assessment.

All statistical tests performed were two-tailed with significance at the 5% level, except the primary variable (VAS $AUC_{0–3\ days}$), which was analyzed at the 1% level. The null hypothesis at all times was the equality of the ibuprofen plaster and the placebo plaster.

Results

Patient disposition and demographics

In total, 130 patients with acute sports-related traumatic blunt soft-tissue injury/contusion were included (ibuprofen 200 mg, $n = 66$; placebo, $n = 64$). No patients withdrew early from the study.

The two treatment groups were relatively well balanced regarding demographics and baseline characteristics (Table 1). Most patients were Caucasian. Distribution of sites of injury was similar between treatment groups.

Pain on movement assessments

The VAS $AUC_{0–3\ days}$ of POM (primary end point) was significantly lower (less pain) for the ibuprofen 200-mg plaster than placebo ($P = 0.0011$) at a two-tailed significance level of 1%; the least squares (LS) mean difference in VAS $AUC_{0–3\ days}$ between treatments was 693.78 mm h (Table 2). The difference between treatments in mean VAS of POM values was observed within the first 24 h following application of the first plaster and was maintained thereafter (Figure 1); and the difference in LS mean VAS AUC values for POM was significant from 0 to 12 h, 0 to 24 h, and 0 to 5 days (P values ≤0.0056) (Table 3). The difference between treatments was also observed at the 12-h (LS mean difference [95% CI], −8.12

Table 1. Baseline characteristics of trial patients.[a]

	Ibuprofen 200-mg plaster ($n = 66$)	Placebo ($n = 64$)
Male, *n* (%)	44 (66.7%)	44 (68.8%)
Race, *n* (%)		
Caucasian	65 (98.5%)	64 (100%)
Other	1 (1.5%)	0 (0%)
Age	34.09 (11.72)	30.08 (11.09)
VAS of POM (mm)	74.21 (11.43)	73.98 (10.24)
Time from injury to first treatment (min)	100.09 (43.44)	98.09 (45.74)
Size of injury/contusion (cm^2) (mean (SD))	51.05 (23.43)	46.48 (19.58)
Pressure algometry injured site (N/cm^2)	1.37 (0.86)	1.46 (0.96)
Pressure algometry contralateral site (N/cm^2)	4.73 (1.47)	4.70 (1.66)
Tenderness ratio (injured/contralateral)	0.28 (0.10)	0.29 (0.11)
Location of injury, *n* (%)		
Feet	1 (1.5)	4 (6.3)
Lower leg	10 (15.2)	14 (21.9)
Knee	6 (9.1)	2 (3.1)
Upper leg	14 (21.2)	16 (25.0)
Hip	4 (6.1)	3 (4.7)
Upper back	1 (1.5)	0
Upper arm	15 (22.7)	12 (18.8)
Forearm	4 (6.1)	5 (7.8)
Chest	3 (4.5)	3 (4.7)
Low back	1 (1.5)	2 (3.1)
Shoulder	7 (10.6)	3 (4.7)
Number of patients with prior medications	6 (9.1)	2 (3.1)
Number of patients with concomitant medications	11 (16.7%)	4 (6.3%)

[a]Values are mean (SD) unless otherwise indicated.
SD: Standard deviation; POM: pain on movement; VAS: visual analog scale.

Table 2. VAS $AUC_{0-3\ days}$.

	Ibuprofen 200-mg plaster (n = 66)	Placebo (n = 64)
VAS $AUC_{0-3\ days}$ [mm h] (mean (SD))	2768.13 (1501.29)	3430.95 (1253.14)
LS mean	2731.74	3425.52
LS mean difference [99% CI]	−693.78 [−1237.28; −150.27]	
P value (ANCOVA*)	0.0011	

*ANCOVA: Analysis-of-covariance test with total sum of RICE duration and VAS at baseline as covariates and treatment and center as fixed effects.
AUC: Area under the curve; CI: confidence interval; LS: least square; VAS: visual analog scale.

[−14.85; −1.39]; P = 0.0184) and 24-h (LS mean difference [95% CI], −10.76 [−16.90; −4.62]; P = 0.0007) time points (Table 3).

Algometry (tenderness) assessments

The ibuprofen plaster was associated with greater improvement in algometry assessments (i.e. reductions in tenderness) at the injured site; the algometry AUC was lower for the ibuprofen than the placebo plaster over the 3-day (LS mean difference [95% CI], 0.94 N/cm^2 day [0.43; 1.44]) and 5-day (LS mean difference [95% CI], 1.87 N/cm^2 day [0.87; 2.88]) periods (P values ≤ 0.0004) (Table 4). The difference between treatments was observed at 24 h following application of the first plaster (LS mean difference [95% CI], 0.30 N/cm^2 [0.14; 0.47]; P = 0.0003). The ratio of the injured to contralateral site in algometry $AUC_{0-3\ days}$ and $AUC_{0-5\ days}$ indicated a greater reduction in tenderness with the ibuprofen 200-mg plaster than the placebo plaster (Table 4).

Time to resolution of pain

Only 23/130 (17.7%) of patients had resolution of pain during the 5 days post-baseline. The ibuprofen plaster was associated with significantly shorter time for the algometry/tenderness value at the injured site to reach that of the contralateral (healthy) value (log-rank test: P = 0.0071). Pain had resolved completely for a higher percentage of the patients in the ibuprofen group (17/66 = 25.8%) than in the placebo group (6/64 = 9.4%).

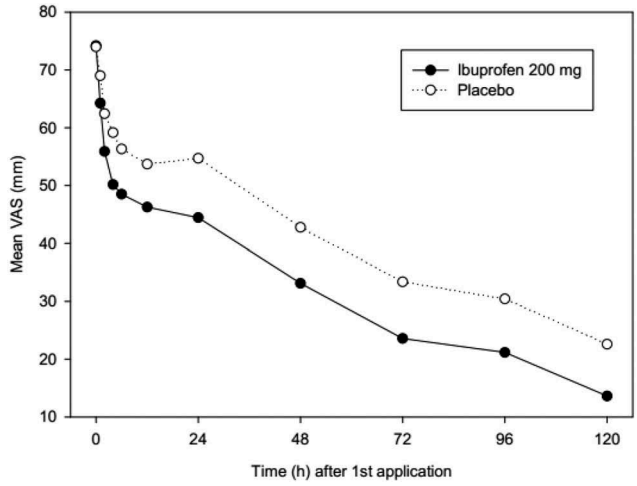

Figure 2. Mean of VAS values over time (FAS/PP).
VAS: Visual Analogue Scale

Patient and investigator global assessment of efficacy

The profiles of the mean of the VAS values over the study period for each treatment are presented in Figure 2. On assessment Days 1, 3, and 5, the treatment efficacy of ibuprofen 200 mg and placebo were assessed globally by the patients and investigators (none, poor, fair, good, excellent). At all time points, a greater

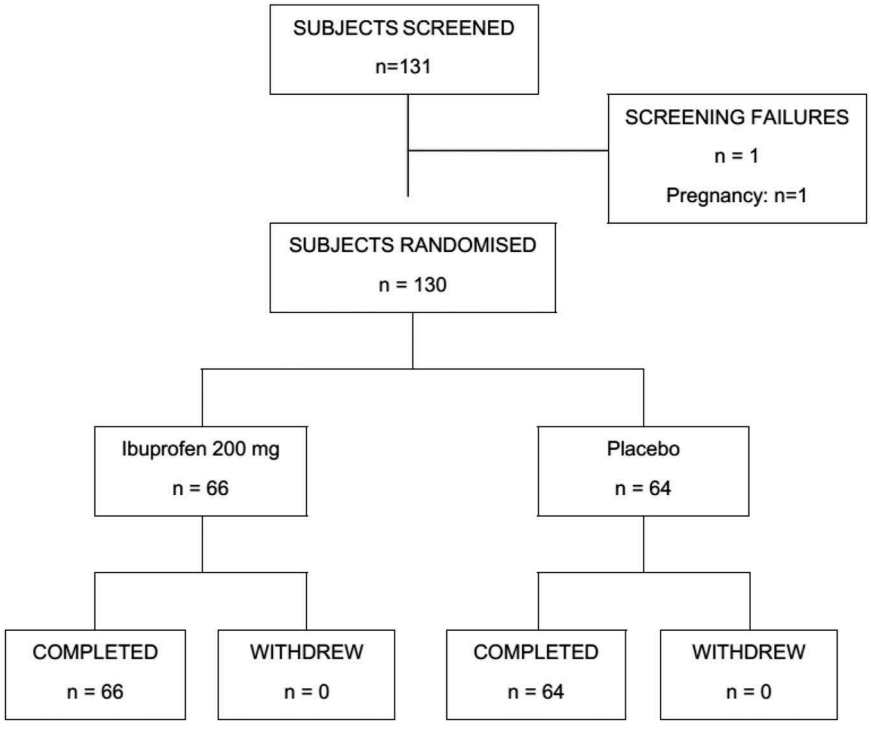

Figure 1. Disposition of subjects.

Table 3. Summary of VAS evaluation of pain on movement (POM).

	LS means (mm h)		LS mean difference (mm h) (95% CI)	
	Ibuprofen 200-mg plaster (n = 66)	Placebo (n = 64)	Ibuprofen 200-mg − placebo	P value
VAS AUC				
$AUC_{0–12\ h}$	607.91	699.37	−91.48 (−155.64; −27.31)	0.0056
$AUC_{0–24\ h}$	1140.90	1345.71	−204.81 (338.00; −71.62)	0.0029
$AUC_{0–5\ days}$	3677.75	4877.55	−1199.80 (−1904.59; −495.01)	0.0010
VAS after initiation of treatment (mm)				
12 h	45.41	53.53	−8.12 (−14.85; −1.39)	0.0184
24 h	43.71	54.47	−10.76 (−16.90; −4.62)	0.0007

AUC: Area under the curve; CI: confidence interval; LS: least square; VAS: visual analog scale.

Table 4. Algometry (tenderness): AUC for the injured site at each time point.

	LS means (N/cm^2 day)		LS mean difference (N/cm^2 day) (95% CI)	
	Ibuprofen 200-mg plaster (n = 66)	Placebo (n = 64)	Ibuprofen 200 mg − placebo	P value
AUC at the injured site				
$AUC_{0–3\ days}$	7.44	6.50	0.94 (0.43; 1.44)	0.0004
$AUC_{0–5\ days}$	14.71	12.84	1.87 (0.87; 2.88)	0.0003
AUC ratio of injured and contralateral site				
$AUC_{0–3\ days}$	1.58	1.35	0.23 (0.11; 0.35)	0.0003
$AUC_{0–5\ days}$	3.13	2.72	0.41 (0.18; 0.64)	0.0006

AUC: Area under the curve; CI: confidence interval; LS: least square.

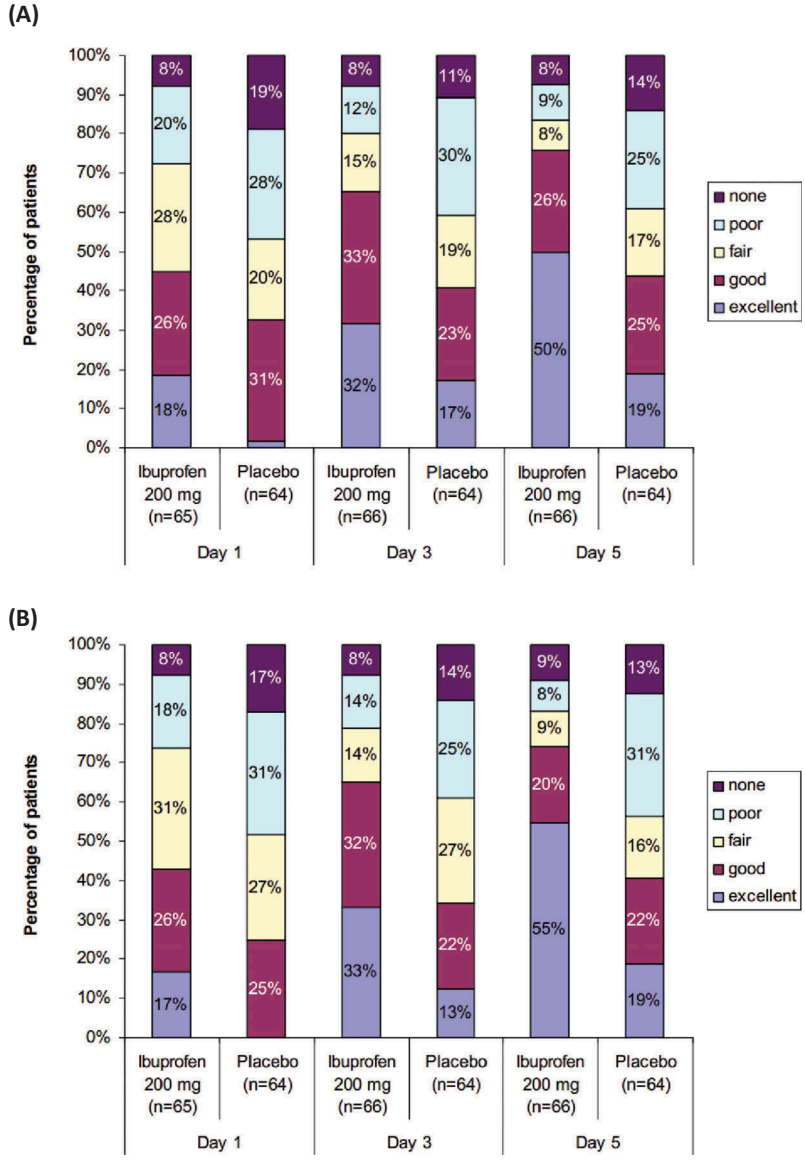

Figure 3. Patient and investigator global assessment of treatment efficacy.

Table 5. Nonserious treatment-emergent adverse events by preferred term (safety population).

	Ibuprofen 200-mg plaster (n = 66)	Placebo (n = 64)
Nasopharyngitis	0	2
Headache	1	1
Application site pruritus	1	1
Application site reaction	0	2
Application site hypersensitivity	2	0
Pain	1	0
Application site erythema	0	1
Toothache	1	0
Application site discomfort	0	1
Angina pectoris	1	0
Vertigo	1	0
Sleep disorder	1	0
Joint swelling	1	0

percentage of patients and investigators rated the effectiveness of the ibuprofen plaster as good/excellent compared with the placebo plaster ($P \leq 0.0048$) (Figure 3). At Day 5, 76% and 44% of patients and 75% and 41% of investigators rated the ibuprofen plaster and placebo plaster, respectively, as good/excellent.

Safety

A total of 15 patients (ibuprofen 200 mg: $n = 7$, Placebo: $n = 8$) had at least one treatment-emergent adverse event (TEAE) during the course of trial (Table 5). The total number of TEAEs was similar between treatment groups. All TEAEs were nonserious and of mild severity. Nine TEAEs were considered by the Investigator to be drug related (possible or probable) (ibuprofen 200 mg: $n = 4$, placebo: $n = 5$). Possible or probably drug-related TEAEs associated with ibuprofen 200-mg plaster were application site hypersensitivity ($n = 2$), joint swelling ($n = 1$), and application site pruritus ($n = 1$). Drug-related TEAEs associated with the placebo plaster were application site reaction ($n = 2$), application site pruritus ($n = 1$), application site erythema ($n = 1$), and application site discomfort ($n = 1$).

Discussion

Ibuprofen is widely used in the treatment of soft-tissue, postoperative, and arthritic pain. Recently, an ibuprofen 200-mg plaster has been developed for the treatment of nonserious pain. The ibuprofen plaster has the advantage over oral administration in acting at the site of need and not systemically. This superiority study evaluated the safety and efficacy of the ibuprofen 200-mg plaster in sports-related traumatic blunt soft-tissue injury/contusion compared with a placebo plaster. The study found that the ibuprofen plaster was superior to placebo in reducing POM; the LS mean difference in VAS $AUC_{0-3\ days}$ for POM (primary end point) was 662.82 mm h in favor of the ibuprofen 200-mg plaster ($P = 0.0011$). The greater reduction in POM with the ibuprofen plaster compared with placebo was observed after 12 h of therapy and was maintained for the remainder of the study. Resolution of pain was more rapid in the ibuprofen than in the placebo group, and a greater percentage of patients treated with the ibuprofen plaster had complete resolution of pain (26%) than those treated with placebo (9%). Reduction in tenderness/pain as evaluated by algometry at the injured site also was significantly greater with the ibuprofen 200-mg plaster than placebo over 5 days of therapy ($P \leq 0.0004$). Across the study, a greater percentage of patients and investigators rated the effectiveness of the ibuprofen 200-mg plaster as good/excellent than the placebo plaster.

The reduction in VAS observed in this study with the ibuprofen plaster compared with the placebo plaster was clinically significant. In an acute pain setting, a clinically significant minimum VAS change is 9 mm [23], which is less than the mean 24-h difference of about 11 mm observed between the ibuprofen 200-mg plaster and the placebo plaster in the current study. Our findings are consistent with two prior controlled studies that found that ibuprofen 5% gel compared with placebo resulted in improvement in walking, resting, and standing in patients with acute ankle sprain [24] and was associated with a significantly shorter time to achieve clinically meaningful reduction in pain in patients with soft-tissue injuries [25]. The gel formulation of ibuprofen has also been found to be as effective as oral ibuprofen in lower pain in patients with osteoarthritis, rheumatic disease, and recurrent knee pain [19,26–28].

In the current study, few TEAEs were observed for either treatment group (≤3.1%) and were mild in intensity. The number of TEAEs was similar between therapies and was mostly associated with administration site reactions. Only application site TEAEs for either therapy were considered by the investigator to be possibly/probably related to treatment. The results of this study are consistent with a systematic review performed by Moore et al. [29] which found that incidence of application site skin reactions associated with topically applied NSAIDS was uncommon (<4%), and the frequency of systemic TEAEs even lower (0.5%). In addition, a systematic review by Massey et al. [6] found that local AEs at the site of application for topical NSAIDs are no worse than that observed with topical placebo; the AEs were mild and transient and occurred in about 6% of patients. Massey et al. also found that systemic AEs, such as nausea and stomach upset, were uncommon and were similar between topical NSAIDs and placebo therapies [6]. The lack of TEAEs associated with application of the ibuprofen 200-mg plaster likely reflects the fact that the topical application results in lower plasma concentrations of the drug. A pharmacokinetic study found that the systematic absorption of ibuprofen from the 200-mg plaster was low but was consistent with levels required for therapeutic relief (personal communication).

The ibuprofen 200-mg plaster has several benefits over the gel and oral formulations. The plaster results in controlled constant administration of the drug, eliminating oscillation in drug levels observed with oral dosing. Although levels of ibuprofen released from the plaster are sufficient to reduce pain, the plasma levels are significantly less than that from oral administration of the drug [30]. For example, the C_{max} for the ibuprofen plaster is about 514 ng/ml and for oral formulations range from 22.9 to 71.34 mg/l [30]. In contrast to the variability of dosing due to inconsistencies in application of the gel formulation, the plaster results in a specific dose of the drug. In addition, the plaster is applied once daily compared with the three times daily administration of the gel formulation. Moreover, the plaster is easily applied. The daily dosing and ease of application with the plaster may result in better adherence of patients to therapy. Sports medicine/injury rehabilitation personnel and patients with blunt soft-tissue injuries agree that the appraisal of pain and subsequent treatment of the pain are important factors in maintaining rehabilitation adherence and improved outcomes [31].

The study has several limitations. The sample size was small and the evaluation of pain and efficacy used subjective measurements. However, the use of VAS to assess pain has been employed extensively and has been demonstrated to reflect clinically important changes in pain. Furthermore, the study enrolled subjects from only four centers in Germany which offers only a limited geographic dispersion on which efficacy claims were based. Larger randomized studies involving other sites and geographies are necessary to further evaluate the use of the ibuprofen 200-mg plaster in treating pain, not only of blunt soft-tissue injuries but also for other nonserious localized pain, as well.

Conclusion

This study supports the use of the ibuprofen 200-mg plaster for the treatment of nonserious localized pain in adults. The results suggest that the new ibuprofen 200-mg plaster is a safe option for the treatment of acute sports-related traumatic blunt soft-tissue injuries/contusions in adults. Patients treated with the new ibuprofen plaster had statistically significant and clinically relevant reductions in pain scores and tenderness reaching a pain-free condition significantly earlier than patients administered placebo. Additionally, the ibuprofen-medicated plaster was well tolerated in this study. Ease of application, few TEAEs, and over-the-counter convenience may help to improve compliance with therapy.

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Declaration of interests

HG Predel was a paid investigator for conducting this study. MP Connolly was paid by the sponsoring organisation for his contributions to the project. MP Connolly holds no financial interest in the sponsoring organisation. F Lewis is an employee of Reckitt Benckiser. A Bhatt is an employee of Reckitt Benckiser, and holds shares in the sponsoring organization. B Giannetti was member of the CRO that managed the study paid by Reckitt Benckiser. B Giannetti declares no financial holdings in Reckitt Benckiser. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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