Risk Factors for Continued Opioid Use in Conservative Versus Surgical Management of Low Back Pain Originating From the Sacroiliac Joint

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Abstract

Study Design: Secondary analysis of data from a randomized controlled trial.

Objectives: To identify risk factors for continued opioid use after conservative management (CM) or minimally invasive surgical management (MISM) of low back pain (LBP) originating from the sacroiliac joint.

Methods: Patients were randomized either to CM (n = 49) or MISM (n = 52). We documented opioid use, pain intensity (visual analogue scale [VAS]), Oswestry Disability Index (ODI), and the Zung depression score (Zung Self-Rating Depression Scale) at baseline and at months 3 and 6 after treatment initiation.

Results: Compared with opioid nonusers, opioid users at baseline had higher mean levels of disability (ODI 61.5, standard deviation [SD] 13.3 vs ODI 51.5, SD 12.8; P < .01) and higher depression scores (Zung 48.5, SD 8.5 vs Zung 42.2, SD 7.2; P < .01). At 6 months, opioid users had higher 6-month pain levels (VAS 60.4, SD 24.0, vs VAS 42.4, SD 28.2; P < .01), higher disability scores (ODI 50.5, SD 16.2, vs ODI 32.7, SD 19.3; P < .01) and higher depression scores (Zung 47.6, SD 8.0, vs Zung 38.8, SD 8.9; P < .01). Risk factors for continued opioid use at 6 months were patient age (odds ratio [OR] for age = 0.91; P = .02) and an increase in LBP (OR 1.08; P = .02) in the CM group and a lack of improvement in depression scores (OR 1.12; P = .03) in the MISM group.

Conclusions: In our patient cohort, the risk of continued opioid use in the treatment of LBP increased not only with pain intensity but also with levels of depression during the course of treatment.

Keywords

opioid use, sacroiliac joint, low back pain, depression

Introduction

The sacroiliac joint (SIJ) is a contributing factor in about 20% of all patients evaluated for low back pain (LBP).1,2 If SIJ pain treatment using nonsteroidal anti-inflammatory drugs, physical therapy, SIJ injections, or radiofrequency ablation fails, therapists frequently resort to the prescription of long-term opioids.3-6 LBP is the most common reason for opioid prescription in the United States and a significant risk factor for ensuing opioid abuse.7-10 Causing more deaths than any other routine medical treatment of nonfatal conditions, prescription opioid use has become a national epidemic in the United States.7,8,11,12

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Opioid prescription for LBP is especially controversial since current evidence suggests no clear-cut long-term benefits versus placebo.13 Risk factors for continued opioid use are rarely reported and predominantly derived from patient cohorts undergoing a specific surgical intervention without comparison to a similar patient cohort undergoing conservative management (CM).14-16 A recent prospective study of 423 patients undergoing either CM or minimally invasive surgical management (MISM) of SIJ pain showed that MISM produced significantly larger improvements in pain and disability than CM.17 The same study also found somewhat less improvement in pain and disability after MISM in opioid users compared with nonusers. To date, however, risk factors for continued opioid use after surgical or nonsurgical treatment of SIJ pain has not been examined. In patients with musculoskeletal pain not related to the SIJ, continued opioid use was shown to be associated with smoking and levels of depression.16

To identify potential risk factors for continued opioid use in patients with SIJ pain, we conducted a secondary analysis of data from an ongoing international randomized controlled trial comparing treatment outcomes after either CM or MISM in patients with LBP originating from the SIJ.18,19 Our specific goal was to describe the prevalence and dosage of opioid use over time and to test the hypothesis that continued opioid use was associated not only with the amount of pain experienced but also with other factors, such as patient age, smoking, and levels of depression.

Materials and Methods

Patients were included in iMIA (iFuse Implant System Minimally Invasive Arthrodesis) between June 2013 and May 2015 at 9 different European centers. The trial was approved by the ethics committee of the Charité–Berlin (EA4/025/14) and by the ethics committees of all participating centers and is registered with ClinicalTrials.gov (NCT01741025). All participating patients gave written informed consent. Patients between the ages 21 and 70 years were eligible if diagnosed with chronic LBP originating from the SIJ with an intensity of at least 50 points on the 0 to 100 visual analogue scale (VAS) as well as a baseline Oswestry Disability Index (ODI) of at least 30 points. The SIJ was identified as the main source of LBP (as opposed to LBP caused by degeneration of facet joints or intervertebral discs) by fluoroscopically guided intraarticular SIJ injection of local anesthetic that provided at least 50% improvement of pain as measured using a VAS. All study centers had agreed prior to study initiation to use the same purely intraarticular injection technique with entry into the joint at its lowest dorsal point without any injection around the joint. Intraarticular placement of the needle was verified by injection of contrast agent under fluoroscopy prior to injection of the local anesthetic. Further details on inclusion and exclusion criteria were previously described.18 Patients were assigned at random (1:1 ratio) to either CM or MISM. Based on published guidelines, CM entailed a combination physical therapy for at least 8 weeks and medical treatment but did not include intraarticular steroid injections or radiofrequency ablation at the SIJ.20 MISM consisted of a minimally invasive lateral fusion of the SIJ by transarticular placement of porous titanium implants (iFuse Implant System, SI-BONE, San Jose, CA; typically 3 implants per SIJ) to reduce micromotion and rotation of the joint.21 Although study follow-up is ongoing, the follow-up time period for this analysis was 6 months, the time period in which no crossover was allowed. Crossover after the month 6 visit occurred in 43% of CM patients. At baseline and at months 3 and 6 after treatment initiation, patients rated LBP intensity using a VAS and disability using ODI.22 Quality of life and the level of depression symptoms were measured by EuroQol Score (EQ-5D-3L, presented as percentage) and the Zung Self-Rating Depression Scale (0-80 points), respectively.23 Clinically important improvement in LBP was defined as a decrease in VAS score of at least 20 points.24

At baseline and all follow-up visits, medications taken on a regular basis for pain were recorded with daily doses. None of the patients’ medication was regulated by the study protocol and there were no recommendations aimed at reducing opioid use. Using previously published standardized conversion factors, we calculated the oral-morphine equivalent daily dose (OME).25

Statistical Analysis

Of the 109 patients enrolled in iMIA, 6-month follow-up data was available in 103 patients. Of these, opioid use data was unavailable in 2, leaving 101 patients for the analyses presented here.18 Data flow is depicted in Figure 1. Variables are reported as means with standard deviation (SD) or standard error (SE), as indicated. T test was used to compare continuous variables between groups, while the Pearson \( \chi^2 \) test was used to compare nominal variables. Changes in frequencies of opioid use over time were assessed using McNemar’s \( \chi^2 \) test. Changes in opioid doses over time were analyzed by Friedman’s test. We applied binomial logistic regression analysis to analyze associations between opioid use at 6 months (dependent variable) and the independent variables patient age, change in LBP, patient gender, smoking status, and levels of depression.
change in ODI, and change in Zung score. In a separate model, we examined whether discontinuation of opioids at 6 months depended on the same independent variables as mentioned above or on total baseline OME. The logistic regression models used are described in more detailed in the appendix. All statistical analyses were conducted using SPSS software, Version 22.0.0.0 (IBM Corp, Armonk, NY).

Results

Baseline Characteristics

Patients using opioids at baseline had higher levels of disability and depression and lower levels of quality of life compared with nonusers (each \( P < .01 \); Table 1). No differences in baseline characteristics were found for age, sex, current smoking, LBP, and the type of treatment allocated (CM vs MISM).

Prevalence of Opioid Use Over Time

In the entire patient cohort, the prevalence of opioid use at baseline was 52.5% (\( n = 53 \)) with no significant difference between CM (46.9%) and MISM (57.7%; \( P = .28 \)). In the CM cohort, the prevalence of opioid use remained unchanged at 46.9% both at 3 and 6 months compared with baseline (\( P = 1.00 \) each). In the MISM cohort, the prevalence of opioid use showed a slight decrease over time from 57.7% at baseline to 44.2% both at 3 months (\( P = .04 \)) and 6 months (\( P = .02 \)).

Opioid Dosage Over Time

In patients taking opioids, OME showed no significant change over time from baseline (57.8 mg; SE 7.3) to month 3 (33.5 mg; SE 7.3) and month 6 (50.0 mg; SE 7.3; \( P = .35 \)). In a separate analysis of opioid users in the CM and MISM cohorts, we found that baseline OME was significantly higher in MISM (73.9 mg; SE 11.3) than in CM (40.4 mg; SE 7.9; \( P = .02 \)). Over time, OME displayed no statistically significant changes in the CM cohort, with 45.8 mg (SE 8.4) at month 3 and 48.8 mg (SE 10.9; \( P = .06 \)) at month 6. In contrast, in MISM, which showed higher levels of OME at baseline than CM, we identified a decrease in OME from a mean of 73.9 mg (SE 11.3) at baseline to 43.4 mg (SE 9.2) at month 3 and 51.1 mg (SE 9.9) at month 6 (\( P = .01 \) vs baseline).

Risk Factors for Opioid Use at 6 Months

Patients using opioids at month 6, when compared with patients without opioid use, showed not only higher disability and lower quality of life at baseline and over time but also higher scores for pain and depression over time (Table 2). Also, the frequency of LBP improvement was significantly lower in patients using opioids at 6 months compared with those without opioid use. There were no differences in age, sex, smoking status, or baseline LBP.

Table 3 describes risk factors for continued opioid use separately for the CM and MISM cohorts. Among CM patients, risk factors for continued opioid use at month 6 were lower age (OR for age \( = 0.91, P = .02 \)) and increases in LBP over time (OR 1.08, \( P = .02 \)). The increase in pain in CM opioid users was 7.2 VAS points (SD 12.1) compared with a decrease in pain in nonusers by 17.1 VAS points (SD 27.0).

In the MISM group, the only risk factor for continued opioid use at month 6 was a lack of improvement in levels of Zung depression scores (OR 1.12, \( P = .03 \)). While opioid users improved in Zung depression scores by only 0.9 points (SD 9.2), patients without opioid use improved by 8.3 points (SD 7.2).

In the entire study cohort, we identified 12 opioid discontinuers and 41 patients with continued opioid use at...
6 months (Table 4). After adjusting for the effects of patient age, sex, and the type of treatment (CM vs MISM), we found that opioid discontinuation was associated with larger decreases both in LBP (OR 0.95, 95% confidence interval 0.92-0.98; P < .01) and in depression scores (OR 0.79, 95% confidence interval 0.68-0.92; P < .01).

Discussion

Risk factors for continued use in chronic pain conditions and specifically in LBP are sparsely reported.14-16 In our study, significant risk factors for continued opioid use at 6 months were younger patient age and increasing LBP in the CM cohort and a lack of improvement in depression scores in the MISM cohort. Our findings confirm our initial hypothesis that opioid was associated with the amount of pain (in CM), patient age (in CM), and levels of depression (in MISM). However, smoking was not a risk factor for continued opioid use in either of the 2 groups.

When discussing the identified differences in risk factors for continued opioid use between CM and MISM, it is important to note that, as previously published, patients undergoing MISM in the iMIA trial showed significant improvements in pain and disability when compared with patients during CM.18,19 This is why we examined risk factors for continued opioid use for both treatment groups separately. The fact that MISM led to better outcomes in LBP than CM, independently of whether patients were using opioids or not, may explain why the degree of LBP led to no significant clinical improvement in LBP over time, predictors of opioid use at 6 months were both the amount of LBP and younger patient age while the degree of depression symptoms was not predictive.

We identified 12 out of 53 (22.6%) opioid users at baseline who were able to discontinue opioid use over time. After adjusting for the effects of age, sex, and the type of treatment (MISM vs CM), we found that opioid discontinuation was associated with a decrease in depression scores and with larger improvements in LBP. These findings are in line with previously published evidence reporting that continued opioid use is not only a function of a specific type of interventional treatment but also of a patient’s mental status and certain sociodemographic factors.14-16 In a cohort of 2104 patients with chronic pain, Goesling and colleagues identified depression symptoms in 43.6% of patients with opioid use and in only 26.8% of nonusers. This is in line with our finding that opioid users had significantly higher Zung depression scores both at baseline and after 6 months. It is important to note that the mean Zung scores observed in our patient cohort represented mild depression (41-47), or moderate depression (>47).23 Even though no major depression was
observed, we still feel that the dynamic changes between different levels of Zung scores over time are valuable to understand interactions between opioid use and depression symptoms in our patient cohort. Goesling and colleagues also showed that pain and depression interact in opioid users to the extent that pain is a predictor of opioid use in nondepressed patients while in depressed patients opioid use is predicted not by the amount of pain but also by the level of depression.26 The idea that the impact of pain may be outweighed by individual interpretation of pain is supported by the results of a recent knee and hip arthroplasty study, which showed that continued opioid use after surgery was predicted by catastrophizing of preoperative pain rather than by the actual level of reported pain.15 Patients with opioid use at 6 months after hip or knee surgery showed catastrophizing levels twice as high as those of patients without opioid use. In a prospective cohort study on 632 patients with musculoskeletal pain, Linton and colleagues showed that pain catastrophizing may be one of the most important cofactors in the relationship between opioid use and depression.27 Scherrer et al found that opioid use not only increases the risk of recurrence of already existing depression but also of developing new-onset depression.28 They examined 355 patients with chronic LBP and found that the proportion of patients with depression among opioid users with an OME of at least 50 mg increased from 8.5% at baseline to 25.8% after 2 years. In our study, the relationship between opioid use and depression symptoms became especially evident at 6 months of follow-up. While opioid users showed no significant improvement in depression scores, those without opioid use had improved substantially (by 8.3 points on the Zung depression scale) over time. The fact that depression scores predicted continued opioid use especially in patients of the MISM cohort, which showed a significant decrease in LBP over time, further supports the view that reported pain levels may be less important in assessing the risk of continued opioid use. Failure to discontinue opioid use over time should therefore prompt therapists to pay attention not only to pain levels but also to depression symptoms when planning further treatment strategies. Another previously reported factor associated with continued opioid use in patients with spine-related pain is smoking.16 Krebs et al examined 2110 patients with painful lumbar spine conditions and found that the relative risk of continued opioid use was 1.5 for smokers after 2 years of follow-up. In our study, we found no association between smoking and continued opioid use. This may be explained by a comparably smaller patient cohort and a shorter period of follow-up in our analysis.

Our overall results confirm that opioid prescription for LBP is a common phenomenon. Previously reported series on patients with LBP reported quite similar prevalences of baseline opioid use of 41.6%9 and 42.3%16 compared with 52.5% in our study.9,16 We found that opioid users showed the same baseline pain levels as nonusers (VAS 76.6 vs 74.6), which is in line with data on patients with chronic pain conditions reported by Hina and colleagues (Numeric Rating Scale 7.6 vs 7.4). However, Hina et al conducted different stimulation tests and found significantly more hyperalgesia in opioid users than in nonusers.29 Even if pain did not differ at baseline in our study, we were able to show that at 6 months of follow-up patients with opioid use reported not only significantly higher levels of pain than nonusers but also showed a decreased frequency of pain improvement when compared with nonusers. These results are in line with the large meta-analyses of randomized controlled trials comparing opioids to placebo in the treatment of LBP, which found no evidence for long-term superiority of opioids.13,28

Opioid use is known to not only affect pain perception but also disability and quality of life. In a large observational longitudinal study, Turner and colleagues showed that continued opioid use for 1 year significantly increased the prevalence of disability, which was 11.7% in patients without or only minimal opioid use compared with 19.3% (P < .01) in patients with higher dose opioid use.30 Our results support this notion in that we found that at baseline and at month 6 opioid users showed significantly higher levels of disability and lower levels of quality of life than nonusers.

One of the most critical aspects of long-term opioid prescription is the risk of dependency.12,31 In our study, opioid use was relatively frequent over time. Only in the MISM cohort did we find a slight decrease in the prevalence of opioid use over time, while in the CM cohort opioid use remained constant. Even though these findings may be somewhat confounded by the fact that the baseline dosage of opioids was higher in MISM than in CM, one may argue that our data suggests that CM may not be beneficial in avoiding opioid dependency, especially in combination with increasing levels of disability and depression observed over time. Interestingly, successful opioid discontinuation did not depend on the dose of opioids used. Similar findings have been made for spine surgery outcome, which does not seem to be associated with the actual dosage of opioids but rather with whether opioids are used or not.32

The main strength of our study is that it was based on a well-selected subgroup of patients with LBP originating from the SIJ and that it presents data on continued opioid use not only on patients undergoing a surgical intervention but also CM. However, certain limitations need to be mentioned. First, our findings may not be generalizable to patients with LBP caused by the fact that the baseline dosage of opioids was higher in MISM than in CM, one may argue that our data suggests that CM may not be beneficial in avoiding opioid dependency, especially in combination with increasing levels of disability and depression observed over time. Interestingly, successful opioid discontinuation did not depend on the dose of opioids used. Similar findings have been made for spine surgery outcome, which does not seem to be associated with the actual dosage of opioids but rather with whether opioids are used or not.32

The main strength of our study is that it was based on a well-selected subgroup of patients with LBP originating from the SIJ and that it presents data on continued opioid use not only on patients undergoing a surgical intervention but also CM. However, certain limitations need to be mentioned. First, our findings may not be generalizable to patients with LBP caused by degeneration of facet joints or intervertebral discs, since all patients in our study suffered from pain originating from the SIJ. Also, in the iMIA trial patients were randomized to either CM or MISM and randomization was not stratified according to baseline opioid use. Therefore, no separate power analysis or sample size estimation was conducted for this specific secondary analysis on opioid use, which limits the validity of our results. However, because the protocol did not dictate opioid behaviors or include opioid reduction programs, our data offers a realistic insight into current habits of opioid prescription, which may also be viewed as a strength of this study. Another limitation is that baseline OME was somewhat higher in the MISM group compared to CM, which may reduce the comparability of changes in OME over time. Furthermore, neither patients nor physicians were blinded to the type of treatment
Conclusions

Significant risk factors for continued opioid use were younger patient age and increases in LBP in the CM cohort and a lack of improvement in levels of depression in the MISM cohort. Our results suggest that patients with LBP and continued opioid use should be evaluated not only for levels of pain but also for depression symptoms.

Appendix

The overall fit of our binomial regression models (model 1: opioid use at 6 months; model 2: opioid discontinuation at 6 months) was examined by omnibus testing of model coefficients, the Nagelkerke $R^2$, and a separate accuracy of classification test of actual versus predicted values.

For model 1, we identified a good overall fit of our model with $\chi^2$ values of 19.59 ($p = .001$) in CM and 14.44 ($p = 0.013$) in MISM in the omnibus test. The Nagelkerke $R^2$ value was 0.46 in CM and 0.33 in MISM. The overall accuracy of classification rate was 80.4% in CM and 70.6% in MISM. In addition to the results presented in Table 3, we identified the following data for the significant independent predictors of opioid use at 6-month “age”/“change in LBP” in the CM group: coefficient $=-0.092/0.074$; SE $0.039/0.031$; Wald $\chi^2$: 5.54/5.89. In the MISM cohort, only “change in Zung” predicted opioid use at 6 months. For this variable, we identified the following data: coefficient 0.10; SE 0.049; Wald $\chi^2$: 4.30.

For model 2, we found the following results for the significant predictors “change in LBP”/“change in Zung” in addition to those mentioned in the Results section. There was a good overall model fit with $\chi^2$ values of 15.98 ($p = .003$)/17.67 ($p = .001$) in the omnibus test. The Nagelkerke $R^2$ values were 0.35/0.41. The overall accuracy of classification rates were 80.0%/86.0%. Further findings were the following: coefficient $-0.052/-0.24$; SE $0.017/0.079$; Wald $\chi^2$: 9.47/8.98.

Authors’ Note

Parts of this project were presented as a talk at the Global Spine Conference 2017 in Milano, Italy, May 5, 2017; and at the Second International Conference on Sacroiliac Joint Surgery (ICSJS) in Hamburg, Germany, September 16, 2016.

The iMIA trial was approved by the ethics committees of all participating centers. The devices and drugs are Food and Drug Administration–cleared or –approved by the corresponding national agencies for this indication.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: BS, DK, and RP have received personal fees from SI-BONE. JD has received a research grant from the German Federal Ministry of Education and Research via a grant from the Center for Stroke Research Berlin for projects not related to this article. PV has received personal fees from Brainlab and Ulrich medical. DC is an SI-BONE employee. EvE is a consultant for SI-BONE. DP, AG, and EE have no conflict of interest to report.

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