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ORIGINAL ARTICLE • ANKLE - FRACTURES

Increased opioid consumption in diabetics with operative ankle fractures: a retrospective case–control study

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Abstract

Introduction Opioids are commonly used for post-operative pain control. It is known that diabetic patients with ankle fractures will experience prolonged healing, higher risk of hardware failure, and an increased risk of infection. However, the opioid requirements amongst this patient cohort have not been previously evaluated. Thus, the purpose of this study is to retrospectively compare opioid utilization amongst ankle fracture patients with and without diabetes mellitus (DM).

Methods An IRB approval was obtained for the retrospective review of patients who presented with an ankle fracture and underwent surgery between November 2013 and January 2017. A total of 180 patients (144 without DM, 36 with DM) with a mean age of 50 years (± 18 years) were included. Opioid consumption was quantified utilizing a morphine-milliequivalent conversion algorithm. A repeated measures ANOVA was conducted to compare opioid consumption. A two-tailed p value of 0.05 was set as the threshold for statistical significance.

Results Repeated measures ANOVA revealed a statistically significant decrease in total opioid consumption during the 4-month duration ($p < 0.001$). The model demonstrated a mean difference in opioid consumption of − 214.3 morphine meq between the patients without and with DM ($p = 0.022$). Post hoc pair-wise comparison revealed less opioid consumption amongst non-diabetic patients at 2 (− 418.5 Meq; $p = 0.009$), 3 months (− 355.6 Meq; $p = 0.021$), and 4 months (− 152.6 Meq; $p = 0.006$) after surgery.

Conclusion Our study revealed increased opioid consumption amongst diabetic patients who are treated surgically for ankle fractures. With increasing efforts aimed at reducing opioid administration, orthopaedic surgeons should be aware of higher opioid consumption amongst this patient cohort. Further studies are needed to verify the results of this study.

Keywords Opioids · Narcotics · Diabetes · Ankle fractures

Introduction

Opioid medications are commonly used for post-operative pain control in patients following ankle fractures. A prolonged duration of opioid treatment has become increasingly common and has resulted in a number of negative outcomes [1–3]. In 2011, more than 40,000 deaths were attributed to drug toxicity poisoning, and 41% of those deaths involved opioid analgesics [4]. In that same year, opioid abuse and dependence in the USA increased in prevalence to 0.24% from 0.095% in 2002 [5]. Despite this, sales of prescription opioids quadrupled from 1999 to 2014. Concerns of a growing opioid dependency epidemic have led to an increasing legislative effort to reduce its administration.

Menendez et al. [6] evaluated the risk of pre-operative opioid abuse in patients undergoing elective orthopaedic surgery. They found a significant increase in inpatient mortality, induced mental disorders, respiratory failure/mechanical ventilation, pneumonia, surgical site infection, myocardial infarction, post-operative ileus, duration of hospital stay and non-routine discharge. While efforts are made to wean patients from pre-operative narcotic doses, prolonged opioid use remains a challenging problem for both the surgeon and

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patient. Many offices have published policies that inform patients of their opioid prescribing policy prior to surgery. To our knowledge, there are no published studies examining the effect, if any, this has on reducing post-operative prescribing practices or patient expectations and satisfaction.

Diabetic patients have been found to report higher pain scores both pre-operatively and post-operatively as compared to non-diabetic patients [7]. This hyperalgesia in diabetic patients is believed to be twofold in nature, with an up-regulation in pronociceptive ion channels and a down-regulation in GABAergic neurons that are used to diminish pain signals [8]. Despite this knowledge, the opioid requirements amongst this patient cohort remain understudied, especially in the setting of orthopaedic surgery.

The purpose of this study was to retrospectively compare opioid utilization amongst ankle fracture patients with and without diabetes mellitus (DM). Using a repeated measures model, we compared the opioid consumption over a 180-day period for post-operative ankle fracture patients who did and did not have a diagnosis of DM.

Methods

Institutional review board approval was obtained for this study. A diagnosis code search was performed for patients who presented with any fracture about the ankle to any of eight institutions in a large mid-atlantic regional hospital system. Exclusion criteria included patients under the age of 18 or for patients in which post-operative medication scripts were unable to be obtained ($n = 38$). Patients with diabetes mellitus (DM) were identified via chart review. These patients were pooled into a single cohort regardless of their given type of insulin resistance. This yielded a total of 180 patients (144 without DM, 36 with DM) identified to have undergone surgical intervention between November of 2013 and January of 2017 (mean age 50 years, SD 18 years).

Univariate analysis was conducted to assess for potential differences between the two groups, in which continuous and categorical variables were assessed with independent samples *t*-test or Chi-square analysis, respectively. A Mann–Whitney *U* test was utilized when comparing non-parametric continuous demographic data. Opioid consumption was quantified utilizing the morphine-milliequivalents of narcotics obtained from a centralized prescription insurance reporting database which is integrated into the electronic medical record [9]. A repeated measures ANOVA was conducted to compare opioid consumption between the two groups. The model was adjusted for age and body mass index (BMI kg/m^2). Post hoc pair-wise comparisons with Bonferroni adjustment were conducted to assess group difference with respect to time. A two-tailed p value of 0.05 was set as the threshold for statistical significance. All analyses were conducted using SPSS version 24 (Armonk, NY USA).

Results

Of the 180 ankle fracture patients analysed, 36 were diabetics (Table 1). There were 4 patients excluded for Pilon fractures and 19 excluded for distal 1/3 tibia fractures because these are more severe injuries, frequently with a higher energy mechanism. Median time to surgery was 6 days for both non-diabetic and diabetic patients ($p = 0.911$). Repeated measures ANOVA revealed a statistically significant

Table 1 Comparison of patient demographics for individuals with and without diabetes mellitus (DM) presenting with an ankle fracture that required surgical intervention

	DM	No DM	*p* value
Median age in years (IQR)	65 (17)	47 (27)	< 0.001
Mean body mass index in kg/m^2 (SD)	31.3 (7.1)	34.1 (6.9)	0.036
Mean rank pre-operative 1-month opioid consumption	81.06	92.86	0.110
Median time till operation in days (IQR)	6 (10)	6 (11)	0.911
Gender			
Male	9 (25.0%)	63 (43.8%)	0.040
Female	27 (75.0%)	81 (56.3%)	
Smoking status			
Yes	32 (88.9%)	98 (68.1%)	0.013
No	4 (11.1%)	36 (31.9%)	
Weber classification			
Weber A	3 (8.3%)	6 (4.2%)	0.367
Weber B	20 (55. 6%)	96 (66.7%)	
Weber C	13 (36.1%)	42 (29.2%)	

IQR inter-quartile range

decrease in total opioid consumption during the 4-month duration ($p < 0.001$) (Fig. 1). The model demonstrated a mean difference in opioid consumption of −214.3 morphine meq between the patients without and with DM ($p = 0.022$). Post hoc pair-wise comparison revealed less opioid consumption amongst non-diabetic patients at 2 months (mean difference = −418.5 Meq; $p = 0.009$), 3 months (mean difference = −355.6 Meq; $p = 0.021$), and 4 months (−152.6 Meq; $p = 0.006$) after surgery (Table 2). No patients had documented EMG results or Semmes–Weinstein monofilament exams. Two of the 35 patients had documented sensory deficits on physical exam.

Discussion

An increasing opioid consumption has spurred legislative efforts to reduce its use [10, 11]. As such, orthopaedists have been challenged with the task of judicious opioid administration that serves to optimize pain control while mitigating opioid-related adverse events. In doing so, it has become important to identify comorbidities associated with prolonged opioid use. Our study compared opioid consumption between non-diabetic and diabetic patients who presented to the ED with an ankle fracture. Our findings reveal higher opioid consumption amongst diabetic patients being treated for ankle fracture when compared to non-diabetic patients.

Similarly, other studies from non-orthopaedic specialties have reported an increased opioid consumption amongst diabetic patients. Karci et al. [12] compared morphine-based patient-controlled analgesia (PCA) usage between 30 diabetic and 30 non-diabetic patients undergoing abdominal hysterectomy. The authors reported higher mean cumulative morphine consumption from PCA in diabetic patients when compared to non-diabetic patients at 48-h follow-up (54.12 ± 25.09 mg and 42.66 ± 20.67 mg, respectively; $p = 0.0015$). Likewise, in a prospective study of 39,140

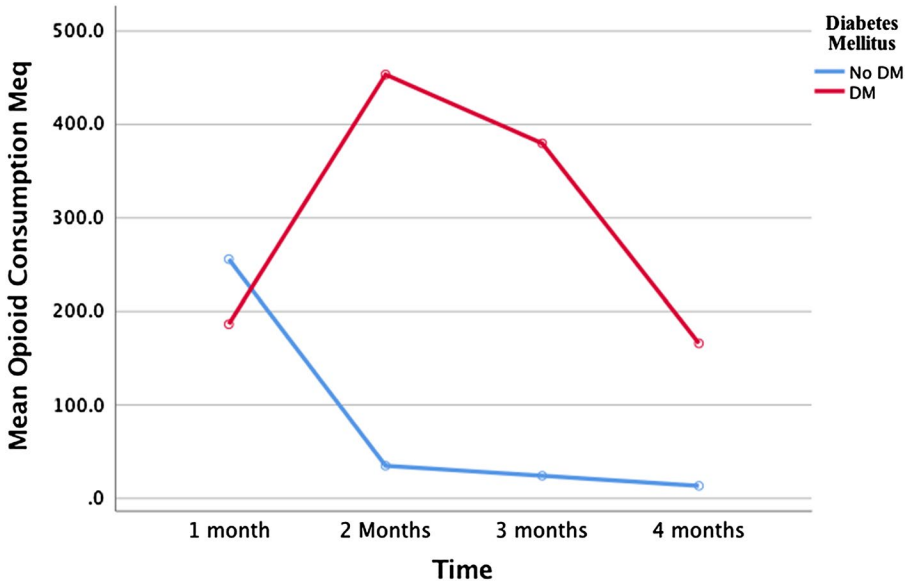

Fig. 1 Repeated measures ANOVA plot comparing opioid consumption of patients with and without diabetes mellitus for 4 months following operative intervention of an ankle fracture. Adjusted for age and BMI. Within-subject factors (time) p value < 0.001. Between-subject factors p value = 0.015

Table 2 Adjusted between-subject pair-wise comparison estimates of opioid consumption (in milliequivalents of morphine) per month for patients with and without diabetes mellitus

Dependent variable	Parameter	Mean difference	Sig.	95% CI	
				Lower bound	Upper bound
Total opioid consumption for month #1	No DM	69.376	0.331	−71.06	209.813
	DM	0[a]	–	–	–
Total opioid consumption for month #2	No DM	−418.516	0.009	−732.592	−104.440
	DM	0[a]	–	–	–
Total opioid consumption for month #3	No DM	−355.553	0.021	−656.967	−54.140
	DM	0[a]	–	–	–
Total opioid consumption for month #4	No DM	−152.560	0.006	−259.706	−45.415
	DM	0[a]	–	–	–

Significant determined by p values < 0.05

0^a reference value of zero

opioid naïve patients who underwent major elective surgery (including cardiac, intra-thoracic, intra-abdominal, and pelvic procedures), Clark et al. [13] assessed factors associated with continued opioid use that persisted more than 90 days after surgery. Following risk adjustment with multivariable logistic regression modelling, the authors identified age (age 66–75 years vs. 86 years and older; OR 1.63; $p=0.03$), lower household income and patient specific comorbidities such as diabetes (OR 1.15; $p=0.04$) as factors associated with an increased risk of opioid consumption.

The increased need for opioid consumption may be due to an altered opioid responsiveness that occurs during a hyperglycaemic state. Raz et al. [14] explored the effects exerted by different hyperglycaemic states on pain threshold and analgesic morphine potential in male Sabra rats. The authors revealed a blunted response to morphine analgesia amongst Sabra rats with both acute and chronic states of streptozocin-induced hyperglycaemia. This attenuated opioid response has been reportedly due to hyperglycaemic-mediated desensitization and reduction in functional mu-1 receptors which may explain our study findings [15, 16].

Additionally, prolonged opioid use has been reported to negatively effect diabetic quality of care. Gautam et al. [17] evaluated the effect of opioid prescription use and diabetic quality of care in their longitudinal study entailing two statewide private insurances databases ($n=152{,}984$). The authors reported decreased adjusted odds for receiving HbA1C tests with increasing daily opioid consumption (OR 0.90 for 20–49 mg/day, $p<0.01$; OR 0.85 for 50–99 mg/day, $p<0.01$; OR 0.81 for ≥ 100 mg/day, $p<0.05$), and increased adjusted odds for diabetes-related hospitalization in diabetic persons with opioid consumption of 50–99 mg/day (OR 2.30; $p<0.001$) and ≥ 100 mg/day (OR 2.16; $p<0.01$).

The greater opioid consumption amongst diabetic patients with ankle fractures should be a cause for concern. Previous reports have demonstrated delayed time to fracture healing and soft tissue healing in diabetic patients [18, 19]. In the setting of increased opioid consumption, this time to healing may be further augmented. Chrastil et al. [20] reported reduced callus strength, and delayed callus maturation and remodelling in rats who received morphine post-operatively after undergoing femoral osteotomy. Martin et al. [21] reported delayed wound healing amongst chronic morphine users through the morphine-mediated inhibition of inflammatory cell recruitment at the wound site. As such, orthopaedists should be vigilant in administering opioids to diabetics with ankle fractures and should have a higher propensity towards non-narcotic alternatives amongst this patient population.

This study is not without its limitations. Our study is retrospective in nature and falls short when compared to randomized controlled trials. Additionally, opiate prescriptions were retrieved from a centralized insurance prescription-reporting database that is integrated into the electronic medical record. This means all prescriptions obtained by paying in cash or outside of insurance reimbursement were not captured. We feel this is a minor concern, because assuming an equal distribution of cash payers among the population we likely would be under-reporting the narcotic use. Lastly, intraoperative anaesthetic and block information was not obtained, nor were inpatient hospital narcotic dispensing data. Despite these limitations, this study is one of the first of its kind and may be useful for orthopaedic surgeons who prescribe opioid-based medications for diabetic patients with ankle fractures.

Conclusion

Our study revealed increased opioid consumption amongst diabetic patients who were treated surgically for ankle fracture. With increasing efforts aimed at reducing opioid administration, coupled with poor healing potential amongst diabetics and chronic opioid users, orthopaedic surgeons should be hyper-vigilant in reducing opioid consumption amongst this patient cohort. Further studies are needed to verify our findings.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical statement The authors involved in this study abided by the current ethical standards of our country.

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