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Differences in analgesia in opioid naïve and tolerant patients with sciatic nerve blockade following elective foot and ankle surgery

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1. Abstract

1.1 Introduction and Purpose: Adequate postoperative analgesia in the opioid tolerant with chronic non-malignant pain is challenging. Multimodal pain relief regimens include regional anesthesia but opioid tolerant patients report increased postoperative pain and opioid consumption. This study compared analgesia in opioid naïve and tolerant patients receiving postoperative sciatic nerve blockade for foot and ankle surgery.

1.2 Method: Preoperative pain scores, trauma, maintenance and intraoperative opioid doses and following postoperative sciatic nerve blockade, patient self-reported pain scores and opioid consumption at discharge from the post-anesthesia unit and 24 hours were recorded.

1.3 Results: 191 patients enrolled. 40.3% were opioid tolerant and 33% had lower extremity trauma. Preoperative, immediate and delayed postoperative pain scores and intraoperative, immediate and 24 hour postoperative consumption of opioids were increased in opioid tolerant patients. Trauma and continuous infusion in opioid naïve and tolerant groups did not result in differences in 24 hour opioid consumption.

1.4 Limitations: Small subgroups and use of the pain score limited the accuracy of results.

1.5 Conclusion: Opioid tolerant patients require greater analgesic doses following sciatic nerve blockade for foot and ankle surgery. 24 hour opioid consumption for opioid naïve and tolerant patients is neither influenced by lower extremity injury nor continuous infusion.

2. Introduction

Opioid therapy for chronic non-malignant pain is becoming more widely prescribed although selection criteria concerning which patient will most benefit from this therapy are still being defined [1,2]. The Opioid Tolerant (OT) patient presenting for surgery poses a challenge for effective perioperative analgesia and a multimodal approach has been advocated which includes alternative pharmacological classes of medications and regional anesthetic techniques [3,4]. Regional anesthesia as an adjunct technique has been shown to improve pain scores but it has not been demonstrated if adequate analgesia in opioid tolerant patients relates to improved quality of recovery [5]. Peripheral nerve blockade does reduce postoperative opioid consumption and related side effects but in opioid tolerant patients who sustained leg amputation the postoperative opioid consumption and phantom limb pain remained elevated a week after surgery when compared to an opioid naïve cohort [6,7]. The purpose of this prospective observational study was to assess postoperative analgesia in opioid naïve and tolerant patients who were administered a popliteal Sciatic Nerve Block (SNB) for elective foot and ankle surgery.

3. Method

After receiving IRB approval from the University of Washington Human Subjects Division, patients provided written informed consent prior to undergoing foot and ankle surgery and were enrolled for participation in a sciatic nerve block study. The preoperative data collected were age, ASA physical status, height, weight, calculated BMI, recent traumatic injury related to the current surgery, preexisting chronic lower extremity pain with worst pain score, and dose of prescribed maintenance opioid medications. All patients received general inhalational endotracheal anesthesia with sevoflurane and intraoperative analgesia in the form of intravenous fentanyl, morphine and/or hydromorphone for their surgery. Postoperative analgesia in those patients with inadequate pain relief

following sciatic nerve blockade was administered as intravenous fentanyl, morphine and/or hydromorphone and oral oxycodone in bolus doses in the immediate postoperative period and as patient controlled analgesic infusions in the 24 hour period following surgery. In order to quantify the opioids administered to patients in equivalent dosing units and to compare the opioid usage between patients as a result of the variety of analgesic narcotic medications administered peri-operatively due to both patient and prescribing practitioner preferences, all dosages were converted to equipotent values in mg of intravenous morphine sulphate using standardized opioid conversion formulae. The dose of intraoperative opioid administered was recorded for each patient. All patients received a popliteal SNB with 25 ml 0.25% bupivacaine upon arrival to the Post-Anesthesia Care Unit (PACU). Nerve blockade was performed under ultrasound guidance with a SonoSite Turbo M using a 38 mm linear array probe and visualizing the nerve using a short axis view with the injection point proximal to the nerve branch point using a Life-Tech ProBloc 20 Gauge 30 degree bevel 100 mm needle. Patients with a hospital stay anticipated to be over 48 hours received a continuous (C-) SNB with an infusion of 0.25% bupivacaine at a rate of 10 ml/hour commenced after a catheter was positioned 3 cm distal to a Life-Tech ProLong 19 Gauge 30 degree bevel 100 mm nerve block needle tip. Supplemental opioid analgesia administered in the PACU and pain score on discharge from the unit were recorded. Patient self-reported pain scores at 24 hours after SNB and total supplemental opioid administration in the intervening time interval from PACU discharge were recorded. Patient controlled analgesia was prescribed for all patients using a 1 mg/ml hydromorphone infusion with settings of 0.2 mg at 6 minute intervals with no 4 hour lockout. All doses of opioid were converted to mg equivalents of intravenous morphine sulphate.

4. Results

There were 191 patients enrolled in this study of which 103 (53.9%) received a single bolus (S) SNB and 88 (46.1%) had a C-SNB. There were 114 (59.7%) Opioid Naïve (ON) and 77 (40.3%) OT patients and within these groups 24 (12.6%) ON and 39 (20.4%) OT patients had traumatic lower extremity related procedures (T) and the remainder had non-trauma related surgery (NT). Demographic characteristics and observed pain scores and opioid dosages for both S-SNB and C-SNB, ON and OT groups are presented in Table 1 and the more specific gender and trauma subgroup data are outlined in Table 2.

OT patients were significantly younger than ON patients in both the general S-SNB and C-SNB groups. Further detailed subgroup analysis demonstrated no meaningful differences by gender for age, ASA status, BMI or preoperative maintenance opioid dosages although the number of patients in the female trauma related groups were too low to permit complete statistical evaluation for these factors. These data are recorded in Table 2.

Preoperative, immediate and 24 hour postoperative pain scores were reported one point higher on the pain scale in S-SNB and C-SNB OT groups (mean pain scores 3 (SD 3) and 4 (SD 2) respectively) compared to the ON groups (mean pain scores 2 (SD 2) and 2 (SD 2) at the same time points). Intraoperative, immediate and 24 hour cumulative analgesic opioid doses were significantly higher in OT patients in both the generally categorized S-SNB and C-SNB groups. The mean intraoperative opioid doses for OT patients were 37.04 (SD 23.17) mg in the S-SNB group and 41.8 (SD 20.72) mg in the C- SNB group and in the ON patients the doses were 22.71 (SD 15.15) mg for the S-SNB group and 32.01 (SD 14.01) mg in the C-SNB group. The mean immediate postoperative opioid doses for OT patients were 11.05 (SD 14.65) mg in the S-SNB group and 24.97 (SD 22.96) mg in the C- SNB group and in the ON patients the doses were 5.39 (SD 8.46) mg for the S-SNB group and 12 (SD 16.16) mg in the C-SNB group. The mean cumulative 24 hour postoperative opioid doses for OT patients were 163.67 (SD 170.25) mg in the S-SNB group and 116.54 (SD 96) mg in the C- SNB group and in the ON patients the doses were 47.15 (SD 44.47) mg for the S-SNB group and 55.64 (SD 50.11) mg in the C-SNB group. Significant differences were noted for immediate postoperative mean opioid analgesic doses in the OT S-SNB group between females (n=20) and males (n=27) of 20.04 *vs* 4.72 mg, ($p < 0.01$). Figure 1 plots the mean perioperative opioid requirements for OT and ON patients in the S-SNB and C-SNB groups.

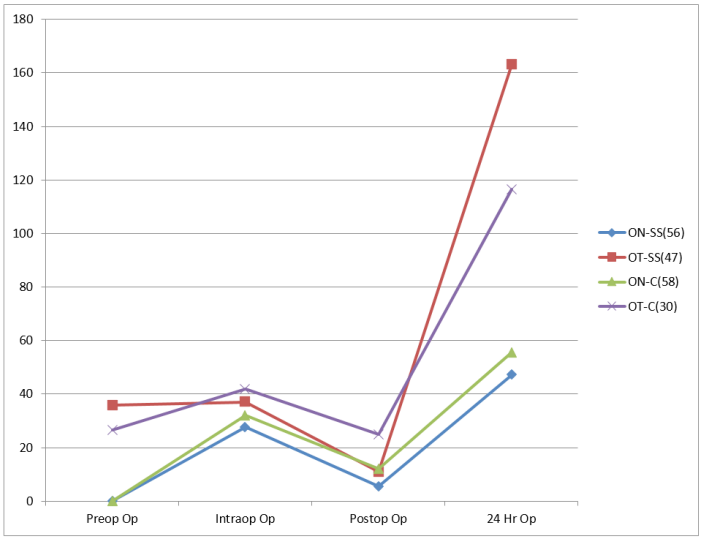

Figure 1: Perioperative opioid analgesic requirements for patients after sciatic nerve blockade. ON – Opioid Naïve, OT – Opioid Tolerant, SS – single bolus injection, C – continuous catheter infusion, Op – Opioid. Y-axis is expressed as mg intravenous morphine sulphate equivalent.

Intraoperative opioid doses were not statistically different between OT and ON groups with reference to gender, trauma, S-SNB or C-SNB. Immediate postoperative opioid doses were significantly higher in female OT NT S-SNB and male OT T C-SNB patients. Compared to their ON counterparts, OT patients in the NT groups had significantly higher 24 hour postoperative opioid requirements except for males in the C-SNB category although the number of subjects in this section may be too low to warrant comparison. The mean perioperative opioid doses for these subcategories are plotted in Figure 2.

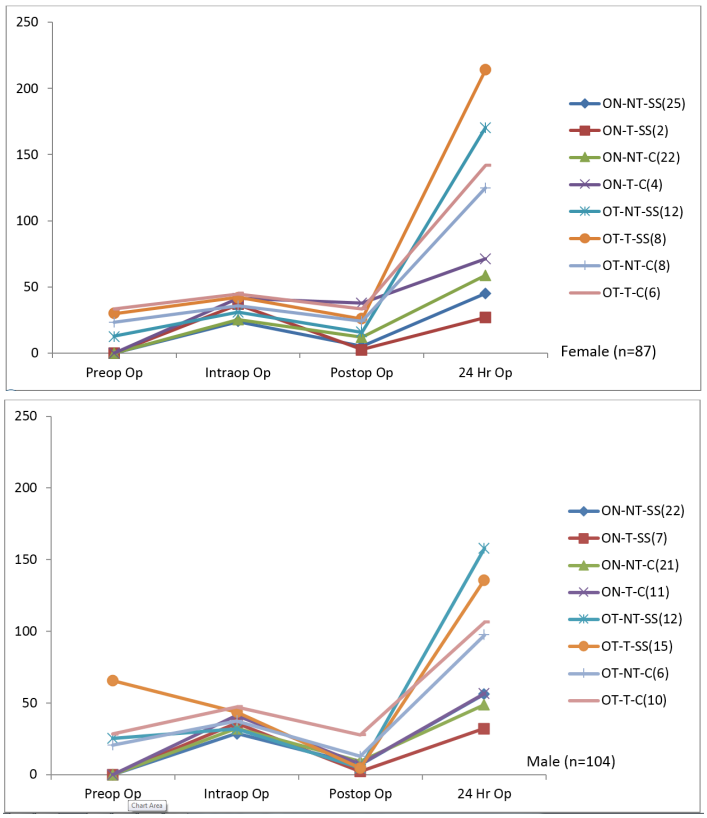

Figure 2: Perioperative opioid analgesic doses in intravenous mg morphine for Opioid Naïve (ON), Opioid Tolerant (OT), Single Dose (SS), Continuous Catheter (C), Non-Trauma (NT) and Trauma (T) patients by gender.

There was no meaningful difference in 24 hour cumulative opioid dose requirements for S-SNB and C-SNB patients regardless of prior opioid exposure or trauma related surgery.

5. Discussion

The data corroborate observations previously reported that increased perioperative opioid doses are necessary in order to achieve effective analgesia in OT patients. The magnitude of the dose of supplemental cumulative 24 hour postoperative opioid analgesia for foot and ankle surgery in OT patients in this study is more than double the amount used by ON patients. This difference in supplemental 24 hour postoperative opioid requirements in OT patients is not affected by the presence of peripheral nerve blockade whether a single bolus dose or continuous catheter infusion is used. Comparison within the ON and OT patient groups that received either S-SNB or C-SNB demonstrated no significant differences in the immediate or 24 hour cumulative opioid doses with regards to whether the elective procedure was for degenerative foot and ankle joint disease or trauma related injury.

The lack of a difference in the 24 hour cumulative postoperative opioid doses in both the ON and OT groups between the S-SNB and C-SNB cohorts indicates that catheter placement and preservation of proximity to the nerve for prolonged local anesthetic blockade was neither adequately achieved nor sustained in most patients.

One limitation of this study is the use of the pain score as opposed to the Visual Analog Scale (VAS) that lends itself to more accurate quantification and analysis. The selection of the pain score was due to ease of use for patient and nursing reporting. Future studies will incorporate the VAS for more precise pain assessment. The small number of patients in some of the cohorts skew and bias the results and this renders group comparison and generalizations inaccurate or erroneous. A large number of practitioners at various levels of training and expertise performed the SNB as opposed to a small consistent group of expert faculty and this introduces performance bias with respect to the outcome of the nerve block with respect to adequate analgesia.

6. Conclusion

Perioperative opioid analgesic supplementation in OT patients receiving SNB after elective foot and ankle surgery is significantly higher than in ON patients. The cumulative 24 hour opioid doses within the ON and OT groups with SNB are not influenced by whether surgery is for lower extremity degenerative joint disease or trauma related injury. No significant differences in the 24 hour cumulative opioid doses in patients receiving either a S-SNB or C-SNB infusion were found within the ON and OT groups. Future studies with larger numbers of subjects, use of VAS as opposed to pain scores, placement of SNB by expert faculty procedure personnel and improved catheter placement and fixation equipment and techniques will lead to improved analgesia for all patients.

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Table 1: Patient demographics, pain scores and perioperative opioid dosages.

N=191	ON-SS(56)	OT-SS(47)	ON-C(58)	OT-C(30)
Age (yrs)	56.5(15.08)	48.13(14.81)*	54.93(14.29)	48.73(11.54)*
ASA	2(1)	2(1)	2(1)	2(1)
BMI (kg/m2)	28.14(9.63)	28.4(6.11)	30.8(11.85)	27.32(5.43)
Pre-op Pain Score	5(3)	6(3)	3(3)	6(2)
Pre-op Opioid	0	35.82(57.96)	0	26.47(22.81)
Intra-op Opioid	22.71(15.15)	37.04(23.17)*	32.01(14.21)	41.8(20.72)*
Post-op Pain Score	2(2)	3(3)	2(2)	4(2)
Post-op Opioid	5.39(8.46)	11.05(14.65)*	12(16.16)^	24.97(22.96)`*
24 Hr Pain Score	4(2)	5(2)	3(2)	5(2)
24 Hr Opioid	47.15(44.47)	163.67(170.25)*	55.64(50.11)	116.54(96)*

Numbers are arithmetic mean (SD). Opioid dosage expressed in mg intravenous morphine.
* $p < 0.05$ between ON and OT, ^ $p < 0.05$ between ON-SS and ON-C groups, ` $p < 0.05$ between OT-SS and OT-C groups.

Table 2: Patient Demographics, Perioperative Pain Scores and Analgesic Opioid Requirements (n = 190).

Female Patients (n=87)	**Opioid Naïve Non Trauma**	**Opioid Tolerant Non Trauma**	**Opioid Naïve Trauma**	**Opioid Tolerant Trauma**
	Single Bolus Dose(47)			
Number (n)	25	12	2	8
Age, years	57.6(15.7)	54.33(13.87)	51.5	41.75(10.42)
ASA Status	2(1)	2(1)	2	2(1)
BMI	27.78(5.09)	29.89(6.32)	33.2	26.33(4.25)
Preop Pain Score	6(3)	7(4)	5	8(3)
Preop Opioid Dose	0	12.65(13.35)	0	29.75(32.71)
Intraop Opioid Dose	23.77(15.91)	30.93(30.4)	36.7	42.04(10.94)
PACU Pain Score	1(1)	3(3)	3	4(2)
PACU Opioid Dose	5.14(5.72)	15.78(16.21)*	2.67	25.9(20.66)
24 Hour Pain Score	4(2)	4(3)	2	7(1)
24 Hour Opioid Dose	44.86(46.42)	170.3(288.48)*	27.05	214(74.45)
	Continuous Infusion(40)			
Number (n)	22	8	4	6
Age, years	60.14(10.87)	49.3(13.35)	45.25(16.21)	43.83(10.94)
ASA Status	2(1)	2(1)	2	2(1)
BMI	26.88(4.45)	34.5(12.81)	25.7(4.38)	26.23(5.87)
Preop Pain score	3(4)	6(3)	5	6(2)
Preop Opioid Dose	0	23.42(19.1)	0	33.19(27.81)
Intraop Opioid Dose	25.33(10.76)	35.79(25.02)	41.25(10.66)	44.78(14.4)

PACU Pain Score	2(3)	4(3)	4(3)	3(2)
PACU Opioid Dose	12.13(14.2)	24.08(19.87)	37.8(35)	33.33(15.59)
24 Hour Pain Score	4(2)	4(3)	4	7(2)
24 Hour Opioid Dose	58.83(60.02)	124.85(112.74)*	71.33(32.08)	141.55(96.84)

Numbers stated are mean (SD), PACU Post Anesthesia Care Unit, Opioid doses in mg intravenous Morphine
*p<0.05 by t-test.

Table 3: (Cont'd) Patient Demographics, Perioperative Pain Scores and Analgesic Opioid Requirements.

Male Patients (n=104)	Opioid Naïve Non Trauma	Opioid Tolerant Non Trauma	Opioid Naïve Trauma	Opioid Tolerant Trauma
	Single Bolus Dose(56)			
Number (n)	22	12	7	15
Age	56.45(16.34)	55(17.27)	54.14(8.13)	41.07(11.41)
ASA Status	2(1)	2(1)	2(1)	2(1)
BMI	29.72(4.464)	31.85(6.79)	36.4(24.5)	25.57(4.77)
Preop Pain Score	6(3)	6(2)	3(3)	5(3)
Preop Opioid Dose	0	25.58(26.37)	0	65.79(91.01)
Intraop Opioid Dose	28.75(11.29)	32.14(13.69)	36(22.07)	43.62(27.09)
PACU Pain Score	2(2)	3(3)	1(1)	2(2)
PACU Opioid Dose	6.88(11.92)	4.67(7.53)	2.38(2.97)	4.76(4.77)
24 Hour Pain Score	4(2)	5(2)	3(2)	5(2)
24 Hour Opioid Dose	56.3(47.37)	158.06(153.77)*	32.34(29.29)	136.03(78.5)*
	Continuous Infusion(48)			
Number (n)	21	6	11	10
Age	54.24(15.61)	55.17(5.27)	49.36(14.72)	47.6(12.77)
ASA Status	2(1)	2(1)	2(1)	2(1)
BMI	32.48(14.28)	28.97(2.81)	27.75(4.25)	27.32(5.43)
Preop Pain Score	4(3)	4(3)	4(3)	6(2)
Preop Opioid Dose	0	20.62(21.27)	0	28.37(25.42)
Intraop Opioid Dose	32.3(16.36)	37.6(11.32)	41.44(10.4)	47.33(25.03)
PACU Pain Score	2(2)	4(3)	1(1)	3(2)
PACU Opioid Dose	9.31(11.24)	13.13(14.55)	7.49(11.89)	27.77(27.34)*
24 Hour Pain Score	2(2)	4(2)	3(2)	6(2)
24 Hour Opioid Dose	48.9(47.03)	97.45(125.26)	56.42(42.41)	106.33(71.05)

Numbers stated are mean (SD), PACU Post Anesthesia Care Unit, Opioid doses in mg intravenous Morphine
*p<0.05 by t-test.