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Patient-perceived duration of effect of lidocaine and bupivacaine following diagnostic medial branch blocks; a multicenter study

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ABSTRACT

Objective: To quantify the duration of pain relief reported in association with lidocaine and bupivacaine in patients suffering from axial back pain, who reported a response of ≥80% relief lasting at least 30 min following medial branch blocks(MBB).

Design: A retrospective review.

Methods: Setting & Subjects: Four academic medical centers utilized a uniform pain diary. It was administered to consecutive patients after undergoing MBB. This pain diary included NRS pain score and percentage of pain relief (PPR) at 12 designated time points.

Results: One hundred and fifty pain diaries were collected and analyzed. 42 blocks were performed in the cervical spine, 7 in the thoracic spine, and 101 in the lumbar spine. By NRS, 32% of pain diaries indicated that the patient experienced ≥80% pain relief at the 30-min and 42.7% (64/150) did so by PPR. Mean duration of ≥80% pain relief as measured by NRS in the bupivacaine subgroup was 3.5 h (SD 8.7, 95% CI 0.6–6.5) versus mean duration of 16.4 h (SD 19.6, 95% CI 5.4–27.4) in the lidocaine subgroup. Mean duration of ≥80% pain relief as measured by PPR in the bupivacaine subgroup was 19.2 h (SD 19.2, 95% CI 13.3–25.1) versus mean duration of 12.2 h (SD 15.9, 95% CI 5.6–18.8) in the lidocaine subgroup.

Conclusions: This study demonstrates that there is no discernable or statistically significant difference in the duration of effect when comparing lidocaine to bupivacaine in patients that experience 80% or more relief following a medial branch block. This data suggests any emphasis on concordant duration of relief from specific anesthetics utilized for diagnostic medial branch blocks should be reconsidered.

1. Introduction

Medial branch radiofrequency neurotomy (MB RFN) is a widely-utilized procedure in the treatment of non-radicular neck and low back pain arising from the zygapophyseal joint (z-joints, facet joints) [1,2]. In the lumbar spine, prevalence of z-joint pain ranges from 5 to 50%. [3–12]. [13] and in the cervical spine 25–60% [14–16] MBBs can be diagnostic and prognostic and are required to make the diagnosis of z-joint pain and thus select patients for therapeutic RFN due to the relatively low sensitivity and specificity of physical exam maneuvers and diagnostic imaging has in making this diagnosis [17].

The interpretation of MBBs as a selection criterion for RFN has been widely debated. In large part, this debate centers around what an acceptable threshold is for the sensitivity and specificity of this diagnostic test, as false positive responses are inherent. The estimates of a false positive response after a single MBB range from range of 15–45% [2–4,9,10,18–22]. The determinate of what constitutes a "positive response" is arbitrary and debated, with increasing thresholds of relief being required to determine a test positive resulting in a more specific but less sensitive test. Similarly, performing the test twice will reduce false positive

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findings. Recent facet guidelines advocate 50% relief after a single MBB for diagnosis, [22]. [23]. North American Spine Society (NASS) current recommendations are consistent with recently updated Medicare LCD guidelines, which call for 80% relief after two sequential MBBs [22–24].

The Spine Intervention Society (SIS) endorses a more rigorous selection criteria via the concept of controlled comparative MBBs [25]. Theoretically, controlled comparative MBBs reduce the false-positive responses by comparing the patient perceived duration of pain relief following blocks using a short-acting (e.g. lidocaine) versus a long-acting (e.g. bupivacaine, ropivacaine). A positive test requires not only that the patient have relief of their pain with MBBs, but that a block with a longer-acting agent has a longer duration of pain relief than a shorter-acting local anesthetic. This is referred to as a "concordant" response [25].

This model of comparative blocks has been evaluated in cervical MBBs [26,27].

In 47 patients with chronic neck pain following whiplash injury who underwent dual anesthetic blocks, 45 had a positive initial block, and 44 had a positive second block (irrespective of duration). Interestingly, 4 patients (9%) had a response with lidocaine longer than bupivacaine, but responses still "consistent with known pharmacology of the drugs" [26]. 13 patients (29%) demonstrated relief for period in excess of the reported durations of action of either lidocaine or bupivacaine, and of that group only 7/13 had longer relief with bupivacaine than lidocaine. Collectively, duration of action varied widely from 35 min to several days. For lidocaine, median duration was 185 min (Q1 98 min and Q3 405 min) and for bupivacaine median 458 min (Q1 240 min and Q3 1365 min).

The same investigative group then considered comparative versus "placebo-controlled" MBBs in fifty consecutive patients with chronic neck pain [28]. In this study, only those patients who responded to both blocks, who obtained longer-lasting relief when the longer-acting agent was used, and had a negative block with placebo, were considered true positive responders. Comparative MBBs considering duration of anesthesia tested against placebo MBBs yielded a specificity of 88%, but only a marginal sensitivity of 54%. If the definition of a positive response was expanded to all patients with reproducible relief on both blocks done with anesthetic, irrespective of duration, sensitivity increased to 100%, but specificity decreased to 65%. It is from this study alone that the validity of dual comparative blocks has been evaluated. This diagnostic paradigm has not been specifically evaluated in the lumbar spine and the translation of the literature from the cervical spine to the lumbar spine has been debated [29]. Perhaps surprisingly, there is a paucity of literature on comparative effects between small volumes of lidocaine and bupivacaine in general. While the merits of a comparative medial branch block paradigm continue to be debated, there is surprisingly little published data on the duration of anesthesia patients experience when undergoing MBB with lidocaine or bupivacaine.

The objective of this study is to quantify the duration of pain relief reported in association with lidocaine and bupivacaine in patients suffering from axial back pain, who reported a response of $\geq$80% relief lasting at least 30 min following MBB.

2. Methods

2.1. Study design

This is a retrospective review from four academic medical centers of prospectively collected data from a uniform pain diary administered to consecutive patients after undergoing MBBs. Internal Review Board (IRB) exemption was granted at all four participating institutions (IRB 181798 Vanderbilt, HSC2018-385E at UT Health San Antonio, 18–25701 at UCSF, 107359 at Emory). The time-period of collection was from January 2018 to June 2019. The pain diary assessed numeric rating scale (NRS) score immediately pre-injection and at 12 different time points post injection up to 48 h (Appendix 1). Routine clinical decision making, including assessing the degree of pain relief, was the sole determinate in patients progressing from MBB to RFN; patients' participation in use of the pain diary in and of itself was not a determinate.

2.2. Participants

Inclusion criteria, consisted of adults (>18YO) with axial pain determined, by history and physical examination, to be most likely secondary to a facetogenic pain generator and scheduled for a MBB. Data was collected for geographic location, sex, body-mass index (BMI), spine segment MBB was performed upon, number of joints targeted, type of anesthetic used, anesthetic volume, needle gauge, and pre-injection NRS pain score. There were no exclusion criteria. Data collection occurred over an 18-month period.

2.2.1. Medial branch block procedure

MBB procedures were performed by Physical Medicine and Rehabilitation Physicians with fellowship training in either Interventional Spine or Pain Medicine. These procedures were conducted according to the Spine Intervention Society's Practice Guidelines for Spinal and diagnostic and Treatment Procedures [30]. All procedures were performed using contrast under live fluoroscopy to minimize the risks of a false negative block. Anesthetics used were either 0.5% bupivacaine or 2% lidocaine at the discretion of the treating physician. Patients continued their standard of care after injection without restriction of co-interventions.

2.3. Outcome measure

A uniform pain diary was agreed upon between the four separate academic centers and used as a part of routine clinical practice (Appendix 1). This pain diary included NRS pain score and percentage of pain relief at 12 designated time points. Pain relief was measured as current pain at the time period specified: relief lasting only 25 min would be recorded as "no relief" at the 30 min mark, complete relief of 35 min or 55 min would equally be recorded as "100%" relief at the 30 min mark. Patients were asked to fill out the diary in full. Missing data points were not included in data analysis. Data was prospectively collected from these diaries.

2.4. Data analysis

Each MBB was considered in isolation, though there were patients who returned for multiple blocks. Greater than or equal to 80% improvement in pain at the 30-min time point was considered a positive block. This was performed based upon both the (1) "calculated" 80% improvement on the traditional NRS score, as well as (2) patient-reported percentage of improvement. The null hypothesis was that there would be no difference in duration of relief between lidocaine and bupivacaine after positive response to a MBB. Mean and standard deviation and median duration of pain relief was extracted with 95% confidence intervals (CI) for means and interquartile ranges (IQR) for medians. Categorical responses based were calculated along with 95% CI to evaluate if utilizing a threshold of pain relief that "wore off" between 61 min and 1 h 59 min and another window that "wore off" between 3 h and 3 h 59 min would be able to discriminate between lidocaine and bupivacaine.

3. Results

One hundred and fifty consecutive uniform pain diaries were collected and analyzed. Eighty-five (56.67%) diaries emanated from a single institution. The average age of subjects was 60.76 years. Seventy-two (48%) of the subjects were female. Average BMI was 30.7 kg/m^2. Regarding spine segment, 42 blocks were performed in the cervical spine, 7 in the thoracic spine, and 101 in the lumbar spine. Ninety percent of procedures were performed with a 25-gauge needle (135/150). A single joint was targeted 29 times, two joints 85 times, and four joints 36 times. In 95.3% of cases, 0.5 mL or less was injected per nerve (143/150). In 66% of cases (99/150), bupivacaine was used as opposed to lidocaine

Table 1
Patient and procedural characteristics.

Age (Mean Years)	60.76
Gender (Female)	72 (48%)
Body Mass Index (Mean kg/m2)	30.7
Segment Blocked Cervical	42 (28.0%)
Segment Blocked Thoracic	7 (4.7%)
Segment Blocked Lumbar	101 (67.3%)
25 Gauge Needle Size	135 (90.0%)
One Joint Blocked	29 (19.3%)
Two Joints Blocked	85 (56.7%)
Four Joints Blocked	36 (24.0%)
Volume Injected ≤0.5 mL	143 (95.3%)
Bupivacaine Used	99 (66.0%)
Lidocaine Used	51 (34.0%)

(Table 1).

Thirty-two percent (48/150) of pain diaries indicated that the patient experienced ≥80% pain relief at the 30-min threshold utilizing calculated data from the traditional NRS score. Two of these 48 diaries included incomplete data and were excluded from analysis. Analysis of the patient reported percentage improvement in pain revealed that 42.7% (64/150) of diaries demonstrated ≥80% relief at the 30-min threshold. Subgroup analysis for those patients whose blocks were performed with lidocaine showed positive response in 14/51 (25.4%) in the traditional NRS score subgroup and 22/51 (43%) in the patient reported percentage improvement subgroup. Similar analysis in the bupivacaine subgroup revealed a 32/99 (32.3%) and 42/99 (42.4%) positive response rate, respectively (Table 2).

When calculating percentage improvement in NRS score based on NRS score changes, the average duration of ≥80% pain relief for positive responses in the bupivacaine subgroup was 3.5 h (SD 8.7, 95% CI 0.6–6.5), and the median duration was 0.5 h (IQR 0.5–3.5). The average duration of≥80% pain relief for the positive responses in the lidocaine subgroup was 16.4 h (SD 19.6, 95% CI 5.4–27.4), and the median duration was 9.0 h (IQR 0.5–48) (Table 3).

When patient-reported percentage improvement was used to define a block as "positive", the average duration of ≥80% pain relief for positive responses in the bupivacaine subgroup was 19.2 h (SD 19.2, 95% CI 13.3–25.1) and the median duration was 9.0 h (IQR 2–48). The average duration of pain relief for the positive responses in the lidocaine subgroup was 12.2 h (SD 15.9, 95% CI 5.6–18.8), and the median duration was 6.0 h (IQR 0.9–13.5) (Table 3).

Two by two tables were also constructed to evaluate the number of positive responses that lasted less than 2 h compared to 2 h or more. As calculated by NRS scores, of the positive lidocaine responders 5 ((35.5%) 95% CI 10.5–60.5%) had a duration of relief of less than 2 h whereas 9 ((64.3%) 95% CI 39%–89%) had a response of at least 2 h or more. For bupivacaine 23 ((71.8%) 95% CI 56.2%–87.4%) had relief for less than 2 h compared to 9 ((28%) 95% CI 12.5%–43.7%) who had relief of 2 h or more (Table 4). Data was also evaluated using patient reported improvements in pain (Table 5). Data was similarly analyzed using a threshold of less than 4 h as compared to 4 h or more for both calculated NRS, and patient reported pain relief (Table 4 and Table 5).

Table 2
Response rates for ≥80% improvement in pain at the 30 min timepoint threshold using numeric rating scale and percentage of pain improvement. Subgroup analysis includes patients who had their block performed with lidocaine and those who had their block performed with bupivacaine.

	Numeric Rating Scale	Percentage Pain Improvement
≥80% Relief All Subjects	48 (32%)	64 (42.7%)
≥80% Relief Lidocaine	14 (25.4%)	22 (43.0%)
≥80% Relief Bupivacaine	32 (32.3%)	42 (42.4%)

Table 3
Mean and median duration of responses in those subjects with positive response to medial branch blocks, categorized by which local anesthetic was used to perform the block.

	Mean Pain Relief Duration (Numeric Rating Scale) In Hours ± Standard Deviation With 95% Confidence Interval	Mean Pain Relief Duration (Percentage Pain Improvement) In Hours ± Standard Deviation With 95% Confidence Interval	Median Pain Relief Duration (Numeric Rating Scale) In Hours ± Interquartile Range	Median Pain Relief Duration (Percentage Pain Improvement) In Hours ± Interquartile Range
Bupivacaine	3.5 ± 8.7 (0.6–6.5)	19.2 ± 19.2 (13.3–25.1)	0.5 (0.5–3.5)	9.0 (2.0–48.0)
Lidocaine	16.4 ± 19.6 (5.4–27.4)	12.2 ± 15.9 (5.6–18.8)	9.0 (0.5–48.0)	6.0 (0.9–13.5)

Table 4
Categorical Evaluation of Anesthetic Duration as Measured by Calculated NRS scores.

	<2 h	≥2 h
Lidocaine	5 (35.5%) 95% CI 10.5–60.5%	9 (64.3%) 95% CI 39%–89%
Bupivacaine	23 (71.8%) 95% CI 56.2%–87.4%	9 (28%) 95% CI 12.5%–43.7%
	<4 h	≥4 h
Lidocaine	5 (35.7%) 95% CI 10.6%–60.8%	9 (64.3%) 95% CI 39.2–89.4%
Bupivacaine	24 (75%) 95% CI 60%–90%	8 (25%) 95% CI 10%–40%

Table 5
Categorical evaluation of anesthetic duration as measured by patient reported improvements in pain.

	<2 h	≥2 h
Lidocaine	6 (27.3%) 95% CI 8.6%–45.9%	16 (72.3%) 95% CI 54%–91%
Bupivacaine	5 (11.9%) 95% CI 2%–22%	37 (88%) 95% CI 78%–98%
	<4 h	≥4 h
Lidocaine	7 (32%) 95% CI 12%–51%	15(68%) 95% CI 49%–88%)
Bupivacaine	13 (30.9%) 95% CI 17%–45%	29 (69%) 95% CI 55%–83%

4. Discussion

In this study, we show that within the confines of a single diagnostic medial branch block, there is no reliable differentiation in the patients' duration of pain relief whether lidocaine or bupivacaine is used. By some measures, it appears the lidocaine response was longer than bupivacaine even. This calls into question the clinical utility of considering the duration of relief when performing dual medial branch blocks. While this study appears in conflict with foundational work by Lord et al. in the performance of cervical medial branch blocks, this study is not equipped to specifically evaluate the sensitivity or specificity of dual medial branch blocks when anchored against a placebo response [28]. In fact, in the work by Barnsley et al., this same phenomenon of discordant responses or unexpectedly prolonged responses was also noted and the authors in fact called for additional research, which we aimed to address [26].

While the pharmacokinetics of short vs long acting anesthetics is well

documented, there is in fact a paucity of literature in general that assesses the duration of action when small volumes of anesthetic are used targeting relatively small targets. Regional anesthesia research utilizing larger volumes of injectate do suggest longer durations of action for bupivacaine; for example one study investigating the duration of effect of a 30 mL injection used for a brachial plexus block found duration of lidocaine to be 172.8 +-/7.8 min compared to 546.4 ± 14.9 min for bupivacaine [31] However, it is unknown if this is applicable to the smaller volumes used in this study.

Two studies have shown that combining smaller volumes of both lidocaine and bupivacaine together does not delay the onset of action relative to lidocaine alone nor decreases the duration of action relative to bupivacaine alone [32,33]. Another study comparing 0.25% bupivacaine and 1% lidocaine given as 0.2 mL of intra-dermal injection found mean duration of effect to be 7.02 ± 1.46 h and 6.63 ± 1.85 h respectively [34]. The onset of action for both anesthetics was less than 30 s. While this study reported a significant p value for duration of effect, clinically a difference of 0.39 h (23 min) is insufficient for a paradigm such as "comparative" blocks. Overall, our findings are largely consistent with this latter study.

In the work by MacVicar et al. on clinical outcomes of lumbar and cervical radiofrequency ablation, two separate blocks using lidocaine or bupivacaine were used as selection criteria, however in both studies the "duration of relief following each block was not a criterion for treatment" [18,35]. In fact, the reasoning for this as published in these studies references commentary from one of the authors also involved in the referenced work by Lord and Barnsley. Specifically, it was noted that "duration of relief has little effect on the diagnostic confidence (posttest probability) of comparative local anesthetic blocks" [36]. In the study by Dreyfuss and colleagues on outcomes following lumbar RFN, patient selection was only that pain relief after lidocaine MBBs last at least 1 h and that relief following subsequent bupivacaine MBBs last at least 2 h. Neither discordant responses between anesthetics nor prolonged duration of relief following MBBs were excluded [9]. Perhaps most interesting from that study, is that the authors reported a median (range) duration of relief from lidocaine and bupivacaine blocks and similar results to our study were seen in that there was little difference. The median duration of relief following lidocaine was 4.4 h (IQ range 1.3–6 h) and following bupivacaine was 4.9 h (IQ range 2–6 h). In that light, our research is in fact consistent with previously published literature on this topic.

Indeed, the findings of this study must also be put in context to the study design. We acknowledge that we did not compare blocks within patients (in those who had two blocks) nor did we utilize a control saline to potentially identify placebo responders as did Lord et al. Certainly, this resulted in some "false positive" responders being included in our analysis. Nonetheless, in this study the incidence of a positive block was only 32% (48/150), which is well within the accepted range of the prevalence of z-joint pain [3–12]. Pragmatically, a physician is not able to the use a placebo block in clinical practice. Even more, after an apparently positive initial medial branch block, a treating physician is in fact only availed to information on the duration of that single block. After in an initial block, no comparison is available, and in that sense, it is helpful to know if unexpectedly long duration of effects of lidocaine or unexpectedly short duration of effects of bupivacaine should be appreciated versus be discounted. Indeed, in this study, the data demonstrates that the duration of that block seems unrelated to the anesthetic agent used.

Weaknesses of this study include its retrospective design; the way data was securely collected limited our ability to extrapolate other potentially interesting information such comparing 2 blocks done on the same patient. We also acknowledge that we did not prospectively follow patients to evaluate if duration of effect was associated with outcomes following radiofrequency ablation. Similarly, this data does not further comment on the utility of performing 1 vs 2 MBBs, or what percentage of pain relief is the best measure. Other limitations include that the investigators were not blinded to the injectate used, though the patients were typically blinded. A modest proportion of patients who had 2 MBBs may have been given the same anesthetic agent for both blocks. We considered cervical, thoracic, and lumbar blocks together, though we are unaware of why the duration of effect would be dependent on the spinal segment blocked. The loss to follow up percentage is also unknown, as while all consecutive patients were given the same pain diaries in a clinical setting across all sites, we did not prospectively enroll patients and thus had no means of tracking those who received the pain diary but did not return it.

Strengths of this study include the pragmatic approach as well as the multi-center design. The data compiled included a large number of pain diaries assessed with rigorously prospectively collected data, which increases the validity of our findings. The overall 'N' of this study is larger than any previously published literature we are aware of that contains data on the duration of effect of anesthetics following MBB. We also used two different means of assessing pain relief in patients, via both a calculated NRS scale as well as a direct assessment of patients' subjective perception of pain relief. While both measures of pain relief failed to show a difference between lidocaine and bupivacaine, it is curious the differences seen when comparing the two different measures of pain relief. Further investigation into the phenomenon is warranted.

5. Conclusion

This study demonstrates that there is no discernable or statistically significant difference in the duration of effect when comparing lidocaine to bupivacaine in patients that experience 80% or more relief following a medial branch block. This data suggests any emphasis on concordant duration of relief from specific anesthetics utilized for diagnostic medial branch blocks should be reconsidered.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Byron Schneider reports a relationship with Spine Intervention Society that includes: board membership, funding grants, and travel reimbursement. Byron Schneider reports a relationship with AIM Specialty Health that includes: consulting or advisory. Byron Schneider reports a relationship with State Farm Insurance Companies that includes: consulting or advisory. Jaymin Patel reports a relationship with Professional Disability Associates that includes: consulting or advisory. Zachary McCormick reports a relationship with Avanos Medical Inc that includes: funding grants. Zachary McCormick reports a relationship with Relievant Medsystems that includes: funding grants. Zachary McCormick reports a relationship with SPR Therapeutics that includes: funding grants. Zachary McCormick reports a relationship with Boston Scientific Corp that includes: funding grants. Zachary McCormick reports a relationship with Soal Therapeutics that includes: consulting or advisory. Zachary McCormick reports a relationship with Stryker Corp that includes: consulting or advisory. Zachary McCormick reports a relationship with FSUMobile that includes: consulting or advisory.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inpm.2022.100083.

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