Retrospective Review

Chronic Low Back Pain: The Therapeutic Benefits of Diagnostic Medial Branch Nerve Blocks

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Background: Chronic low back pain (CLBP) is an extremely prevalent disease, whose etiology is often multifactorial. Facet joint arthropathy is one of the most common causes of CLBP. Facet joints are innervated by the medial branches of the primary and adjacent level dorsal rami and are, therefore, key potential targets for the symptomatic management of CLBP. A lumbar medial branch nerve block (MBB) procedure is often used to assist in the diagnosis of facet mediated CLBP. For unclear reasons, some patients experience protracted relief of CLBP after diagnostic MBBs alone.

Objective: To describe the phenomenon of protracted relief of CLBP after diagnostic MBBs and search for predictors of this response.

Study Design: A retrospective chart review of patients who underwent MBB procedures by a single practitioner, over a 2 year period, was conducted.

Setting: All patients were seen at the Montefiore Multidisciplinary Pain Program, Bronx, NY.

Methods: Data from follow up visits was used to categorize patient's response to MBBs as having no relief (NR), transient relief (TR) or protracted relief (PR). Patient demographics and characteristics were collected, and a multivariate analysis investigating associations with PR was conducted.
Results: 146 patients met inclusion criteria. 41 patients (28%) had NR, 54 (37%) had TR, and 51 (35%) had PR. CLBP symptom duration of < 6 months ($P = 0.013$) and unilateral back pain symptoms ($P = 0.0253$) were significantly associated with PR after MBB.

Limitation: This is a retrospective study with a relatively small sample size conducted on patients belonging to a single practitioner. Outcomes were based largely on subjective patient satisfaction scores.

Conclusions: In select patients, MBB may produce protracted relief of CLBP symptoms. The authors present distinct hypotheses which may help explain the therapeutic effects of diagnostic MBB procedures.

Key words: Chronic low back pain, facet joint, medial branch nerve block

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Chronic low back pain (CLBP) is an extremely prevalent, clinically, and economically burdensome ailment, that carries a lifetime prevalence of 30–85% in the aging population, (1,2), and is one of the leading causes of activity limitation, lost work hours, and disability in the United States (3) CLBP generally refers to pain located in the lumbar region, lasting > 3 months, without associated radicular symptoms. Lumbar facet joint arthropathy is one of the most common causes of CLBP, although these symptoms are often multifactorial and can be myofascial in origin, due to intervertebral disc degeneration or referred

from hip or sacroiliac joint pathology (4). Facet joints are paired synovial joints, located in the posterolateral spine and formed between adjacent vertebral level, whose biomechanical function is to guide and limit movement of the spinal segments (5). Each facet joint is innervated by both the medial branch of the primary dorsal ramus of the nerve exiting at its level, and the medial branch of the above vertebral level (6). Conservative therapies including home exercise, formal physical therapy, and topical or oral pharmacotherapy, are the first line therapies for the management of CLBP. In refractory cases and under certain circumstances, CLBP caused by lumbar facet arthropathy may be managed by percutaneous lumbar medial branch nerve radiofrequency ablation (RFA), a procedure resulting in lumbar facet joint denervation (7). Often, history of present illness, physical examination, and radiologic evidence are insufficient in correctly diagnosing facet mediated CLBP, therefore positive responses to a series of diagnostic lumbar medial branch blocks (MBB) with local anesthetics is a necessary precursor to lumbar medial branch nerve RFA (8,9). Positive diagnostic lumbar MBB is loosely defined as experiencing transient > 80% pain relief of CLBP on a single or series of 2 diagnostic lumbar MBBs. Interestingly, some patients with CLBP achieve significant and protracted pain relief and/or functional improvement after diagnostic lumbar MBBs alone and do not require lumbar RFA. In these patients, analgesic effects of local anesthetics appears to be prolonged, providing pain relief to some for weeks to months, long outlasting the pharmacokinetics of the anesthetics employed (10). Manchikanti and colleagues have described the phenomenon in detail and written extensively about the therapeutic effects of MBBs with local anesthetics, and with or without steroids (11-14). Furthermore, the recent facet joint interventions guidelines set forth by the American Society of Interventional Pain Physicians provide level II (moderate strength) evidence for therapeutic lumbar facet joint nerve blocks, with inclusion of 3 relevant randomized controlled trials with long-term improvement (13-16). Interestingly, the mechanism for this protracted pain relief response is not known and it should be noted that local anesthetics may have a differential impact on acute versus chronic pain (17). Herein, we aim to describe the phenomenon of protracted pain relief after diagnostic lumbar MBBs, search for predictors of this response in our patient population, and suggest possible mechanisms that may help explain this response.

Methods

Patient Population

Institutional review board approval was obtained from Albert Einstein College of Medicine, Bronx, NY. A retrospective chart review was conducted. Candidate patients were identified by searching medical records of patients who underwent lumbar MMB (CPT code 64493), by a single provider (JRH), at the Montefiore Multidisciplinary Pain Program, Bronx, NY, during a 2 year period (2017-2019). All patients included were diagnosed as having suspected facet mediated CLBP based on history, physical examination and radiological findings. Included in the analysis were charts that contained the following: a) an initial visit, b) a complete series of 2 lumbar MBB procedures and c) at least 1 post procedure follow-up visit. All patients were 1) at least 18 years of age, 2) had pain in the lower back without radicular symptoms, and 3) had no meaningful pain relief after at least 2 conservative therapies (oral pharmacotherapy and a full course of physical therapy or home exercise program). Microsoft Excel® was employed to record pertinent patient demographics, such as age, gender, body mass index (BMI), duration of lower back pain symptoms (in months), degree of lumbar spondylosis on imaging as described by a radiologist (mild, moderate or severe), comorbid medical and psychiatric history, smoking history, number of nerves blocked during procedure (3 or 4), and laterality of pain (unilateral or bilateral).

Procedures

All diagnostic lumbar medial branch block procedures were performed in a series of 2 injections, 2 - 3 weeks apart, using the following standardized and validated technique (18). The patient was placed prone on the fluoroscopy table, skin was sterilized, draped, and then anesthetized with 0.5-1 mL of 1% lidocaine. Then, under fluoroscopic guidance, the interventionalist (JRH) targeted the medial branches of the lumbar level(s) of concern with a 22G 3.5- inch or 5-inch spinal needle, located at the junction of the superior articular process and the transverse process. Oblique and anterior posterior views of the lumbar spine were obtained to confirm the correct location of the needle tip. Next, 0.5 mL of Omnipaque 180 (Iohexol) contrast dye was injected at each level to confirm the position of the needle and to ensure the absence of vascular or epidural flow. Finally, 0.25 - 0.5 mL of 0.5% bupivacaine was injected at each level during the first MBB procedure in the series. The identical technique was employed for

a second confirmatory lumbar MBB procedure, except 0.75% bupivacaine was used as the injectate. Different concentrations of local anesthetics were selected for diagnostic purposes, 0.5% bupivacaine typically producing shorter periods of transient pain relief, relative to 0.75% bupivacaine. Low volumes of higher concentrated local anesthetics were employed in order to decrease the false positive rate of diagnostic MBB (19).

Outcome Measurement

Follow-up visits after the second set of MBBs occurred at 4 to 8 weeks. Although pre- and post- MBB numeric rating scores (NRS) were documented by the patients, to account for the subjective nature of pain perception, the final decision to proceed to RFA was based solely on the patients' individual experience. Patients who reported no relief after both the first or second MBB were classified as having no relief (NR) and not offered lumbar RFA. Patients who reported transient (> 12 hours to ~1 week) of satisfactory pain relief (at least 50% or greater relative to baseline) and functional improvement (such as distance of walking or completing activities of daily living) were classified as having transient relief (TR). Patients who reported continued significant pain relief and functional improvement at follow-up, occurring at least 4 weeks after the second procedure, were classified as having protracted relief (PR) and not offered RFA. Formal physical therapy and topical and oral pharmacotherapy was included as part of every patient's comprehensive multimodal treatment plan, before and after the diagnostic MBBs (20).

Statistical Analysis

All data collected was aggregated into a Microsoft Excel® spreadsheet database. Data tables were generated and populated based on the analysis of patient information. Descriptive statistics were calculated using Microsoft Excel®. Patient demographics, characteristics, and response to diagnostic lumbar MBBs were reported as percentages. To determine if any patient characteristics or clinical features are predictive of PR, we performed unadjusted logistic regression analysis for each predictor of interest as the sole independent variable to measure and test the association with the PR. Then, we used best-subset strategy to select predictors from 10 candidate variables for multivariate logistic regression. The selection procedure compares Akaike Information Criterion (AIC) between the complete enumerations of 210 models. The best-subset strategy selected age, gender, unilateral MBB (either right or left side), and longer symptom duration (> 6 months). The resulting unadjusted and adjusted odds ratio was subsequently tabulated. All statistical analyses were performed by R version 3.6.2.

Results

Patient Selection

One hundred and seventy-seven patients were initially identified. Based on the aforementioned criteria (see Methods), 146 charts were considered complete and, therefore, included in the analysis. The remaining 31 charts were excluded for various reasons, most commonly because of lack of documented patient follow-up after a single or series of MBBs. Other reasons for exclusion included: relocation, interruption of insurance coverage, and patients who refused to have a second diagnostic block because of increased pain after the first procedure.

Demographics

Patient demographics and clinical characteristics are summarized in Table 1. The average patient age was 61 years old (range 34 - 97). Sixty-six point four percent (97) of patients were women. The average BMI was 31.6 (range 20 - 54.9). 50.7% of patients (74) were smokers or had a positive history of smoking. Forty-six point six percent of patients (68) carried a concurrent diagnosis of depression. Only 8.2% (12) were diagnosed as having fibromyalgia. Eighty-three point six percent (122) of patients had radiographic evidence of facet arthropathy or spondylosis on x ray, CT, or MRI of the lumbar spine. Twenty-one point 2 percent (31) of patients received unilateral MBB (for exclusively unilateral pain), the remainder 78.8% (115) received bilateral MBB.

MBB Outcomes

One hundred and forty-six patients underwent a series of 2 diagnostic MBBs. At follow-up, 28% (41) of patients reported NR, and 72% (105) had a positive response to the diagnostic block. Of those who had a positive response, 37% (54) had TR while 35% (51) had PR (Fig. 1.1). Data was then stratified to include only patients with positive response to diagnostic block. One hundred and five patients were included in the positive response group and 51% (54) had TR, while 49% (51) had PR (Fig. 1.2).

PR Predictors

In a multivariate logistic regression, unilateral MBB [Adjusted OR 3.366 (1.232, 9.917); Adjusted *P*

Table 1. *Patient demographics are tabulated for total population and stratified according to response group (NR: no relief, TR: transient relief, PR: protracted relief).*

	Total (n = 146)	NR (n = 41)	TR (n = 54)	PR (n = 51)
Mean Age [range]	61 [34, 97]	61 [34, 85]	60 [41, 84]	60 [39, 97]
Women	97 (66.4%)	14 (34.1%)	32 (59.2%)	13 (25.5%)
Men	49 (33.6%)	27 (65.9%)	22 (40.7%)	38 (74.5%)
Mean BMI [range]	31.6 [20, 54.9]	32.6 [21.9, 49.4]	31.5 [20.4, 54.9]	30.9 [20.1, 46.5]
Smoker	74 (50.7%)	22 (53.7%)	31 (57.4%)	22 (43.1%)
Depression	68 (46.6%)	24 (58.5%)	22 (40.7%)	22 (43.1%)
Fibromyalgia	12 (8.2%)	5 (12.2%)	5 (9.3%)	2 (3.9%)
Facet arthropathy on imaging	122 (83.6%)	38 (92.7%)	41 (75.9%)	43 (84.3%)
Unilateral MBB	31 (21.2%)	4 (9.8%)	11 (20.4%)	16 (31.4%)
Bilateral MBB	115 (78.8%)	37 (90.2%)	43 (79.6%)	35 (68.6%)
Symptoms ≤ 6 months	14 (9.6%)	0 (0%)	3 (5.6%)	11 (21.6%)

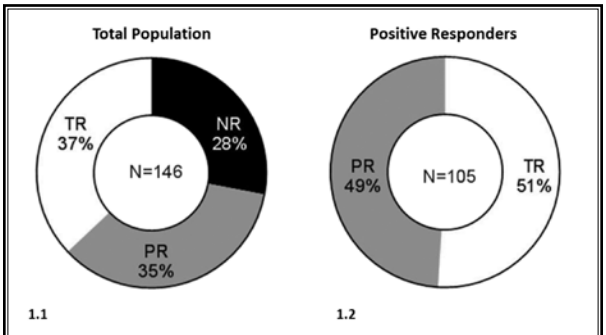

Fig. 1. *Depicted is the response distribution of total patient population (1.1) and positive responders only (1.2) to diagnostic lumbar MBBs. NR: no relief; TR: transient relief; PR: protracted relief.*

value 0.0174] was found to be significantly associated with PR and symptom duration > 6 months [adjusted OR 0.194 (0.039, 0.73); adjusted *P* -value 0.0142] negatively associated with PR ($P < 0.02$), indicating that symptom duration of < 6 months was associated with PR. The remaining predictors did not reach statistical significance (Table 2). The adjusted and unadjusted odds ratio and their 95% confidence intervals are tabulated (Table 2). For the adjusted odds ratios, the odds ratios are shown only for the 4 variables from the model with the optimal AIC. To visualize the association between PR and the continuous variables (age, BMI), we estimated the probability of PR by age and BMI using locally estimated scatterplot smoothing (LOESS). Neither age nor BMI was significantly associated with PR, however, an unexpected trend ($P < 0.1$) did suggest a direct relationship between increasing age and PR (Fig. 2).

Discussion

Interventional pain practitioners sometimes encounter patients with CLBP who experience therapeutic relief after diagnostic lumbar MBB procedures, though the mechanism(s) for this phenomenon remain ill-defined. In the current retrospective chart review, the following important observations related to this phenomenon were made: 35% of all patients who met the study inclusion criteria (n = 146) had PR and 49% of patients who had positive response to diagnostic lumbar MBBs (n = 105) had PR; unilateral pain symptoms were found to be a significant positive predictor of PR, while symptom duration of > 6 months was a negative predictor of PR; neither age nor BMI significantly correlated with PR, though a trend was observed suggesting a direct association between age and PR.

Herein, we observed a surprisingly prevalent PR response involving 1/3 of the total population under investigation and in nearly half of the positive responders. In the PR group, the analgesic effects of local anesthetics appear to provide pain relief to some for weeks to months, far outlasting the pharmacokinetics of the anesthetics employed. In clinical practice, the impact of expectancy and placebo effects on pain disorders is an important consideration and may account for up to 50% of the effectiveness of pain treatments (21). However, we opine that the placebo effect alone cannot entirely explain the observed PR response. We, therefore, present the following alternate hypotheses which may help explain the PR response.

Deep Trigger Point Hypothesis

Trigger points are hyperirritable areas of taut skeletal muscle bands that produce both local and re-

Table 2. *The adjusted and unadjusted odds ratio and their 95% confidence intervals are shown. For the adjusted odds ratios, the odds ratios are shown only for the 4 variables from the model with the optimal AIC. BMI: body mass index; Unilateral MBB: blocks performed on either right or left side for unilateral symptoms; 3 facet MBB: 4 medial branches blocked instead of 2 facets or 3 medial branches blocked*

Predictor	Unadjusted Odds Ratio	Unadjusted *P* value	Adjusted Odds Ratio	Adjusted *P* value
Age	1.024 [0.993, 1.058]	0.1323	1.029 [0.992, 1.068]	0.1269
BMI	0.982 [0.921, 1.046]	0.5791		
Depression	1.103 [0.507, 2.405]	0.8036		
History of smoking	0.563 [0.257, 1.214]	0.1431		
Facet arthropathy on imaging	1.049 [0.121, 9.073]	0.4832		
Fibromyalgia	0.400 [0.055, 1.953]	0.2650		
Men	0.498 [0.213, 1.131]	0.0961	0.488 [0.191, 1.194]	0.1169
Unilateral MBB	1.787 [0.741, 4.436]	0.1966	3.366 [1.232, 9.917]	0.0174
3 facet MBB	1.152 [0.524, 2.531]	0.7392		
Symptom > 6 months.	0.213 [0.046,0.736]	0.0132	0.194 [0.039, 0.73]	0.0142

ferred pain patterns and are common causes of chronic musculoskeletal pain (22). Acute strain or repetitive microtrauma to the quadratus lumborum, multifidus and erector spinae muscles may lead to the development of stress on muscle fibers and the formation of trigger points in the lumbar region which are a leading cause of CLBP. Trigger-point injection is one of the most effective treatments for painful trigger points often providing prompt and lengthy relief of symptoms. The lumbar MBB procedure may be viewed as a form of deep trigger point therapy, as it involves directing spinal needles towards the lumbar facet joints and traversing numerous layers of lumbar paraspinal musculature. Therefore, PR response may be an indirect consequence of concurrent deep trigger point injections during the MBB procedure.

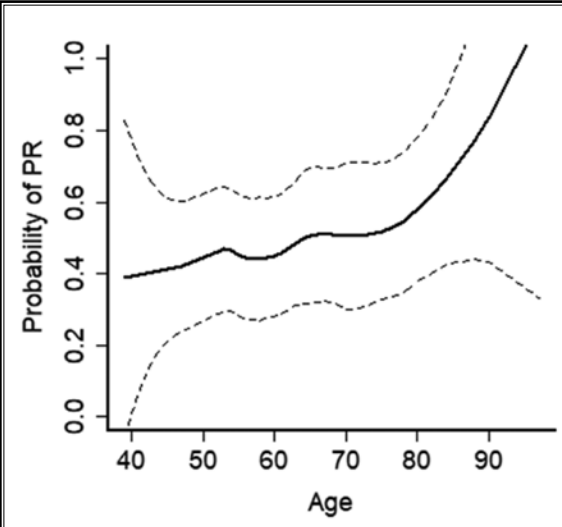

Fig. 2. *Locally estimated scatterplot smoothing (LOESS) are fit to visualize the probability of PR as a function of recorded continuous variables age and the 95% confidence intervals.*

Lysis of Adhesions Hypothesis

Manipulation under anesthesia (MUA) is a technique that can be used to break up fibrous or scar tissues to relieve pain and improve range of motion. MUA consists of a series of mobilization, stretching, and traction procedures performed while the patient receives anesthesia (23), and is commonly used to treat arthrofibrosis after total knee replacement (24,25) and recurrent or treatment refractory adhesive capsulitis of the shoulder (26). A lumbar MBB procedure involves the application of local anesthetics adjacent to the facet joints, after which patients are encouraged to resume activities of daily living, specifically those that normally produce pain. The immediate pain relief effects of the local anesthetics applied along with resumption of otherwise pain producing activities, including range of motion, mimics MUA (local anesthesia), which may produce a lysis of adhesion to the lumbar facet joints and produce a PR response.

Medial Branch Hypersensitivity Hypothesis

Peripheral and central sensitization can explain

pain hypersensitivity states that cause symptoms of hyperalgesia and allodynia in a variety of pain producing conditions including CLBP (27,28). Nociceptor inputs affecting the peripheral lumbar medial branch nerves, produced by repetitive strain injury or progressive arthropathy to the facet joints, may produce both peripheral and central sensitization, by triggering a prolonged but reversible increase in the excitability and synaptic efficacy of the peripheral nerves (medial branch nerve hypersensitivity) and central nociceptive pathways. Conceivably, medial branch nerve blockade may interrupt this pain cycle and subsequently reduce the sensitivity of nociceptive afferents at the peripheral tissue resulting in the desensitization of hypersensitive medial branch nerves thereby producing the PR.

Local Anesthetic Chemical Neurolysis Hypothesis

Low volume and higher concentrations of local anesthetics may increase the specificity of diagnostic lumbar MBBs (19) and is therefore often employed. Local anesthetic neurotoxicity has been previously described (17,29), and may be related to a host of mechanisms including local anesthetic induced elevation of intracellular calcium concentrations (30), direct induction of certain kinases (31) and inhibition of mitochondrial energy production (32). Therefore, a series of diagnostic MBBs employing concentrated local anesthetics may inadvertently produce a medial branch nerve chemical neurolysis, mimicking that of thermal neurolysis during lumbar RFA and resulting in a PR response.

In order to determine if the PR response could be reliably predicted, we employed a multivariate analysis to test for an association between patient demographics and PR. Unilateral pain symptoms significantly correlated with PR response, while symptom duration of > 6 months negatively predicts PR. Under normal spinal conditions (i.e., no scoliosis, no prior spine surgery, no leg length discrepancy), throughout the course of a lifetime, equal distribution of forces is applied to the lower lumbar facet joints. Therefore, lumbar facet arthropathy should occur more often bilaterally and produce bilateral pain symptoms (as observed in our population, > 75% of patients have bilateral pain (Table 1)). Consequently, the etiology of unilateral CLBP may be myofascial in origin rather than arthropathic. Hence, when PR response is achieved while treating unilateral pain symptoms, the deep trigger point hypothesis may be invoked. Similarly, symptom duration of > 6 months is significantly negatively associated with PR. In other words, shorter symptom duration is predictive of PR response. Considering the medial branch hypersensitivity hypothesis, this observation might be related to peripheral and central sensitization, such that shorter symptom duration is less likely to produce significant peripheral and central sensitization. As a result, this increases the impact of a local anesthetic blockade on the desensitization of the medial branch nerves.

Although not statistically significant, we chose to visualize the association between PR and the continuous variables, BMI and age, because we observed a counterintuitive noteworthy trend suggesting increased age is associated with PR. Age being a well-established risk factor for arthropathy (33), we initially hypothesized that age would be inversely associated with PR, since the likelihood of having CLBP due to facet arthropathy increases with age. It is possible that senescent medial branch nerve endings are more susceptible to the potentially neurotoxic effects of 0.75% bupivacaine, thereby producing a chemical neurolysis and PR in this age group. Alternatively, the Prospect Theory by Kahneman and Tversky (34) suggests that decision making is not based on absolute outcomes, but rather on relative perceptions of gain and loss, and thus may help explain this unexpected trend in the following manner. Chronic pain often affects the older adult and geriatric population by producing pronounced functional limitations, whereas younger adults, under similar conditions of chronic pain, may experience fewer physical limitations because of increased compensatory abilities. Thus, older adult and geriatric population may experience more noticeable functional gains after MBB and report greater outcome satisfaction relative to younger patients (reference-dependent evaluations).

Limitations

Our study has several important limitations. First, this is a retrospective study with a relatively small sample size of 146 patients and thus may have been underpowered to detect major predictors of the PR response in the population. Second, the chart review was conducted on patients belonging to a single practitioner, leading to an inherent patient selection bias. For instance, patients with CLBP and fibromyalgia were significantly underrepresented in the sample, though patients with fibromyalgia are not less susceptible to facet mediated CLBP. This could indicate that the interventionalist was less likely to perform interventional procedures on patients with fibromyalgia. Third, in our cohort the decision to proceed to RFA was based

largely on subjective overall patient satisfaction, as opposed to objective pain scores or disability indices, which themselves have limitations. Finally, a subset of patient likely did have PR after a single lumbar MBB procedure, but these patients were excluded from the analysis as they did not meet the strict inclusion criteria of having at least 2 blocks and one follow-up visit. While our hypothesis may also apply to a single MBB, this was a retrospective study on patients who underwent the second MBB, as is routinely done at the practice location.

Conclusion

Facet mediated CLBP is one of the most physically burdensome and pharmacotherapeutically challenging pain conditions to date. Thus far, treatment modalities are largely focused on symptom management and often the mechanisms by which pain relief is achieved are not always entirely understood. We describe a patient population suffering from CLBP who experience protracted pain relief after diagnostic lumbar MBBs and suggest possible mechanisms for this protracted pain response. The current standard of care is to treat facet mediated CLBP with lumbar medial branch (MB) RFA after a series of 2 positive diagnostic lumbar medial branches. However, based on our findings, if a patient has PR after a series of lumbar MBBs at follow-up, a watch-and-wait approach might be a reasonable alternative to direct referral for lumbar MB RFA. Furthermore, going forward practitioners may consider educating patients about the potential therapeutic benefits of lumbar MBBs, as opposed to presenting MB RFA as an absolute, if diagnostic blocks are positive. Future research should focus on better understanding the genetic, epigenetic, and environmental risk factors associated with the development of facet mediated CLPB, such that future treatments could focus on disease prevention rather than symptom management and possibly reversal of disease progression altogether.

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