ORIGINAL ARTICLE

Differential Epidural Block Predicts the Success of Visceral Block in Patients with Chronic Visceral Abdominal Pain

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■ **Abstract:** *Background and Aims:* Differential thoracic epidural regional block, also known as a differential neural block (DNB), involves the placement of an epidural catheter placed in the thoracic epidural space to achieve appropriate anesthesia in a dermatomal distribution. This is a retrospective case series evaluating how well a DNB may predict success of subsequent visceral blockade in patients with chronic abdominal pain of visceral origin.

Methods: Of 402 patients who had a DNB performed for unexplained abdominal pain from January 2000 to January 2009, 81 patients were found to have results consistent with visceral pain and thus underwent subsequent visceral blockade. Basic demographic data, years of chronic pain, history of psychosocial issues, initial visual analog scale (VAS) pain score, pain location, and medication usage were documented in our electronic medical record database. Parameters regarding DNB and visceral blocks also were documented. Descriptive statistics were computed for all variables. The positive predictive value (PPV) for DNB for whom visceral block was successful (at least a 50% reduction in VAS) was calculated. Additionally, subjects with successful visceral blocks were compared to those with unsuccessful visceral blocks.

Participants: All patients with chronic abdominal pain with normal gastrointestinal studies who underwent DNB.

Setting: Tertiary Outpatient Pain Management Clinic.

Design: Retrospective Cohort Study.

Results: Mean age of patients was 46 (± 15) years, 73% were female, and median duration of pain was 5 years. 67% of subjects were taking opioid analgesics. PPV of DNB was 70.4%. Only factor found to be statistically significant with visceral block success was baseline VAS with higher scores associated with DNB predictive success (6.8 ± 1.7 vs. 5.5, 1.8; $P = 0.004$). Use of membrane stabilizing medications was significantly more common in subjects for whom visceral block was not successful (46% vs. 25%; $P = 0.058$).

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Area underneath curve (AUC) for VAS was found to be 0.70 (95% CI: 0.57, 0.82), which signifies fair discrimination.
Conclusion: Differential neural block is fairly predictive of subsequent visceral block success in patients with chronic abdominal pain of visceral origin. An initial VAS ≥ 5 provides a sensitivity of 93%, which implies that VAS < 5 may predict unsuccessful visceral block. Contrarily, a value of ≥ 8 would provide a specificity of 92% and may be used to predict success of subsequent visceral block. ■

Key Words: abdominal pain, visceral pain, differential block, differential nerve block, visceral block

INTRODUCTION

There is a certain degree of frustration among patients, gastroenterologists, and chronic pain physicians regarding the difficulties of evaluation and treatment of chronic abdominal pain. This frustration is multifactorial, as some of the reasons include an inability to properly diagnose the nature of the pain (visceral, somatosensory, or central/psychogenic), inadequacy of available treatment options, and the frequent concomitant use of opioids in this patient population. There is a need for a reliable tool to identify the nature of chronic abdominal pain after extensive gastrointestinal evaluations fail to show correctible pathology. This is owing to the complexities of visceral innervation and the fact that some chronic abdominal pain may not be visceral in origin, but rather may be central or somatosensory. The hope is that differentiating the types of abdominal pain will assist in developing an effective approach to addressing the pain adequately. In the pain medicine literature, retrograde differential neural block (DNB) is considered to be a valuable tool in the diagnosis of chronic abdominal pain, chronic pelvic pain, and thoracic pain of unknown origin,[1–6] although technical limitations and interpretation made the diagnostic tool difficult to use. However, a modified thoracic epidural retrograde differential block has been described where an epidural catheter is placed in the mid-thoracic epidural space to obtain appropriate thoracic anesthesia and to achieve a block in the dermatomal distribution of the patient's pain complaints. Using such an approach, incremental doses of local anesthetic are injected via an epidural catheter to prevent excessive blockade and to maintain hemodynamic stability.[1] The premise of this test is based on the fact that nerves vary in their response to local anesthetics based on their diameter and state of myelination. Small unmyelinated C-fibers (which transmit visceral pain sensation) are blocked by lower concentrations of local anesthetics and take longer period of time to recover than the A-delta fibers. A-delta fibers (which are responsible for somatosensory pain) require larger concentrations of local anesthetics, become blocked faster but also recover faster. The interpretation of such neural blockade has been standardized and published previously.[1–4] If the patient responds to placebo injection, the DNB should be aborted and may be repeated at a later date. If pain persists in spite of achieving adequate segmental regional anesthesia above the level of the pain, the pain is interpreted as central pain and subsequent neuropsychiatric evaluation and treatment should be considered. If the patient has initial improvement of abdominal pain with thoracic anesthesia and the pain returns with resolution of the sensory block, the test is interpreted as somatosensory pain, which can be treated by transversus abdominis plane blockade using ultrasound guidance or more conservative therapies including trigger point injection, NSAIDs, physical therapy, and weight loss if indicated. If the patient has initial improvement of abdominal pain with thoracic anesthesia but has delayed return of the pain after the recovery of somatosensory function, the pain is considered to be visceral in origin and can be treated with, among other modalities, nerve blocks that target the sympathetic chain or visceral fibers.

Monitoring successes of visceral blocks following DNB may reveal the positive predictive value (PPV) of differential nerve block.[4] This can result in proper identification of pain source and in improving the likelihood that a therapeutic intervention will improve symptoms.

MATERIALS AND METHODS

Procedure

Differential neural block is administered by an interventional pain medicine specialist. After appropriate informed consent is obtained, an intravenous line is established and appropriate intravenous fluids are started. The patient's blood pressure, oxygenation, and electrocardiogram (ECG) are monitored. An epidural catheter is inserted into the thoracic epidural space up to a level 2 to 3 segments above the dermatomal supply of the patient's site of pain, typically in the thoracic spine for upper abdominal and epigastric pain. The patient is then transferred to the recovery area and monitored for the response to injections of normal

saline (placebo is administered twice), and local anesthetics (eg, 2% to 3%-chloroprocaine). Local anesthetics are injected in stepwise fashion to achieve motor and sensory anesthesia in the segmental distribution that overlaps the patient's abdominal pain complaint.[4] If the patient responds to placebo injection, the test may be repeated in another day. If pain persists in spite of achieving adequate segmental regional anesthesia above the level of the pain, the pain is interpreted as being central in origin. If the patient has initial improvement of abdominal pain with thoracic anesthesia and the pain returns with resolution of the sensory block, the test is interpreted as somatosensory pain. If the patient has initial improvement of abdominal pain with thoracic anesthesia but has delayed return of the pain beyond the recovery of somatosensory function, the pain is considered to be visceral in origin. On the basis of the response to local anesthetic administration, pain is characterized as visceral or nonvisceral (somatosensory, central) in origin. Occasionally, pain is classified as mixed (visceral and nonvisceral components) if pain origins cannot be clearly separated.[4]

Retrospective Chart Review

After Institutional Review Board approval, we reviewed electronic medical records of 402 patients who had diagnostic differential epidural block for otherwise unexplained abdominal pain from January 2000 to January 2009. Recorded data included patients' age, gender, years of chronic pain, diagnosis as a possible source of chronic pain, recorded initial visual analog scale (VAS) pain score, pain location, use of oral opioids (in morphine sulfate mg equivalents), antidepressants, and membrane stabilizing medications for pain (in quantity). History of depression, drug, or alcohol abuse was also noted. Other data collected include number of patient's other pain sources (if other than in abdomen), dermatomal level of her/his abdominal pain, vertebral level where the epidural catheter was inserted, pain scores recorded after placebo injections, and pain scores after local anesthetic injection. Volume of the local anesthetic injected was recorded, as well as vertebral level of sympathetic block achieved. Diagnosis that was suggested by the DNB was noted. Inclusion criteria for this chart review were all patients who underwent DNB to establish diagnosis of their abdominal pain and subsequently received visceral nerve block as the therapeutic treatment. One hundred and thirteen patients were diagnosed with visceral pain by DNB. Of the 113 patients, 81 patients subsequently underwent visceral blockade of some sort (celiac plexus, hypogastric, or splanchnic blocks). From the 81 patients who were diagnosed with visceral pain by DNB and subsequently underwent visceral blockade, we extracted the type of the visceral block used, vertebral level at which visceral block was conducted, volume of the local anesthetic used, and pain score following the visceral block. Success was defined as an improvement in abdominal pain by > 50% by VAS.

Statistical Analysis

Descriptive statistics were computed for all variables. These include means, standard deviations, and percentiles for continuous factors and frequencies and percentiles for categorical variables. The PPV for DNB for whom visceral block was successful (at least a 50% reduction in VAS) was calculated along with its corresponding 95% confidence interval. In addition, subjects with a successful visceral blockade were compared to those for with an unsuccessful visceral blockade to assess whether there was any factor that was associated with success of treatment. A receiver operating characteristics (ROC) analysis was performed to assess utility of VAS (alone or in combination of other baseline characteristics) could be used to predict treatment success. The ROC curves were plotted, and the areas under the curves are reported. An automated bootstrap variable selection method was performed on 1,000 bootstrap samples to choose the final model. All baseline variables were considered for inclusion, and the 2 factors with highest inclusion rates were included in the model. A $P < 0.05$ was considered statistically significant. All analyses were performed using SAS version 9.2 (The SAS Institute, Cary, NC, U.S.A.).

RESULTS

The mean age of patients receiving the DNB was 46 (± 15) years and 73% were female. Sixty-seven percent of subjects were on a morphine equivalent, and median duration of pain was 5 years (P25, P75:2, 9).

A total of 81 subjects diagnosed with visceral pain by DNB received a visceral block. Table 1 presents a breakdown of subject characteristics by outcome of block. Of the 24 patients that did not achieve at least

Table 1. Demographic and Clinical Characteristics of Subjects Undergoing Visceral Block for Visceral Pain as Diagnosed by Differential Neural Block

Factors	All (*N* = 81)	Successful visceral block (*N* = 57)	Unsuccessful visceral block (*N* = 24)	*P*-value
Age	46.1 ± 14.5	47.5 ± 12.3	42.8 ± 18.5	0.26
Female	59 (72.8)	43 (75.4)	16 (66.7)	0.42
H/o depression	17 (21.0)	11 (19.3)	6 (25.0)	0.57
H/o drug abuse	3 (3.7)	2 (3.5)	1 (4.2)	0.99
H/o alcohol use	8 (9.9)	7 (12.3)	1 (4.2)	0.43
Antidepressants	26 (32.1)	18 (31.6)	8 (33.3)	0.88
Membrane stabilizers	25 (30.9)	14 (24.6)	11 (45.8)	0.058
Mso4 equivalent	30.0 [0.0, 70.0]	36.0 [0.0, 70.0]	25.0 [0.0, 75.0]	0.53
Any morphine equivalent	54 (66.7)	40 (70.2)	14 (58.3)	0.3
Years of pain*	5.0 [2.0, 9.0]	4.0 [2.0, 9.0]	6.0 [2.0, 9.0]	0.43
Preblock visual analog scale	6.4 ± 1.8	6.8 ± 1.7	5.5 ± 1.8	**0.004**
Pain location				
Generalized	12 (14.8)	7 (12.3)	5 (20.8)	0.8
Epigastric	12 (14.8)	8 (14.0)	4 (16.7)	
RUQ	12 (14.8)	8 (14.0)	4 (16.7)	
LLQ	10 (12.4)	8 (14.0)	2 (8.3)	
LUQ	5 (6.2)	3 (5.3)	2 (8.3)	
Periumbilical	10 (12.4)	7 (12.3)	3 (12.5)	
RLQ	8 (9.9)	7 (12.3)	1 (4.2)	
Pelvis	9 (11.1)	7 (12.3)	2 (8.3)	
Flank	2 (2.5)	2 (3.5)	0 (0.0)	
Groin	1 (1.2)	0 (0.0)	1 (4.2)	
No. of other pain locations				
0	47 (58.0)	33 (57.9)	14 (58.3)	0.9
1	24 (29.6)	17 (29.8)	7 (29.2)	
2	7 (8.6)	5 (8.8)	2 (8.3)	
3	1 (1.2)	1 (1.8)	0 (0.0)	
4	2 (2.5)	1 (1.8)	1 (4.2)	
Any response to placebos	10 (12.4)	9 (15.8)	1 (4.2)	0.27
Visceral block				
Celiac	37 (43.2)	24 (38.6)	13 (54.2)	0.8
Hypogastric	26 (30.9)	19 (31.6)	7 (29.2)	
Splanchnic	16 (18.5)	12 (21.1)	4 (12.5)	
Celiac/splanchnic	2(2.5)	2 (3.5)	0(0.0)	
Multiple blocks	8 (9.9)	7 (12.3)	1 (4.2)	0.43

*Years of pain missing for 8 subjects.
Continuous variables presented as Mean ± SD with *t*-tests or Median [25th, 75th percentiles] with Wilcoxon rank sum tests.
Categorical factors presented as *N* (%) with *P* values corresponding to Mantel–Haenszel chi-square test for no. of other pain locations, Fisher's Exact test for history of drug or alcohol abuse, pain location, response to placebo, type of block and use of multiple blocks, and Pearson's chi-square tests otherwise.
The bold value emphasizes the only factor that was found to be statistically significant and highlights a higher baseline VAS score is associated with visceral block success (6.8 ± 1.7 vs. 5.5, 1.8; P = 0.004).

50% improvement in VAS, 5 had worsening, 4 had no change, and 15 had < 50% improvement.

The only factor that was found to be statistically significant with visceral block success was baseline VAS with higher scores associated with visceral block success (6.8 ± 1.7 vs. 5.5, 1.8; $P = 0.004$). In addition, although it just fell short of statistical significance, use of membrane stabilizing medications was significantly more common in subjects for whom visceral block was not successful (46% vs. 25%; $P = 0.058$). After adjusting for use of membrane stabilizing medications, baseline VAS was found to be associated with higher likelihood of DNB success ($P = 0.010$).

Area under the ROC curve (AUC) for VAS was found to be 0.70 (95% CI: 0.57, 0.82), which signifies fair discrimination between successful and unsuccessful visceral block (Figure 1). Adding use of membrane stabilizers did not significantly improve discrimination (AUC [95% CI]: 0.71 [0.60, 0.83]). No single point provided high sensitivity and specificity. A VAS ≥ 5 gives a sensitivity of 93%, which means that values < 5 would be useful to rule out success. On the other hand, a value of ≥ 8 would provide a specificity of 92%, which means that it could be used to rule in success (PPV = 89%).

DISCUSSION

Differential epidural nerve block has been used by our group for the interpretation of chronic abdominal pain type. It was initially described in 1998[7] as a method to stratify patients who would benefit from surgical splanchnicectomy by way of videoscopic thoracoscopy. Since then the interpretation of such neural blockade

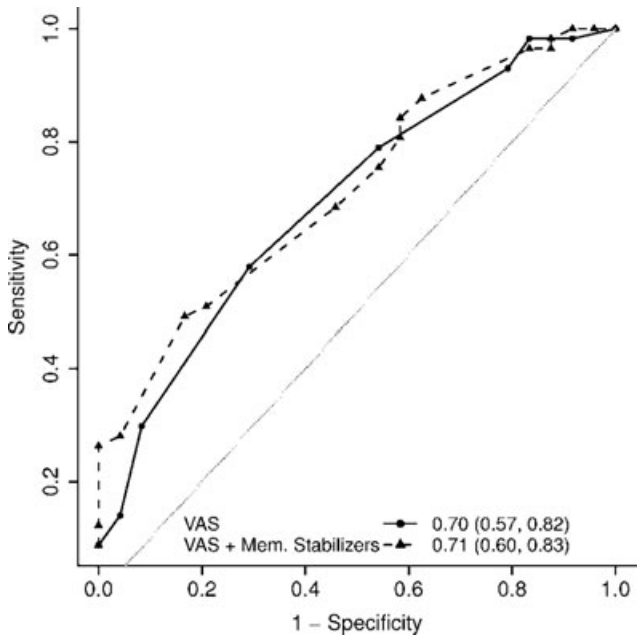

Figure 1. Receiver operating characteristics curves evaluating the utility of pre-procedure visual analog scale (VAS) to predict visceral block success.

has been standardized and previously published.[1–4] Side effects and complications under well-experienced clinicians are low (hypotension, bradycardia, headache, back pain, neurological complications), and the safety of the technique has been reviewed.[8]

Visceral blocks used in this study include celiac, hypogastric, and splanchnic blocks. The celiac plexus originates from the preganglionic sympathetic fibers of the greater (T5 to T9), lesser (T10 to T11), and least (T12) splanchnic nerves. Both the celiac and thoracic splanchnic nerves represent a target point for blockage of nociceptive transmission from the upper abdomen.[9] For example, celiac plexus block has been described for the treatment of pain for patients with upper abdominal malignancies.[10–12] Splanchnic nerve block can be performed using different approaches including percutaneous,[13] videothoracoscopic,[14,15] intraoperative,[16] and transdiscal.[17] Transdiscal approach of splanchnic nerve block gives an effective alternative for the management of chronic upper abdominal pain in patients with cancer.[17]

The effectiveness of visceral blocks is highly variable, and studies have included few patients.[17–21] One study of 23 patients with chronic pancreatitis[4] found that the majority of patients in their cohort had nonvisceral pain (18 of 23, 78%) and only 22% (5 of 23) had visceral pain by differential neuroaxial block. Four of 5 patients (80%) with visceral pain responded to therapy, whereas only 5 of 17 (29%) of patients with nonvisceral pain responded. A meta-analysis of 9 studies evaluated the efficacy of endoscopic ultrasound (EUS)-guided celiac plexus block for chronic pancreatitis and pancreatic cancers. For chronic pancreatitis, 6 relevant studies were identified, comprising a total of 221 patients. EUS-guided CPB was effective in alleviating abdominal pain in 51.46% of patients. For pancreatic cancer, 5 relevant studies were identified with a total of 119 patients. EUS-guided CPN was effective in alleviating abdominal pain in 72.54% of patients.[22] Needless to say, better pain differentiation may improve the success rate of visceral blocks. This will allow patients to avoid unnecessary interventions and allow physicians to be more selective of patients who should undergo visceral blocks.

Unlike the celiac block, which interrupts visceral afferent impulses traveling through the celiac plexus, a differential neuroaxial blockade is a diagnostic temporary block that uses the variable effects of typically short-acting local anesthetics on the nerve fibers to identify the etiology of pain. Our study demonstrates the effectiveness of the DNB as a diagnostic modality for visceral abdominal pain. Of 402 patients enrolled in this study, 81 patients were diagnosed with visceral pain using DNB. Those patients diagnosed with visceral pain then subsequently underwent celiac, splanchnic, or hypogastric plexus block depending upon the location of the abdominal pain. Of 81 patients, 57 patients (70.4%) had successful block (at least 50% reduction in VAS), while 24 patients had unsuccessful block (either < 50% reduction in VAS, no change in VAS or worsening in VAS).

Although not statistically significant, it was also noted that use of membrane stabilizing medications was significantly more common in subjects for whom visceral block was unsuccessful (46% vs. 25%; $P = 0.058$). That might trigger the attention for the need to limit the use of membrane stabilizing medications prior to planned visceral blocks. It should be noted, however, that some patients may be taking membrane stabilizing medications for pain sources other than the abdomen.

This is the first study of its kind to evaluate the positive predictive value for DNB in patients diagnosed with visceral pain. Additionally, it is a sizeable cohort (81 patients), and data were aggregated over an extended period of time (9 years). Although the number of patients does not allow for subgroup analysis of the different types of visceral blocks used, it does demonstrate

the success rate we have in unknown abdominal pain of visceral type. This is invaluable to a pain physician, gastroenterologist, or a surgeon for whom an evaluation for obvious gastrointestinal etiologies is unyielding. DNB can be a diagnostic study that, although may not answer why a patient has somatosensory, central, or visceral pain, may differentiate and guide treatment. In our study, 70.4% of patients who underwent a visceral block after being diagnosed by DNB with visceral pain obtained at least a 50% reduction in their level of pain. This is comparable to Conwell's study in which 78% of patients with chronic pancreatitis who responded to celiac plexus block after being diagnosed with visceral pain by DNB and is far > 29% of patients in his study who responded to celiac block after being diagnosed with nonvisceral pain by DNB.

The ROC curve for DNB to determine success of visceral blocks is similar to that of other commonly used tests for relatively common issues. For example, the AUC for CRP used to stratify ICU admissions is 0.691 (CI: 0.608 to 0.775).[23] Another example is the use of Lp(a), having the largest AUC, as the best marker for unstable angina.[24] Although the result of the ROC for our study is only 0.71, it is comparable to that of the previous 2 markers mentioned, and it is still the best available study up to date.

Additionally, although somewhat intuitive, this is the first study to demonstrate that the more intense the visceral abdominal pain, the more likely a visceral block will improve symptoms. Of clinical relevance, an initial VAS ≥ 5 gives high sensitivity (93%), while an initial VAS ≥ 8 provides a high specificity (92%). Thus, patients with low-grade pain as rated by VAS may not be ideal candidates for visceral block success. This would not preclude such a patient from undergoing these blocks but allows the physician to temper expectations.

This study also demonstrates the usefulness of DNB in predicting success to visceral blocks despite patients having a history of depression, antidepressant medication use, narcotic medications, drug abuse, or alcohol use, all of which can make the assessment of pain more difficult because of its subjective nature. For example, depressive symptoms are related to abdominal pain in school children, while anxiety problems seem to be a comorbid complaint for functional abdominal pain in children.[25] The presence of psychological disorder in inflammatory bowel disease contributes to poor health-related quality of life.[26]

Despite the aforementioned findings, if a patient is prescribed opioid medications, it is intuitive to have them stop the medications for a period of time prior to DNB. This is to minimize the subjective alterations that occur with mu and other opioid receptor regulation. For example, studies in rats showed that chronic morphine treatment induces functional delta opioid receptors in amygdala neurons that project to periaqueductal grey matter.[27] Another study shows that molecular adaptation in mu opioid receptor function occurs because of chronic pain status.[28]

Controversy regarding DNB still exists among anesthesiologists and pain physicians owing to its limitation and drawbacks. Some of those drawbacks include the risk of any neuroaxial procedure including infection, bleeding, epidural hematoma, dural puncture, and sympathectomy. Sometimes if the catheter tip is at higher level like T5 or T6, this may lead to blockage of cardiac accelerator fibers at T1 to T4, if enough local anesthetic dose was administered. This may cause significant hypotension and bradycardia requiring vasopressor therapies. In addition, the procedure is time-consuming, and it requires the attention of a devoted nursing team in the recovery area. This can limit the use of DNB in a smaller private practice setting. Soliman and Narouze[29] suggest to proceeding with transversus abdominis plane (TAP) blockade as an initial diagnostic tool to help differentiating between somatosensory and visceral abdominal pain. However, TAP blockade does not clearly identify centralized pain. Another drawback is that visceral pain can occasionally be transmitted through the vagus nerve. The vagus nerve is not blocked during the DNB, and so if the patient does not have a significant pain reduction after DNB, it could be because it is transmitted by the vagus nerve rather than the pain being merely central in origin. Despite the controversies regarding DNB, the study describes that DNB can be fairly predictive of the success of the subsequent visceral block. Authors suggest that DNB is a useful tool for diagnosing abdominal pain of unknown origin but may be best used on a case by case basis, recognizing the existing controversy.

In conclusion, DNB is a useful tool for to determine whether a patient has visceral abdominal pain of unknown etiology. In patients who do have visceral abdominal pain confirmed by DNB results, the likelihood that a visceral block of some kind may improve their pain by > 50% is approximately 70%. The higher the initial VAS, the higher the chance that the symptoms will improve after visceral block. Physicians may consider discontinuing membrane stabilizing medications in patients in whom they are considering visceral blockade.

Further prospective studies are needed to confirm the aforementioned findings, and to additionally determine the location and modality of visceral blockade that is most effective for different pain locations.

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