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Intravenous Regional Anesthesia with Ketorolac-Lidocaine for the Management of Sympathetically-Mediated Pain

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This retrospective study was undertaken to determine the usefulness of intravenous regional anesthetic (IVRA) blocks containing ketorolac and lidocaine in the management of sympathetically-mediated pain, and to determine what factors, if any, predicted success with this technique. Sixty-one patients with reflex sympathetic dystrophy presenting to a university-affiliated teaching hospital's pain management center were evaluated. Patients underwent one or more treatments with IVRA blocks containing ketorolac and lidocaine. The duration of pain, site of extremity affected, pain symptomatology, duration of relief from the first IVRA block, absence of pain following a series of IVRA blocks and side-effects from the IVRA blocks were determined. Of the 61 patients, 16 had complete response (26 percent), 26 had a partial response (43 percent) and 19 had no response (31 percent) to the ketorolac-containing IVRA. The only symptom which predicted a failure with this therapy was allodynia. No patient had serious side effects from the IVRA block; dizziness following tourniquet release occurred in 41 percent (n = 25) of the patients. IVRA block containing ketorolac is a useful and minimally invasive technique for the management of patients with reflex sympathetic dystrophy.

INTRODUCTION

The multitude of therapeutic modalities that have been advocated for the treatment of sympathetically-mediated pain attests to the relative lack of efficacy and difficulty of treatment. Intravenous regional anesthetic (IVRA)[c] block is one such therapeutic technique, and a variety of agents have been used in conjunction with local anesthetics, including guanethidine, steroids and ketorolac [1-7]. Over the past year, we have utilized a combination of ketorolac and lidocaine for IVRA blocks in the treatment of 61 patients presenting with sympathetically-mediated pain. We report here the results of our management of these patients.

MATERIALS AND METHODS

Institutional human investigational committee approval was obtained prior to performing this retrospective chart review. Informed consent was obtained from all patients prior to procedural intervention. Patients were offered an IVRA block if they had clinical symptoms of sympathetically-mediated pain (i.e., allodynia, hyperalgesia, hyperpathia, edema, vasomotor changes, pain with a burning quality, sudomotor changes or temperature difference between extremities).

A 22-g catheter was inserted in a vein of the affected extremity, and the catheter was flushed with 3 ml of a heparinized (10 u/ml) solution. Intravenous access then was established with a peripherally placed 20-g indwelling catheter in the contralateral extremity.

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[c]*Abbreviations:* IVRA, intravenous regional anesthetic.

After application of routine monitors (including electrocardiogram, pulse oximeter and oscillometric non-invasive blood pressure cuff), the painful extremity was exsanguinated by elevating the extremity and wrapping it with an Esmarch bandage. A single tourniquet was placed on the upper arm and was then inflated to 300 mm Hg. Following removal of the Esmarch bandage, 52 ml of solution containing 60 mg (2 ml) of ketorolac and 50 ml of 0.5 percent lidocaine was administered intravenously via the 22-g catheter. The tourniquet was kept inflated for a minimum of 30 min after injection. All patients were monitored for an additional minimum of 60 min prior to discharge from the clinic.

IVRA blocks were offered to each patient up to six times (maximum of once a week for six weeks). Success was defined as a complete resolution of pain not requiring interventions other than the IVRA block (responders group). Partial success was defined as a resolution of the pain that was not long-lasting. A failure was defined as no subjective improvement following the IVRA block. Partial success and failure patients were classified as "non-responders." If there were no beneficial effects obtained, or if the patient desired, other types of therapeutic intervention were offered (e.g., stellate ganglion block, peripheral nerve blocks, brachial plexus blocks, etc.).

The duration of the pain symptoms was noted prior to administration of the IVRA. The therapeutic benefits of the IVRA blocks were evaluated in all the patients; benefits were also separately evaluated in patients with a duration of symptoms less than, and greater than, six months. Using chi-square analysis, the presence or absence of an antecedent insult (surgery, trauma or both) was evaluated in an attempt to determine which patients benefited from the IVRA block. The symptoms that resulted in patient referral to the pain clinic were noted, and chi-square analysis was used to determine which of these symptoms correlated with success or failure of the IVRA blocks. Data were analyzed using unpaired t-test to determine which demographic characteristics were associated with a high probability of therapeutic success.

The duration of the pain state was compared between the responders and non-responders using an unpaired t-test. The duration of success of the first IVRA block was evaluated similarly. The number of IVRA treatments received by patients in each group was compared using Mann-Whitney U test.

Data are presented as mean ± SD or mean (10th to 90th percentiles), where appropriate. For all evaluations, $p < .05$ was considered statistically significant.

RESULTS

Demographics of the patients are presented in Table 1. There was no significant difference between the two groups with respect to any of the demographic data.

Of the patients who presented to the pain center, 16 (26 percent) had complete response with the IVRA, 26 (43 percent) had a partial response and 19 (31 percent) had no response. The duration of follow-up is presently 18 months for all patients, and none of the complete responders has required further therapy.

Table 1: Age, height, and weight of all patients, complete responders and non-responders. Patients who achieved either partial success or failure from the IVRA were classified as "non-responders."

	Number	Age	Height (in)	Weight (kg)
All patients	61	44 ± 17	66 ± 4	76 ± 28
Complete responders	16	51 ± 17	67 ± 4	85 ± 26
Non-responders	45	41 ± 17	66 ± 4	72 ± 28

The responders had a median of four (1-6) treatments, whereas the non-responders had a median of one (1-4) treatment ($p = .016$). If no benefit was realized from the first IVRA block, we tended not to perform a series of IVRA blocks.

The patients who presented to the pain clinic and participated in this evaluation had a mean duration of pain symptoms of 80 ± 146 weeks. The responders had a mean duration of pain of 44 ± 84 weeks, while the non-responders had a duration of pain of 93 ± 161 weeks (p = NS). Three patients achieved complete relief with the first IVRA treatment and were subsequently discharged from the pain clinic. The duration of pain in these three patients was 12, 12 and 56 weeks, respectively. Of the other patients who achieved complete degree of relief after more than one IVRA treatment, the duration of relief following the first IVRA was 3.6 ± 2.1 days, whereas in the non-responders, the mean duration of pain relief was 2.2 ± 3.1 days. There was no significant difference between the responders and non-responders with respect to the duration of relief following the first IVRA.

When only evaluating patients who had pain for less than six months, 12 of 32 (38 percent) patients achieved complete success, 13 patients achieved partial success (40 percent), and seven patients were classified as failing to respond (22 percent).

When evaluating the symptoms with which the patients presented to the pain clinic, the only symptom that significantly predicted a lower chance of complete success with the IVRA was the presence of allodynia ($p < .024$). Of the 22 patients who presented with allodynia, only two (9 percent) experienced complete relief, whereas 14 of the 49 patients (29 percent) without allodynia had complete relief. The following signs and symptoms were not associated with a higher or lower chance of success following IVRA: burning pain, edema, skin color changes, sweating changes, temperature changes, hyperalgesia and hyperpathia. Similarly, site of affected extremity (upper vs. lower) and history of antecedent trauma or surgery were not significant predictors of success of IVRA.

No patient had a life-threatening side effect from the IVRA block. Of the side effects, dizziness and lightheadedness upon deflation of the tourniquet occurred in 41 percent (n = 25) of the patients. These symptoms were unaccompanied by significant hemodynamic changes. The next most common complaint was a numb extremity following deflation of the tourniquet (16 percent, n = 10 patients). Three patients (5 percent) experienced nausea upon release of the tourniquet. All side effects completely resolved within one-half hour following tourniquet deflation.

DISCUSSION

The use of intravenous regional anesthesia in the management of sympathetically-mediated pain is not new. Previous reports have documented success with injectates containing lidocaine and solumedrol [5, 7], bretylium [8], guanethidine [2], reserpine [9], ketorolac and lidocaine [1], and non-steroidal anti-inflammatory drugs in saline [1,4]. We have previously used IVRA blocks with solutions containing solumedrol but were concerned about systemic side effects due to multiple doses of steroids over a relatively short period of time. IVRA blocks with bretylium had been part of our therapeutic practice but were discontinued because of the high incidence of orthostatic hypotension, which prevented the discharge of our patients from the outpatient clinic in a timely fashion. We have not utilized guanethidine and reserpine in our practice because of the lack of availability of these intravenous medications in the United States. Thus, our therapeutic choices of IVRA injectate for the treatment of sympathetically-mediated pain are limited to local anesthetics and ketorolac.

The one previous report utilizing IVRA with ketorolac detailed their experience in seven patients. Only one of these patients had complete relief of symptoms (this one patient had 36 days of relief, which was continuing at the time of the report) [1]. It is thus interesting to note that 26 percent of our patients experienced complete relief. This is similar to

the incidence of complete relief reported with stellate ganglion blockade [10] or with guanethidine IVRA blocks [2]. However, the success rates from individual reports are difficult to compare because of the patients' varying severity and duration of symptoms when referred to different pain management centers. In addition, stellate ganglion blocks also may have significant morbidity such as pneumothorax, subarachnoid block and vertebral artery injection. Furthermore, such blocks may be relatively contraindicated in the anticoagulated patient. Based on the results reported presently, we feel that the risk of IVRA is much lower, while the only major side effect was dizziness upon tourniquet deflation, which was short-lived and did not prolong discharge from our pain clinic.

The issue arises whether the relief obtained in our center resulted from the lidocaine or the ketorolac in the IVRA. We believe that the therapeutic benefit is derived from the use of ketorolac. Vanos et al. [1] found that IVRA block containing ketorolac was successful and that the combination with lidocaine provided short-term additional analgesia, allowing the patients to undergo physical therapy. We do not think that the lidocaine alone resulted in significant long-term benefit. Hord et al. [11], who combined lidocaine with bretylium, found that the lidocaine IVRA blocks produced a mean pain relief of 2.7 days, whereas the combination with bretylium produced a mean relief of 20.0 days. Furthermore, McKain et al. [12] found that lidocaine IVRA failed to produce pain relief beyond the duration of the block. There is thus a general consensus that IVRA blocks that only contain lidocaine will provide short-term relief and that the mixture of two drugs is necessary for prolonged relief.

It is impossible to state emphatically that the results in our patients were due to ketorolac, and not from lidocaine or the combination of the two; however, when ketorolac was diluted with normal saline rather than lidocaine, similar results have been reported [1]. We do believe that lidocaine is a useful part of the injectate; in our patients who were classified as IVRA "failures," the IVRA lidocaine allowed them to successfully complete a physical therapy session. Also, the lidocaine decreased the burning of ketorolac on injection and also raised the threshold for tourniquet pain.

The precise cellular mechanism responsible for the alteration in peripheral nociceptor sensitivity following tissue trauma are not known [13]. Chemical mediators such as prostaglandins are believed to modify nociceptor input leading to mechanical allodynia [14]. The only symptom that was predictive of failure with IVRA lidocaine and ketorolac was allodynia. Success of ketorolac in these patients would thus be expected by an inhibition of this peripheral sensitization; this, however, was not the case in our patients.

The dose of ketorolac was arbitrarily chosen; an increase or decrease in the dose may affect the results. The one previous report of the use of IVRA ketorolac also used 60 mg [1]. It remains to be determined whether a lower dose may achieve the same effect, or if a higher dose may result in a greater percentage of complete responders. It also remains to be determined whether systemically, rather than locally, administered ketorolac may be an effective treatment.

In conclusion, we have presented our results of IVRA blocks containing ketorolac and lidocaine in the management of sympathetically-mediated pain states. Approximately 69 percent of the patients had at least partial relief with this therapy. Of all patients, 26 percent had complete resolution of their pain symptoms, while the side effects were minimal and short-lived.

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