Original Research Articles

Clinical Effectiveness of Botulinum Toxin A Compared to a Mixture of Steroid and Local Anesthetics as a Treatment for Sacroiliac Joint Pain

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Abstract

Objective. The sacroiliac joint (SIJ) is one of the sources of low back pain and referred pain to the lower limb. Steroid injections have been used to treat SIJ pain, but this frequently necessitates repeated injections. Botulinum toxin (BT) type A has been shown to provide significant reduction of joint pain, and functional improvements. This study investigated the efficacy of BT for reducing SIJ pain and maintaining a clinical effect, compared with steroid injections.

Design. Prospective case control study.

Setting. Spine hospital.

Patients. Patients who were diagnosed with SIJ syndrome based on physical examination and diagnostic SIJ injection were selected.

Interventions. Either Dysport® (BT group) or a mixture of triamcinolone and lidocaine (triamcinolone and local anesthetics [TA] group) was injected into the posterior sacroiliac ligaments under C-arm fluoroscopy.

Outcome Measures. Numeric Rating Scale (NRS) and Oswestry Disability Index (ODI) were used for evaluation at pretreatment, 1 month, 2 months, and 3 months after treatment.

Results. At 1 month, the BT and TA group showed no significant differences in NRS or ODI. However, at 2 and 3 months, the BT group had significantly lower scores in NRS and ODI than did the TA group.

Conclusion. BT shows clinical usefulness in pain reduction and for functional improvement in patients with SIJ pain. This effect was maintained for 3 months following the injection, by which time the effects of TA had diminished.

Key Words. Botulinum Toxin; Steroid; Local Anesthetics; Sacroiliac Joint Pain

Introduction

The sacroiliac joint (SIJ) can be a source of low back pain and referred pain to the lower limb, with a reported prevalence rate varying from 7% to 30% [1]. SIJ pain is usually perceived in the buttock and is occasionally referred to the posterior aspect of the ipsilateral thigh. Thus, it can mimic pain originating from sources in the lumbar spine, such as the zygapophysial joints or intervertebral discs [2,3], but the lack of valid physical or radiological tests prevents SIJ pain from being distinguished from other sources of lumbar pain [4,5]. Although some studies have demonstrated that various clinical features are indicative of SIJ pain [1,6–8], the criterion standard for diagnosis is relief of pain after diagnostic blocks.

Some investigators have used intra-articular blocks to diagnose SIJ pain [4,6,7], but positive responses would occur only in patients with a source of pain restricted to the synovial portion of the joint. Intra-articular blocks do not test for pain that might arise from the ligaments behind the joint. For this reason other investigators have
SIJ pain has been treated with injections of steroids, into the joint alone [9], into the posterior ligaments as well as the joint [10], or into the posterior ligaments alone [11,12]. Two small studies have shown that injections of steroids into the posterior ligaments achieve significantly greater reduction in pain than equivalent injections of normal saline [11,12], but the proportions of patients who achieved relief were not reported. However, the therapeutic effects of injections of steroids attenuate by 3 months [10] and seldom last beyond this duration. Consequently, repeated injections are required to reinstate and maintain benefits [9]. Under these conditions, injections of steroids can have a number of adverse effects, including hypertension, glucose intolerance, osteoporosis, or Cushing syndrome. Because of these properties of steroids, another injectate that is equally as effective but without these problems would be welcome.

Recently, botulinum toxin (BT) has been used to treat headache, back pain, and other regional pains [13–16]. BT has also been used for pain arising from various joints, including the knee, ankle, or shoulder joint, for which it has demonstrated significant pain reduction and functional improvements without any appreciable side effects [17–19]. The analgesic effects of BT have persisted for over 3 months [17,19,20]. These properties promote BT as a possibly effective, and safer, alternative to injections of steroids for SIJ pain.

The primary objective of the present study was to investigate the effectiveness of BT, compared with that of injections of steroids, in reducing SIJ pain. A second objective was to determine the duration of effect of each treatment.

Methods

Injection Technique

The periartricular injection was performed using C-arm fluoroscopy. The patient lied under the C-arm in a prone position with a pillow placed under the abdomen at the iliac crests. The C-arm was tilted 10–30 degree to the involved side and slanted cranially so that SIJ margin could be detected clearly. The periartricular portion of the SIJ was divided into three equal sections including upper, middle, and lower sections; the middle section was selected as the injection target [5]. After marking the skin at an appropriate spot lateral to the midline, the area was sterilized and anesthetized with 2% lidocaine. A 90-mm 23-gauge spinal needle penetrated the skin mark and was then advanced laterally into the middle section of the periartricular portion using intermittent C-arm image guidance. When the spinal needle had penetrated through the posterior sacroiliac ligaments, it was positioned in the middle periartricular space [5]. Next, 0.2–0.3 mL of contrast medium (Iohexol Bonorex®, CMS, Seoul, Korea) was injected, and the position of the needle and the spread of contrast medium was confirmed by fluoroscopy (Figure 2). A diagnostic injection was performed with 2 cc of 2% lidocaine and the intensity of pain was measured before and 30 minutes after the injection, in order to evaluate the effect of the diagnostic injection. Only patients who reported a reduction in their characteristic pain of 50%, or

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more, as calculated from a numerical pain rating scale, were scheduled for a therapeutic injection [1]. Therapeutic injection was performed using 100 U of BT type A (Dysport®, Ipsen, Paris, France) in the BT group, or a mixture of 40 mg of triamcinolone and 2 cc of 0.5% lidocaine in the TA group. Patients were not informed as to which of the two injectates they were given.

Evaluation of Patients

The intensity of pain was evaluated before the therapeutic injection using a standard 100 mm Numeric Rating Scale (NRS) that ranged from 0 (no pain) to 10 (excruciating pain) [21]. All patients were asked to report the average severity of their symptoms over the immediate past 1-week period [22]. For assessment of function, before and after injection, the Korean version of the Oswestry Disability Index (ODI) was used [23]. These evaluations were conducted by a nurse who was blinded to the injectates. The value and validity of the NRS and ODI have been reported previously [24,25], and ODI has previously been used for evaluation of patients with SIJ disorder [26,27]. In the current study, ODI consisted of 10 sections, each with a total score of 5. The first statement was
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scored as 0 and the last statement was scored as 5. If all 10 sections were completed by each patient, the score was calculated as a percentage. For example, if the total score from 10 sections for one patient was 16, the score of that patient would be 32% (16/50 (maximal possible score) × 100) [25].

The patients were reexamined at 1 month, 2 months, and 3 months after treatment by the nurse who had conducted the evaluation before treatment. Both mean NRS and ODI (%) at pretreatment, 1, 2, and 3 months post injection were compared between BT and TA group, respectively. In addition, the proportions of patients who obtained successful results in NRS and ODI (%) were compared between two groups. Successful results in NRS was defined as 50% or more reduction of NRS, and successful results in ODI (%) was defined as 40% or more reduction of ODI (%) as compared with values at pretreatment [21].

Statistical Analysis

The SPSS Version 12.0 statistical package was used for statistical analysis. A chi-squared test was used to compare gender proportion, side of pain, and the proportions of patients with successful results in NRS and ODI (%) in the two groups. A Mann–Whitney test was used to test the differences in age, duration of pain, NRS, and ODI (%) before treatment. Repeated measure of ANOVA was used to compare NRS and ODI (%) at 1, 2, and 3 months after treatment. Results were considered as statistically significant for \( P \leq 0.05 \).

Results

There were no significant differences between the BT and TA group in terms of gender proportion, age, duration of symptoms, NRS or ODI (%) before treatment (Table 1). At 1 month after treatment, no significant differences in NRS or ODI (%) were seen between the BT and TA groups. However, by 2 months following treatment, the BT group had significantly lower scores for both NRS and ODI (%) than the TA group (Figures 3 and 4). The two groups did not demonstrate significant difference in proportion of successful results in NRS and ODI (%) at 1 month after treatment, but the BT group had a significantly higher proportion of successful results in NRS and ODI (%) at both 2 months and 3 months (Figure 5). There were five patients in BT group who achieved complete pain relief (NRS = 0) at 1 month, whereas no patient in TA group did so. At 2 and 3 months, there were three patients who maintained complete pain relief in BT group.

Two patients in the BT group reported mild flu-like symptoms for 1 or 2 days, but these symptoms were not serious as they did not interrupt their daily activities or require any special management.

Discussion

Periarticular injection was used in the present study because it has been reported as providing comparable or better results in pain control and functional improvement, compared to intra-articular injection [5,10,11,12]. The rationale for periarticular injection is that SIJ pain might arise not only from intra-articular structure but also from periarticular structures, such as the posterior interosseous ligament, and that the latter contribute more to SIJ pain [5].

The middle section of the posterior ligaments was targeted because this section is exposed to greater stress during daily life and is therefore more likely to become responsible for SIJ pain [5]. Furthermore, the middle section includes the axial posterior interosseous ligament which is susceptible to degenerative changes [28,29].

Botulinum toxin was used because of emerging evidence of possible analgesic effects. The paralytic effects of BT are well-known, and for this reason, BT was introduced to treat spasticity. Subsequently, it was noted that BT also alleviated pain in patients with dystonia or spasticity [30]. Therefore, it was suggested that pain relief could be attributed to reduction of muscle overactivity [31]. However, BT also alleviated pain in conditions not associated with excess muscle activity [32]. Recently, other mechanisms for the analgesic effect of BT have been proposed aside from simple reduction of muscle activity. BT might reduce the local release of nociceptive neuropeptides, which would inhibit activation of neurogenic inflammation. Also, BT could lead to a reduction in central sensitization associated with pain by controlling sensory input into and autonomic output from spinal cord neurons and by a
NRS of BT group at 2 months and 3 months after treatment is significantly lower than VAS of TA group although there is no significant difference at pretreatment and 1 month after treatment. BT = botulinum toxin; TA = triamcinolone and local anesthetics; NRS = Numeric Rating Scale. * $P < 0.05$.

<table>
<thead>
<tr>
<th></th>
<th>BT group</th>
<th>TA group</th>
<th>p score</th>
</tr>
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<tbody>
<tr>
<td>Pretreatment</td>
<td>6.4 ± 1.6</td>
<td>6.1 ± 1.2</td>
<td>0.500</td>
</tr>
<tr>
<td>1 month after treatment</td>
<td>2.2 ± 1.9</td>
<td>2.8 ± 1.9</td>
<td>0.15</td>
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<tr>
<td>2 month after treatment</td>
<td>1.8 ± 1.7</td>
<td>3.7 ± 1.7</td>
<td>&lt;0.001</td>
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<tr>
<td>3 month after treatment</td>
<td>1.9 ± 2.0</td>
<td>4.9 ± 1.7</td>
<td>&lt;0.001</td>
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Figure 3

ODI (%) of BT group at 2 months and 3 months after treatment is significantly lower than ODI (%) of TA group although there is no significant difference at pretreatment and 1 month after treatment. BT = botulinum toxin; TA = triamcinolone and local anesthetics; ODI = Oswestry Disability Index. * $P < 0.05$.

<table>
<thead>
<tr>
<th></th>
<th>BT group</th>
<th>TA group</th>
<th>p score</th>
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<tbody>
<tr>
<td>Pretreatment</td>
<td>32.5 ± 14.6</td>
<td>28.4 ± 11.9</td>
<td>0.432</td>
</tr>
<tr>
<td>1 month after treatment</td>
<td>13.0 ± 10.0</td>
<td>17.1 ± 10.5</td>
<td>0.12</td>
</tr>
<tr>
<td>2 month after treatment</td>
<td>11.1 ± 10.0</td>
<td>20.4 ± 11.1</td>
<td>0.006</td>
</tr>
<tr>
<td>3 month after treatment</td>
<td>11.9 ± 9.1</td>
<td>24.0 ± 10.6</td>
<td>&lt;0.001</td>
</tr>
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Figure 4
direct effect upon spinal cord neurons [32–35]. BT could also stimulate naturally secreted analgesics such as enkephalin [36,37].

It remains to be demonstrated whether or not such mechanisms operate after injection of BT into the sacroiliac ligaments. However, it is obvious that injections into ligaments would not exert their effect by paralyzing muscles, because the agent is not delivered into any muscle.

Whatever the mechanism, the analgesic effects of BT appear to be enduring. A study of patients with tennis elbow showed that BT produced good or excellent 12-month outcomes [20]. Intra-articular BT (Botox®, Allergan, Irvine, CA) injection in patients with knee, ankle, or shoulder pain provided pain relief for between 3 and 12 months [17,19]. In a study of back pain, the analgesic effect of BT persisted for about 3–4 months, and although back pain might have remained after 6–12 months, the degree of pain was less severe than before treatment [13]. Our results in the current study also demonstrated that the clinical benefits of BT persisted over a longer time period than did those of steroid. Although the BT group did not show significantly better results than the TA group at 1 month, the BT group maintained the proportion of successful results after 2 months, whereas, the TA group showed reduction of proportion. The attenuation of steroid effects, which was observed in the present study, is consistent with what others have encountered [10] or commented upon [9]. The long-lasting effect of BT makes it possible to lessen the number of treatment sessions, which helps to avoid the increased risk of side effects resulting from repetitive injections.

It has been reported that muscle soreness was most common side-effect of BT, but short lived [38]. Muscle weakness occurred in some patients in one study [18], but not in another study [13]. In the present study only two patients in the BT group reported mild and transient flu-like symptoms. These results suggested that BT could be utilized without concern of serious side-effects.

The appropriate dose of BT should be determined as that which obtains clinical effectiveness and avoids side effects. One study has shown that knee or ankle joints could be treated with 25–50 units of toxin, and shoulder joints with 50–100 units (Botox®) without any significant side effects [17]. We used 100 units of BT (Dysport®, Ipsen) because this dose was considered to be safe and appropriate to cover the periarticular area. Side effects, including unwanted weakness of gluteal muscles, were possible because toxin injected into the periarticular area of SIJ had the potential to spread over neighboring

Figure 5 (a) The proportion of successful results in NRS (defined as 50% or more reduction of NRS as compared with NRS at pre-treatment) of BT group was significantly higher than that of TA group at 2 and 3 months after treatment. (b) The proportion of successful results in ODI (%) (defined as 40% or more reduction of ODI (%) as compared with ODI (%) at pre-treatment) of BT group was significantly higher than that of TA group at 2 and 3 months after treatment. BT = botulinum toxin; TA = triamcinolone and local anesthetics; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index. * $P < 0.05.$
muscles. However, according to one study that investigated the effect of 150 U of BT (Dysport®, Ipsen) on piriformis syndrome, no appreciable side effects were noted [39]. Thus, it was expected that even if a part of the 100 units of toxin used in the current study was released and spread into the gluteal muscles, it would not be sufficient to lead to significant muscle weakness or functional impairment. Our study suggested that 100 units were sufficient for pain reduction and functional improvement without inducing any significant side effects.

Considering the treatment effects, statistically significant change does not always mean that the change is clinically important. The minimal clinically important difference (MCID) has been introduced in an effort to define what is the smallest meaningful score change [40]. Published MCID values ranged from 5–16 points for ODI, and 2–4 points for the NRS pain [40–45]. We established clinically important difference as 40% reduction of ODI and 50% reduction of NRS according to the other references because this degree of change was supposed to be enough to avoid overestimation of functional improvement and pain reduction [21,41,46]. In this respect, 88% of our patients exceeded the MCID for both pain and disability after treatment with BT.

For a variety of reasons, the present study falls short of proving the efficacy of BT for SIJ pain. These reasons can be categorized under diagnosis, control, and plausibility. The diagnostic test used to select patients for the present study has not been validated. It has not been determined how reliably or how selectively injections of local anesthetic into the intersosseus ligament succeed in anaesthetizing a putative source of pain. Nor has it been established that 50% relief of pain is a sufficiently specific criterion for a positive response. Moreover, single diagnostic blocks may be subject to false-positive responses, and the false-positive rate of blocks of the sacroiliac ligaments has not been measured. However, these considerations affect only the validity of the conceptual diagnosis. Whether or not ligament blocks are diagnostic of a particular source of pain has yet to be determined. Nevertheless, positive responses to ligament blocks do serve empirically as a nominal selection criterion for treatment with BT. Applying such a selection criterion guards against indiscriminate or wholesale use of BT treatment.

A placebo control was not used in the present study. Instead, BT was compared with injection of steroids. Although used by some, if not many, injection of steroids is not yet a proven treatment for SIJ pain. Only one small study of patients with idiopathic back pain has reported superiority of steroids over placebo [12]. However, that study reported only a significantly greater change in pain; it did not report group scores after treatment, or the proportions of patients with satisfying relief; nor were any other outcome measures reported. Although these deficiencies were redressed in the present study, the absence of a placebo arm severely limits the validity of the present study. Superiority over placebo still has to be demonstrated. Nevertheless, the present study did show differences in favor of BT over steroids, at 2 and 3 months. Whereas responses attenuated after treatment with steroids, they remained stable after treatment with BT.

The results of the present study are shared with readers not because they prove efficacy of BT for the treatment of SIJ pain, but because they raise an intriguing, possible alternative to steroids. BT was clearly more effective than injection of steroids, and could prove to be safer than steroids, because of its longer duration of effect. Others might care to explore this alternative, either to corroborate its apparent effectiveness or to demonstrate an attributable effect greater than that of placebo.

Conflict of Interest

There are no potential conflicts of interests with respect to financial or personal relationships.

Acknowledgments

This research was supported by Wooridul Spine Foundation.

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