HSP Injection Therapies in Stroke

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Submitted by: Ke-Vin Chang

Definition

Hemiplegic shoulder pain (HSP) is one of the most debilitating complications after stroke [1]. Hemiplegic shoulder pain (HSP) hampers post-stroke functional recovery and is not well managed with conservative treatments.

1. Introduction

Hemiplegic shoulder pain (HSP) is one of the most debilitating complications after stroke [1]. Its reported incidence varies from 30% to 72% at one-year follow-up across different studies [2][3][4]. HSP is mostly graded as ranging from moderate to severe intensity [4] and rarely resolves spontaneously [3]. Stroke patients with poor upper extremity function have an increased risk of HSP [5]. Various theories have been proposed for the development of HSP, including deficiency in pain adaption [6], central sensitization to normal or subthreshold sensory stimuli [7], and impaired neuromuscular control of the scapula [8]. Spasticity over the hemiplegic limbs, shoulder subluxation, concomitant rotator cuff pathology, and prolonged immobilization of the affected limbs are also reported to be associated with HSP [9]. Without adequate management, HSP further worsens the function of the upper extremities and can prolong the hospital stay [2].

Shoulder slings, passive range of motion exercises, analgesics, and electrical stimulation have been commonly applied for treating HSP, although their effects are usually limited [10]. In recent years, various injection therapies have been proposed in its management. For instance, suprascapular nerve block (SSNB) using local anesthetics can be performed to decrease nociception from the glenohumeral joint [11]. Intramuscular botulinum toxin (BoNT) injections are also effective in reducing spasticity of the hemiplegic limbs and the associated pain [12]. On the other hand, BoNT injections are beneficial for decreasing chronic shoulder pain, possibly through inhibition of the release of pain mediators [13]. Corticosteroid injections have long been used to treat painful shoulders owing to their anti-inflammatory potential, while intra-articular hyaluronic acid (HA) injections might prevent adhesions and reduce synovitis inside the glenohumeral joint [14].

2. Injection Therapies for Hemiplegic Shoulder Pain in Stroke

At the fourth-week following the interventions, SSNB was likely to rank first, followed by intramuscular BoNT injections. Concerning the period between the 4th and 24th weeks, intramuscular BoNT injections appeared to be the most effective alternative for treating HSP.

Intra-bursal BoNT injections ranked second in relieving the symptoms of HSP between the 4th and 24th weeks. The main concern is that in our network meta-analysis, only one study [15] employed intra-bursal BoNT injections. Furthermore, the aforementioned study did not use a randomized controlled design. Therefore, the effect of intra-bursal BoNT injections could not be confirmed though the sensitivity analysis by excluding non-RCTs. Although a recent meta-analysis reported the superiority of intra-articular/bursal injections of BoNT over corticosteroids in the management of chronic shoulder pain between the first and third months after treatment [13], more evidence is still needed to validate the benefits of intra-bursal BoNT injections for treating HSP.

The best relief of HSP seemed to be provided by SSNB at the fourth post-injection week. According to our included studies, local anesthetics, including lidocaine [11][16][17] and bupivacaine [18][19], were the main regimens used for SSNB. The onset time ranged between two (lidocaine) and five (bupivacaine) minutes [20], enabling SSNB to take effect rapidly. Although the maximum effective duration ranges from one (lidocaine) to four (bupivacaine) hours [20], the clinical effect of SSNB seemed to persist in the fourth week

in our analysis. The mechanism of extended symptom relief is not clear. We also observed that some of the included trials also added corticosteroids or physiological serum into the injectate [11][16][18][17], which might reduce neurogenic inflammation and potentiate the effective duration of SSNB [21].

Intramuscular BoNT injections ranked second in the treatment outcomes of HSP at the fourth post-intervention week. Spasticity, defined as a velocity-dependent increase in muscle tone [9], commonly involves the muscles over the shoulder girdle, e.g., subscapularis, teres major, pectoralis major, latissimus dorsi muscles after stroke [9]. Accordingly, the spasticity of such muscles frequently leads to painful/limited shoulder motions. BoNT is an exotoxin produced by Clostridium botulinum, and its intramuscular injection inhibits the release of acetylcholine at the neuromuscular junction [22]. The maximum effectiveness of intramuscular BoNT injections is usually seen in the second or third post-intervention week but may be delayed due to muscle fibrosis after prolonged paresis in patients that have had a stroke [23]. This issue might have accounted for its lower rank than SSNB in the fourth-week.

Nonetheless, between the fourth and twenty-fourth weeks, intramuscular BoNT injections were found to be the best treatment for HSP. This finding is consistent with our prior assumptions. First, spasticity accounts for the leading cause of persistent HSP. A reduction of spasticity facilitates the normalization of shoulder motion and the reduction of the associated pain. Second, the maximum effect of intramuscular BoNT injections had been achieved in most of our included studies one month after the injection. The active duration of BoNT is at least three months [24], further enabling patients that have had a stroke to benefit from sustained relief of spasticity-related pain.

The doses and target muscles for intra-muscular BoNT injections varied among the included studies. Although we pooled them together for the purpose of network comparisons, the grouped finding of pain control might not be attributed to the motor inhibition only. Aside from neuromuscular blockade, animal studies found that the administration of BoNT was associated with a reduction of substance P release as well as subsequent neurogenic inflammation [25][26]. More basic research is needed to investigate the mechanism of relieving HSP through intra-muscular administration of BoNT.

Corticosteroid injections were consistently better than a placebo at both time points. Considering its well-established effects and thoroughly investigated adverse reactions in treating musculoskeletal pain [27], intra-articular/bursal corticosteroid injections can be considered as useful alternatives for HSP, especially in patients with concomitant rotator cuff or glenohumeral joint pathologies. Compared with corticosteroid injections, a previous meta-analysis revealed the non-superiority of intra-articular HA for shoulder pain management [28]. In our analysis, HA injections mostly ranked behind other non-placebo treatments, and as such, they cannot be recommended for the management of HSP.

Furthermore, SSNB was found to be the least effective among all the non-placebo treatments between the 4th and 24th weeks. This finding can be attributed to the fading effect of local anesthetics. Although SSNB is effective in pain relief by blocking sensory impulses, it does not treat the underlying causes of pain. On the other hand, intramuscular/bursal/articular administration of BoNT or corticosteroid intervenes potential pain generators (spasticity or rotator cuff pathologies).

If the treatment was a combination of two therapies, and this combination was shown in only one arm of the included studies, we would discard this therapeutic arm from the pooled analysis due to its low representativeness [19]. Furthermore, a recent systematic review reported that addition of corticosteroid to local anesthetics had only a small or no effect on the improvement of chronic non-cancer pain compared with local anesthetics alone [29]. Therefore, if one study comprised two similar treatment arms (e.g., one group received SSNB with local anesthetic and the other group underwent the same block with additional corticosteroids) [17], we combined the data from both arms for the analysis.

First, SSNB can be used as the first-line injection therapy in HSP due to its rapid onset. However, its effect is less sustaining, and repeat blocks or subsequent treatments targeting the underlying pain generators

might be required. Second, if there is concomitant upper extremity spasticity, BoNT injections for the spastic periarticular muscles should be prioritized in managing HSP.

3. Conclusions

SSNB was likely to rank first in relieving HSP at the fourth post-treatment week although the probability of being the best treatment was approximately 50%. Furthermore, care should be taken due to its short duration of effectiveness and a lack of enough studies with head-to-head comparisons of SSNB vs. other injection regimens. Intra-muscular BoNT injections seem to be the best treatment in the post-injection period between the 4th and 24th weeks. Concomitant spasticity in the shoulder girdle muscles should be evaluated as a potential source of HSP and properly managed using intra-muscular BoNT injections. If rotator cuff pathologies are suspected clinically, intra-articular/bursal corticosteroid injections can be administered. Further prospective studies are warranted to investigate the combined efficacy of different injections and their long-term therapeutic efficacy in treating HSP.

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Keywords

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