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A COMPARATIVE STUDY BETWEEN EFFICACIES OF USG GUIDED BOTULINUM TOXIN INJECTION INTO THE SUBSCAPULARIS MUSCLE AND THE CONSERVATIVE TREATMENT IN HEMIPLEGIC SHOULDER PAIN

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ABSTRACT

Introduction: Hemiplegic shoulder pain (HSP) is a common complication after stroke. HSP inhibits recovery and rehabilitation and impairs the quality of life of stroke survivors. Although the etiology of HSP is not well known, it has been suggested that multiple factors contribute to HSP. Our approach is to compare the efficacy of USG guided Botulinum toxin injection into the subscapularis muscle and conservative treatment in case of intractable hemiplegic shoulder pain.

Material and methods: In this Parallel Group Open Level Randomized Controlled Trial**,** conducted in the Department of Physical Medicine and Rehabilitation, IPGME&R, SSKM Hospital, Kolkata between September, 2017 to September, 2018 (Twelve months) on 34 (17 in each group) patients with intractable (persistent pain for more than 3 months) hemiplegic shoulder pain. In group 1, Botulinum toxin injection was given in subscapularis muscle by USG guided lateral approach. In group 2, managed conservatively with Physical therapy (stretching, passive range of motion exercise), Modality (hot pack, infrared, IFT), pain medications (NSAIDS, oral opioids) and Neuromuscular electrical stimulation of shoulder. Parameters used: 1. Pain intensity - measured by Numerical Rating Scale (NRS) [Score 0- 10], 2. Spasticity measured by - Modified Ashworth Scale (MAS) [score 0-4], 3. Shoulder range of motion - External rotation (ER) [score 0- 90] assessed. The patients attending the Physical Medicine and Rehabilitation OPD at IPGME&R and SSKM Hospital, Kolkata were included and studied if they fulfilled the inclusion and exclusion criteria after getting Institutional Ethics Committee clearance and informed written consent. After initial visit, followed up on 2nd week, 4th week and 12th week. Comparison done considering all the parameters considering basal and follow up data to compare the efficacy of intra-muscular botulinum toxin injection and those with in group 2, managed conservatively.

Results: All the data collected during this study period were analyzed by using statistical software Statistica vertsion 6 [Tulsa, Oklahoma: StatSoft Inc., 2001] and GraphPad Prism version 4 [San Diego, California: GraphPad Software Inc., 2005]. There was statistically significant difference (group 1 is statistically superior than group 2) between two groups at 2nd, 4th and 12th week in respect to NRS, MAS of subscapularis and ER of shoulder joint (p value<0.05).

Conclusion: There was significant short-term improvement of shoulder pain, spasticity of shoulder internal rotator(subscapularis) and range of motion in the form of external rotation after Botulinum toxin injection compared to conservative treatment. But in terms of intermediate-term and long-term follow-up although both groups showed significant improvement but Botulinum toxin injection group was statistically superior than conservative treatment.

KEYWORDS

Hemiplegic Shoulder Pain, Botulinum Toxin Injection, Subscapularis Muscle, Modified Ashworth Score, Numerical Rating Scale.

INTRODUCTION:

Hemiplegic shoulder pain (HSP) is a common complication after stroke with a reported prevalence of 29%–65%.[1,2] HSP inhibits recovery and rehabilitation and impairs the quality of life of stroke survivors. Although the etiology of HSP is not well known, it has been suggested that multiple factors contribute to HSP such as adhesive capsulitis, rotator cuff disorder, myofascial pain, complex regional pain syndrome and spasticity. HSP in the first 6 months after stroke has a favorable outcome in 80% of patients.[3,4,5] Yelnik et al. reported that Botulinum Toxin (BTX) injections into the subscapularis muscle for spastic HSP result in better improvements in shoulder pain, range of motion (ROM) and spasticity compared to the placebo group.[6] So, this is our humble approach to compare the efficacy of USG guided Botulinum toxin injection into the subscapularis muscle and conservative treatment in case of hemiplegic shoulder pain.

REVIEW OF LITERATURE:

As per Richard D Wilson, et al. hemiplegic shoulder pain is a common complaint for stroke survivors. Many pathologies are included in the diagnosis of hemiplegic shoulder pain. So, shoulder pain has a multifactorial cause.[7] In a prospective population-based study on incidence and associations of hemiplegic shoulder pain poststroke published in *Arch Phys Med Rehabil.* 2015, done by Zoe Adey-Wakeling et al. it has been shown that the frequency of poststroke shoulder pain is almost 30%. Peak onset and severity of hemiplegic shoulder pain in this study was at 4 months and more often associated with movement at later time points. Objective passive range-of-motion tests elicited higher frequencies of pain than did self-report and predicted later subjective shoulder pain.[1] Study done by Ilke Coskun Benlidayi, Sibel Basaran opined that hemiplegic shoulder pain (HSP) is common in stroke survivors, developing in up to 54% of patients. The underlying mechanisms include soft tissue lesions, impaired motor function and central nervous system-related phenomena. Hemiplegic shoulder pain has many underlying causes and is challenging to manage, requiring a team approach, including physicians, therapists and caregivers. The management strategy must target the underlying causes.[8] As per study by Meltem Dalyan Aras et al. shoulder pain can limit the patients' ability to reach their maximum functional potential and impede rehabilitation. The contributing factors such as glenohumeral subluxation, reflex sympathetic dystrophy, tonus changes, motor functional level, limitation in shoulder range of motion, thalamic pain, neglect, and time since onset of hemiplegia. Of the 85 patients with stroke, 54 patients (54/85, 63.5%) were found to have shoulder pain. Limitation of external rotation and flexion of shoulder was also a significant factor in the development of shoulder pain. To prevent and alleviate shoulder pain, efforts should be directed toward proper positioning of the shoulder, range of motion activities, and the avoidance of immobilization.[2] In a study where thirty-two consecutive patients with hemiplegic shoulder pain within a 1-year period after first stroke were recruited to identify the etiology of hemiplegic shoulder pain by arthrographic and clinical examinations and to determine the correlation between arthrographic measurements and clinical findings in patients with hemiplegic shoulder pain; showed significant restriction of passive shoulder external rotation and abduction. Muscle spasticity of the upper extremity was slightly negatively correlated with shoulder PROM (Passive Range of Motion). Shoulder joint volume was moderately positively correlated with shoulder PROM. They have concluded that Greater PROM of the shoulder joint, associated with larger joint volume, decreased the occurrence of adhesive capsulitis. Proper

physical therapy and cautious handling of stroke patients to preserve shoulder mobility and function during early rehabilitation are important for a good outcome.[3] Yelnik et al.[6] reported that Botulinum Toxin (BTX) injections into the subscapularis muscle for spastic HSP result in better improvements in shoulder pain, range of motion (ROM) and spasticity compared to the placebo group. Various studies showed BTX injection as a novel treatment option for a variety of pain syndromes including shoulder pain[6,9,10].

AIMS & OBJECTIVES:
To compare the efficacy of USG guided Botulinum toxin injection into the subscapularis muscle and conservative treatment in case of hemiplegic shoulder pain.

METHODOLOGY:
Institutional ethics committee clearance was taken. Individual written informed consents of patients were taken.

TYPE OF STUDY: Parallel Group Open Level Randomised Controlled Trial.

PLACE OF STUDY: Department of Physical Medicine and Rehabilitation, IPGME&R and SSKM Hospital, Kolkata.

STUDY PERIOD:12 months (September 2017 to September 2018).

SAMPLE SIZE :17 subjects(in each group).

ASSESSMENT PERIOD : Baseline, 2nd week, 4th week and 12th week.

STUDY PARAMETERS :
1. Pain intensity - Numerical Rating Scale (NRS) [Score 0- 10],
2. Spasticity - Modified Ashworth Scale (MAS) [score 0-4],
3. Shoulder range of motion - External rotation (ER) [score 0- 90].

INCLUSION CRITERIA:
1. Post stroke shoulder pain > 3 months.
2. Brunnstrom stage 3 of recovery.
3. Restricted external rotation of shoulder.
3. Unilateral involvement.
4. NRS >5/10.
5. 18 -70 Years of age.

EXCLUSION CRITERIA:
1. Patients without consent or uncooperative patients.
2. Any active infection, malignancy or uncontrolled systemic diseases.
3. Immunocompromised patients.
4. Pregnancy.
5. Blood coagulation disorder or taking oral anticoagulants.
6. Known allergy to botulinum toxin.
7. Patients receiving botulinum toxin injection into subscapularis muscle within last 6 months.
8. Other shoulder joint pathologies.

MATERIALS:
1. Disposable syringes (1 ml).
2. 18 Gauge 10 cm needle.
3. 0.9% Normal Saline.
4. Sterile surgical gloves.
5. Gauze pieces.
6. Injection Botulinum toxin type A.
7. USG machine.

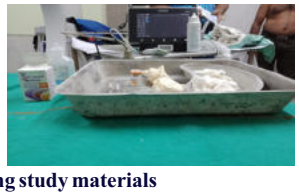

Figure: 1 showing study materials

STUDY TECHNIQUE:
In group 1, Botulinum toxin injection was given in subscapularis muscle by USG guided lateral approach. Dosage was calculated by body weight and spasticity severity (MAS score). Total 200 units of BTX were given in divided doses (each 60-70 unit) at 3 different motor points. Post injection stretching programme was done and continued.

In group 2, Physical therapy (stretching, passive range of motion exercise), Modality (hot pack, infrared, IFT), Pain medications (NSAIDS, oral opioids) and Neuromuscular electrical stimulation of shoulder muscles like deltoid, supraspinatus, teres major, pectoralis major, were administered and continued in the follow-up period.

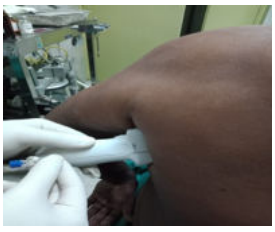

Figure: 2 showing USG guided injection procedure in subscapularis muscle

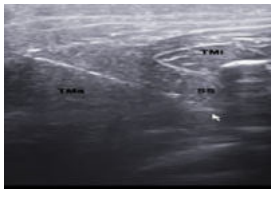

Figure: 3 showing USG guided injection procedure and needle placement in subscapularis muscle

RESULT & ANALYSIS:
Table 1: Basic Parameters

PARAMETERS	GROUP 1	GROUP 2	P Value
AGE	55.24	58.65	0.195
MALE: FEMALE	1.43	1.13	1
DURATION	8.46	8.46	1
NRS-BASELINE	7.49	7.49	1
MAS-BASELINE	2.12	2.12	1
ER-BASELINE	32.23	35.75	0.054

Repeated measures analysis of variance (ANOVA) with Tukey's test as post hoc test used to compare between individual time points for assessment of basic parameters over time. Both groups were comparable in respect to Age, Sex, Disease duration, NRS, MAS of subscapularis and shoulder External Rotation (ER) at baseline.

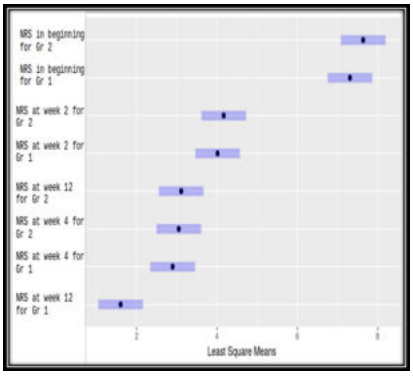

Figure 4: Intervention group wise range of Numerical Rating Scale (NRS) according to different stages of treatment (2nd week, 4th week and 12th week)

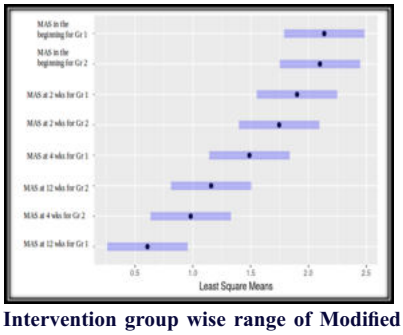

Figure 5: Intervention group wise range of Modified Ashworth Score (MAS) according to different stages of treatment (2nd week, 4th week and 12th week)

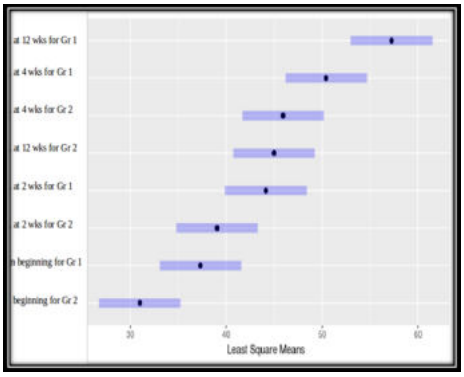

Figure 6: Intervention group wise range of External Rotation (ER) of Shoulder according to different stages of treatment (2nd week, 4th week and 12th week)

Figure 4, 5 and 6 shows NRS and MAS scores were decreased and ER of the shoulder joint was increased after Botulinum toxin injection as compared to conservative treatment. There was statistically significant difference (group 1 is statistically superior than group 2) between two groups at 2nd week, 4th week and 12th week in respect to NRS, MAS of subscapularis and ER of shoulder joint (p value<0.05).

DISCUSSIONS:

This Parallel Group Open Level Randomized Controlled Trial aiming to compare the efficacy of USG guided Botulinum toxin injection into the subscapularis muscle and conservative treatment in case of hemiplegic shoulder pain (HSP) conducted in the Department of Physical Medicine and Rehabilitation, IPGME&R, SSKM Hospital, Kolkata between September, 2017 to September, 2018 (Twelve months) on 34 (17 in each group) patients with intractable hemiplegic shoulder pain. In group 1, Botulinum toxin injection was given in subscapularis muscle by USG guided lateral approach. In group 2, managed conservatively with Physical therapy (stretching, passive range of motion exercise), Modality (hot pack, infrared, IFT), pain medications (NSAIDS, oral opioids) and Neuromuscular electrical stimulation of shoulder.

Parameters used:1. Pain intensity - measured by Numerical Rating Scale (NRS) [Score 0- 10], 2.Spasticity measured by - Modified Ashworth Scale (MAS) [score 0-4], 3. Shoulder range of motion - External rotation (ER) [score 0- 90] assessed. After initial visit, followed up on 2nd week, 4th week and 12th week. Comparison done considering all the parameters considering basal and follow up data. Patients included are of Post stroke shoulder pain > 3 months, Brunnstrom stage 3 of recovery, with Restricted external rotation of shoulder, Unilateral involvement, and pain with NRS >5/10.

In our study patients were in between 18 -70 years of age with the mean age of 55.24 in Group 1 and 58.65 in Group 2 and Male female ratio 1.43 and 1.13 respectively. Repeated measures analysis of variance (ANOVA) with Tukey's test as post hoc test used to compare between individual time points for assessment of basic parameters over time. Both groups were comparable in respect to Age, Sex, Disease duration, NRS, MAS of subscapularis and shoulder External Rotation (ER) at baseline. NRS and MAS scores were decreased and ER of the shoulder joint was increased after Botulinum toxin injection as compared to conservative treatment. There was statistically significant difference (group 1 is statistically superior than group 2) between two groups at 2ndweek, 4thweek and 12thweek in respect to NRS, MAS of subscapularis and ER of shoulder joint (p value<0.05).

Rajiv R. Shah et al. studied a total of 89 stroke survivors. MRI scan evaluations of their painful poststroke shoulders were performed. The mean age was 57.8±11.0 years (SD), 67% were men, mean BPI 12 score was 7.1±1.9, mean time from stroke onset to study entry was 61.1±79.3 weeks, and the mean duration of pain was 53.4±7.5 weeks. Sixty-seven percent sustained non-hemorrhagic strokes. Sixty-five percent exhibited left hemiparesis. The mean motor score was 49±29%.[11] As per a retrospective study on sonographic findings of painful hemiplegic shoulder after stroke by Pei-Hsin Lin; hemiplegic shoulder pain is common in stroke patients and can influence rehabilitation outcome. The underlying pathology can be various: in addition to impaired motor control and altered peripheral and central nervous activity, soft tissue lesions may also play an important role. Study suggested that the mechanism through which soft tissue lesions causes hemiplegic shoulder pain may be independent of the mechanisms through which changes of muscle tone and nervous activity causes shoulder pain.[12] In another study done by In Sook Lee et al. on sonography of patients with hemiplegic shoulder pain after stroke: correlation with motor recovery stage published in Am J Roentgenol, 2009; concluded that the cause of shoulder pain was variable and there was no correlation between the stages of motor recovery and the grades of sonographic findings in patients with hemiplegic shoulder pain.[13] In a prospective longitudinal study published in J Rehabil Med. 2012; done by Ya-Ping Pong et al. where seventy-six (76) stroke patients with hemiplegic shoulders evaluated. Hemiplegic shoulder pain and clinical, physical, and sonography results were recorded at admission and during both acute (before discharge) and chronic stages (6 months after discharge). Their results showed that during the acute stage, hemiplegic shoulder pain correlated significantly with shoulder motor function level and range of motion limitations. During the chronic stage, hemiplegic shoulder pain correlated significantly with shoulder motor function level, range of motion limitations, spasticity and abnormal sonographic findings. They concluded that hemiplegic shoulder pain was correlated with lower motor function level and shoulder range of motion limitation in both stages. Shoulder spasticity and abnormal sonographic findings were correlated with hemiplegic shoulder pain during the chronic stage.[14]

Study by I A Snels et al. showed that Rehabilitation physicians used additional local (anti-inflammatory) injections which includes corticosteroids alone (51.2%), in combination with a local anaesthetic (37.2%) or a local anaesthetic only (9.3%).[15] M Murie-Fernández et al. in their study on painful hemiplegic shoulder in stroke patients: causes and management published in Neurologia, 2012; conducted a literature search of various databases between 1980 and 2008. The articles were evaluated using the PEDro scoring system. They opined that hemiplegic shoulder pain is common after a stroke. Its appearance limits daily living activities as well as participation in specific neuro-rehabilitation programs and may lead to a worse functional outcome. Well planned management of patients can reduce both the frequency and intensity of shoulder pain, improving functional outcome. They concluded that Shoulder subluxation, occurs at an early stage after stroke and is associated with subluxation of the shoulder joint and spasticity (mainly subscapularis and pectoralis).The injection of corticosteroids does not improve pain and range of motion in hemiplegic patients, while botulinum toxin combined with physical therapy appears to reduce hemiplegic shoulder pain.[5] In a study done by Jeong-Gue Choi et al. to evaluate the beneficial effect of Botulinum toxin A (BTX) injection into the subscapularis muscle on intractable hemiplegic shoulder pain; Botulinum toxin A was injected into the subscapularis muscle. Intractable hemiplegic shoulder pain was evaluated using an 11-point numerical rating scale. Pain-free range of motion was assessed for shoulder abduction and external rotation. The spasticity of the shoulder internal rotator was measured using the modified Ashworth scale. Assessments were carried out at baseline and at 1, 2, 4, and, if possible, 8 weeks. Their results showed that intractable hemiplegic shoulder pain was improved (p=0.004) after botulinum toxin injection into the subscapularis muscle. Restricted shoulder abduction (p=0.003), external rotation (p=0.005), and spasticity of the shoulder internal rotator (p=0.005) were also improved. Improved hemiplegic shoulder pain was correlated with improved shoulder abduction (r=–1.0, p<0.001), external rotation (r=–1.0, p<0.001), and spasticity of the internal rotator (r=1.0, p<0.001). They concluded that Botulinum toxin A injection into the subscapularis muscle appears to be valuable in the management of intractable hemiplegic shoulder pain.[16] A systematic review and meta-analysis published in Arch Phys Med Rehabil, concluded that BTX injections had a better effect on shoulder pain than conventional therapies (steroid or placebo injection)[17]

The subscapularis muscle is one of the primary internal rotators of the shoulder and plays a key role in synergic patterns.[18] Interestingly, restricted shoulder ROM is reportedly an important element in a vicious cycle leading to persistent HSP (>6 months).[19] Injection BTX showed significant improvement in shoulder PROM of abduction/ external rotation and pain, including one study by de Boer et al.[20] The BTX injection show efficacy due to less severe pain and spasticity. Another postulated mechanism of our result was the anti-nociceptive effect of BTX. It (BTX) has a direct analgesic effect by inhibiting

neuropeptide release at nociceptive nerve endings, although the pathogenic mechanism of spasticity-associated pain and its alleviating effect have not yet been fully established.[21] Yelnik et al. also reported that BTX injections into the subscapularis muscle for spastic HSP result in better improvements in shoulder pain, range of motion (ROM) and spasticity compared to the placebo Group.[6] BTX injection acts by diffusion from the injection site to the adjacent areas, and the estimated diffusion area is 4.5 centimeter square (4.5CM2).[22] For this reason, not only the subscapularis muscle but also the adjacent soft tissue influenced by the BTX injection might have contributed to the results of this study. Therefore, injections into other soft tissues could be considered in future studies.

As per study done by Jeong-Gue Choi, Joon-Ho Shin, and Bo-Ra Kim; on Botulinum Toxin an Injection into the Subscapularis Muscle to treat Intractable Hemiplegic Shoulder Pain published in Annals of Rehabilitation Medicine 2016; the main source of iHSP (Intractable Hemiplegic Shoulder Pain) was spasticity of the shoulder internal rotator. BTX injection into the subscapularis might decrease the spasticity of the strong shoulder internal rotator, leading to restoration of restricted ROM for shoulder external rotation and finally alleviating iHSP by breaking its vicious cycle. This was supported by the high correlation between ROM or spasticity and pain. Their study shows that BTX injection into the subscapularis muscle improved shoulder pain, ROM, and spasticity in patients with iHSP. The improved shoulder pain was correlated with improved pain-free PROM of the shoulder and spasticity of the shoulder internal rotator. An ultrasonography guided lateral approach or conventional medial approach was made according to the patients' anatomical differences. The needle was used as a stimulation electrode to detect the motor point at which minimal stimulation induces maximal internal rotation. BTX dosage was selected by various patient characteristics such as body weight and spasticity severity. Thus, 60–80 units of BTX were administered in each injection. Pain severity was measured on an 11-point pain intensity numeric rating scale (PI-NRS), where 0 is no pain and 10 is the worst possible pain. Pain-free PROM of abduction and external rotation were assessed. Spasticity of shoulder internal rotator was measured using the Modified Ashworth Scale (MAS) rated on a scale of 0 (normal) to 4 (extreme). These measurements were carried out at baseline and at 1, 2, 4, and, if possible, 8 weeks after the intervention. The results showed; PI-NRS and MAS for the shoulder internal rotator were decreased and pain-free PROM for the shoulder were increased after BTX injection into the subscapularis muscle. Statistically significant differences were found between baseline and follow-up measurements after 1, 2, and 4 weeks in PI-NRS ($p=0.004$), pain-free PROM of shoulder abduction ($p=0.003$), external rotation ($p=0.005$), and MAS for the shoulder internal rotator ($p=0.005$) using the Freidman test. Post-hoc testing showed no statistically significant differences in measurements. There were significant correlations between PI-NRS for iHSP and pain-free PROM for shoulder abduction ($r=-1.0$, $p<0.001$), external rotation ($r=-1.0$, $p<0.001$), and MAS for the shoulder internal rotator ($r=1.0$, $p<0.001$) using the Spearman test.[16]

In a prospective, comparative, randomized, multicenter trial, done by SophieLarrazet et al. where 21 patients with hemiplegic shoulder pain after a recent stroke (less 6 months) were screened at baseline, then post-injection (BTX 150 units pectoralis major, 100 units subscapularis) at 1, 4 and 12 weeks. Outcomes were pain (assessed by visual analogic scale), range of motion, spasticity (Ashworth). The aim of this study was to compare the analgesic effectiveness of 1 month injection after botulinum toxin in the pectoralis major muscle or subscapularis. The result showed that pain improve significatively in subscapularis injection since the first month ($P = 0.027$), but without significant difference between both groups ($P = 0.50$). Pain score decreases from baseline, at respectively 4 and 12 weeks, of 16.3 and 24 points in subscapularis group versus 19.2 and 7.6 points in pectoralis major group. They concluded that Subscapularis injection offers a more linear evolution of pain and shoulder range of motion than pectoralis major injection. This study points out a role of toxin in the management hemiplegic shoulder pain.[23] In a recent Review done by Ke-Vin Chang published in *Pain Management,* Volume 10, in October, 2020 where a total of 19 clinical studies were included; observed that intramuscular BTX injections were helpful in stroke patients with hemiplegic shoulder pain. In shoulder joint pain, intra-articular and intrabursal BTX injections achieved a longer period of pain relief than corticosteroid injections.[24]

In a multicentre open-label parallel-group randomized controlled trial and economic evaluation done by L Shaw et al. to compare the clinical effectiveness and cost-effectiveness of treating upper limb spasticity due to stroke with botulinum toxin type A plus an upper limb therapy programme with the upper limb therapy programme alone; three hundred and thirty-three (333) adults included. The intervention group received botulinum toxin type A injection(s) plus a 4-week programme of upper limb therapy. The control group received the upper limb therapy programme alone. Participants were clinically reassessed at 3, 6 and 9 months to determine the need for repeat botulinum toxin type A injection(s) and/or therapy. They concluded that: the addition of Botulinum toxin type A to an upper limb therapy programme to treat spasticity due to stroke did not enhance improvement in upper limb function when assessed by the prespecified primary outcome measure at 1 month. However, improvements were seen in muscle tone at 1-month, upper limb strength at 3 months, upper limb functional activities related to undertaking specific basic functional tasks at 1, 3 and 12 months, and upper limb pain at 12 months. Botulinum toxin was well tolerated and side effects were minor.[25] In another trial published in Stroke. 2011, to see the effect on impairment, activity limitation, and pain; significant differences in favour of the intervention group with botulinum toxin were seen in muscle tone at 1 month; upper limb strength at 3 months; basic arm functional tasks (hand hygiene, facilitation of dressing) at 1, 3, and 12 months; and pain at 12 months. There was improvement in basic upper limb tasks (hand hygiene, facilitation of dressing) and pain.[26] Study conducted by Phil Shackley et al. published in *Toxins* (Basel) compared the cost-effectiveness of treating post-stroke upper limb spasticity with botulinum toxin type A plus an upper limb therapy programme against the therapy programme alone. Data on resource use and health outcomes were prospectively collected for 333 patients with post-stroke upper limb spasticity taking part in a randomized trial and combined to estimate the incremental cost per quality adjusted life year (QALY) gained of botulinum toxin type A plus therapy relative to therapy alone. They concluded that treatment with botulinum toxin type A plus therapy being cost-effective. The point estimates of the ICER remained above £20,000 per QALY for a range of sensitivity analyses, and the probability of botulinum toxin type A plus therapy being cost-effective at the threshold value did not exceed 0.39, regardless of the assumptions made.[27] As per study of J Wissel et al. target muscles for BTX A were selected on the basis of clinical examination. Intramuscular BTX A injections were placed in muscles exhibiting increased muscle tone in combination with pain during passive joint movement. Baseline and follow-up (mean 5.9 weeks) measures included a patient self-assessment of pain and function on a five-level scale, a physician's evaluation of function, and a global rating of response to BTX A. Fifty-four of sixty patients experienced improvement in pain without subjective functional improvement. The effects were comparable in acute ($n = 17$) and chronic ($n = 43$) spasticity. Physician's assessment of gain in function increased significantly ($p < 0.05$) only in patients with chronic spasticity. No serious adverse event was observed. Mild reversible side effects (local pain, hematoma, edema, mild weakness) were observed in four patients. In conclusion, they showed that intramuscular BTX A injections are a potent, well-tolerated treatment modality to significantly reduce spasticity-related local pain. This problem may be a main indication, especially in patients with poor response or intolerable side effects to oral medication.[10] A randomized, placebo-controlled study done by A M Bakheit et al. patients received either placebo injections or a total of 1000 IU of BTX A into five muscles of the affected arm. Muscle tone was assessed using the Modified Ashworth Scale (MAS). Other outcome measures were the change in the joint range of motion (ROM), the Barthel index, pain score, goal attainment and the subjective evaluation of benefit by patients and investigators. The patients were assessed blind to randomization at baseline and 4th, 8th, 12th and 16th week after treatment. The group of patients who received BTX A had a significant reduction in the summed MAS score at week 4 compared with the placebo group ($P=0.004$). The findings of the present study suggest that treatment with BTX A in a dose of 1000 units reduces muscle tone in patients with post-stroke upper limb spasticity. This effect is sustained for at least 16 weeks. BTX A is safe in the dose used in this study.[28]

In a very recent Systematic Review and Meta-analysis. done by Hui-Min Xie et al. published in Arch Phys Med Rehabil. January, 2021 to evaluate the effectiveness of botulinum toxin A (BTX-A) in the treatment of hemiplegic shoulder pain where Randomized controlled trials that compared shoulder BTX-A injections vs a control intervention in patients with a history of hemiplegic shoulder pain after stroke were selected. Among the 620 records screened, 9 trials with

301 eligible patients were included. Outcome data were pooled according to follow-up intervals (1, 2, 4, and 12 wk.). The primary evaluation indices were pain reduction (visual analog scale [VAS] score) and range of motion (ROM) improvement. The second evaluation indices were upper limb functional improvement, spasticity improvement, and incidence of adverse events. Cochrane risk-of-bias was used to assess the methodological quality of studies independently by 2 evaluators. Meta-analysis revealed a statistically significant decrease in the VAS score in the BTX group vs the control group at 1-, 4-, and 12-weeks post-injection (wk 1: standardized mean difference [SMD], 0.91; 95% confidence interval [CI], 0.27 to 1.54; wk 4: SMD, 1.63; 95% CI, 0.76 to 2.51; wk 12: SMD, 1.96; 95% CI, 1.44 to 2.47). Furthermore, the meta-analysis demonstrated a statistically significant increase in abduction at 1-, 4-, and 12-weeks post-injection (wk 1: SMD, 3.71; 95% CI, 0 to 7.41; wk 4: SMD, 8.8; 95% CI, 2.22 to 15.37; wk 12: SMD, 19.59; 95% CI, 9.05 to 30.13) and external rotation at 1, 2, 4 weeks post-injection (wk 1: SMD, 5.67; 95% CI, 0.88 to 10.47; wk 2: SMD, 9.62; 95% CI, 5.57 to 13; wk 4: SMD, 6.89; 95% CI, 2.45 to 11.33) in the BTX group. The Conclusions was that BTX-A injection provided greater analgesic effects and increased shoulder abduction and external rotation ROM compared with steroid or placebo injection for the treatment of HSP.[29]

HSP inhibits recovery and rehabilitation and impairs the quality of life of stroke survivors.[3,4,5] Study done by Leonid Kalichman, Motti Ratmansky published in Am J Phys Med Rehabil. 2011, showed that the prevalence of hemiplegic shoulder pain is approximately 22%-23% in the general population of stroke survivors and approximately 54%-55% among stroke patients in rehabilitation settings. Hemiplegic shoulder pain causes a reduced quality-of-life, poor functional recovery, depression, disturbed sleep, and prolonged hospitalization.[30] As our study shows that NRS and MAS scores were decreased and ER of the shoulder joint was increased after Botulinum toxin injection as compared to conservative treatment which was statistically significant. So, intervention with injection BTX A definitely improves not only clinical and functional outcome but also rehabilitation outcome as well as quality of life.

CONCLUSIONS:

There was significant short-term improvement of shoulder pain, spasticity of shoulder internal rotator (subscapularis) and range of motion in the form of external rotation after Botulinum toxin injection compared to conservative treatment.

But in terms of intermediate-term and long-term follow-up although both groups showed significant improvement but Botulinum toxin injection group was statistically superior to conservative treatment.

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