



COMPARATIVE EVALUATION OF INTRA ARTICULAR AUTOLOGUS PLATELET RICH PLASMA VERSUS BOTULINUM TOXIN TYPE A FOR RELIEF OF KNEE PAIN DUE TO EARLY OSTEOARTHRITIS

Dr. Nimisha Verma*

MD Anesthesiology, PDCC Pain & Palliative care Assistant Professor Anesthesiology, IMS BHU *Corresponding Author

Dr. Vinoth Kumar SP

MD Anesthesiology Senior Resident, Ganga Hospital, Coimbatore

ABSTRACT

Knee osteoarthritis is a common ailment in the age group above 45 years. Various surgical and non surgical methods have been tried to relieve the pain and disability of OA knee, the joint which is most commonly affected. This study aims to study the pain relieving effects of a single intra articular injection of autologous platelet rich plasma as compared to botulinum toxin type A. Thirty patients of ages from 40 to 70 years, of either sex who were diagnosed with osteoarthritis of knee joint based on X-ray and clinical examination, were included in the study. Both the groups received a single injection of either autologous platelet rich plasma or botulinum toxin type A. All patients were followed for a period of 6 months and the results were analyzed statistically. We found that there was statistically significant pain relief in both these groups from the baseline value that persisted upto six months post treatment ($p < 0.001$). The Oxford knee score was less in PRP group as compared to Botox group at six months and more patients in the PRP group were satisfied with the treatment. Hence, we can conclude that PRP is a better intra articular treatment option than botox for knee joint pain due to osteoarthritis.

KEYWORDS : osteoarthritis, autologous platelet rich plasma, botulinum toxin type A

INTRODUCTION:

Knee osteoarthritis (OA) is a chronic progressive disease that affects more than 20% of people older than 45 years. With an increase in life expectancy, it is estimated that the need for knee arthroplasty would rise to more than six times by 2030¹. The targets of OA treatment are pain decrement, function and mobility increment, prevention or correction of the deformity, and slowing the progression of the disease. The established treatment options for Knee OA (intra articular corticosteroids and NSAIDs) often fail to provide adequate pain relief for long and are fraught with side effects². In this scenario, alternative treatments to relieve pain of knee OA have become very relevant. The two newer intra articular treatment options for OA are autologous Platelet Rich Plasma which is proposed to act by supplying a supra physiologic dose of growth factors into the knee joint^{3,4} and Botulinum toxin type A which by unclear mechanisms mollates knee pain⁵. Botox suppresses the secretion of neurotransmitters thus decreasing peripheral and central sensitization. It may have the potential for inhibiting the release of substance P, calcitonin gene related peptide (CGRP) and glutamate⁶.

So we planned a study to compare the efficacy of intra articular platelet rich plasma with intra articular botulinum toxin type A for pain relief in knee osteoarthritis. To our knowledge this study is the first of its kind that aims to evaluate the comparative efficacy of PRP versus Botox intra-articularly for knee pain due to OA.

MATERIAL & METHODS:

This study was conducted in the Division of Pain and Palliative Care, Department of Anesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi from January 2017 to January 2018. The OPD attendance of Knee OA patients during this period was 67 in number. Of these, thirty patients of both sexes in the age group of 40 to 70 who were not relieved of knee pain by NSAIDs, with grade 1 Ahlback OA severity grading (patients with joint space narrowing less than 3 mm) were included in the study. Patients with inflammatory arthritis, neoplasm or recent trauma, those with suspected pregnancy, lactating females and those with history of intra-articular injection in the study joint in the past 6 months were excluded from the study. Those with local infections, coagulopathies or major psychopathology were also not included in the study. X-ray knee (AP and Lateral view) routine Complete Blood Count (CBC), ESR, Anti CCP were done in all patients. Pain improvement was measured based on VAS (Visual Analog Scale), Oxford Knee Score and Subjective Pain Relief at pretreatment and one, three and six months following a single intra articular injection. Triangle technique under fluoroscopic guidance was used for

injection after taking all aseptic precautions. Patients were divided into two groups. Group I received autologous PRP 2ml and Group II received 100 units of Botulinum toxin A.

The statistical analysis was done using SPSS for Windows version 16.0 software. For non-continuous data Chi-square test was used. The mean and standard deviation of the parameters studied during observation period were calculated for two treatment groups and compared using FISHER test. The critical value of 'p' indicating the probability of significant difference was taken as < 0.05 for comparison.

RESULTS:

A total of thirty patients with early knee OA were included in the study and all patients were followed till the completion of study period. There were no significant age or sex difference between the groups ($p = 0.841$). The pre injection pain intensity as measured by VAS was comparable in the two treatment groups (7.8 ± 0.414 in group I versus 7.93 ± 0.594 in group II) Table 1.

On comparison of VAS score during the follow-up period, it was seen that there was no significant difference in between the groups up to 3 months interval. The Botox group scored better in terms of pain relief at 6 months as compared to PRP group (Table 2). However, this difference was highly significant ($p < 0.001$) when the pre treatment VAS values were compared to the values at six months in both the groups (Table 3).

When we compared the Oxford knee scores in the two groups, we observed that there was a highly significant improvement from the pretreatment levels. There was no significant improvement amongst the two groups at one month post treatment but this difference became noticeable at three months and continued at six months follow up. The group that received botox scored better on Oxford Knee Score at 6 months (group I 28.7 ± 0.458 vs 27.3 ± 0.352 in group II).

On estimation of the subjective pain relief at six months, 7 patients in intra articular PRP reported excellent pain relief and only one of the 15 patients in botox group reported excellent pain relief (Table 4). Good pain relief was observed in 5 patients in PRP group and 2 patients in Botox group. There were two patients who were unsatisfied with PRP treatment as compared to six patients in Botox group.

DISCUSSION:

Osteoarthritis is a degenerative joint disease in which articular

cartilage, subchondral bone, synovium, ligaments and articular capsule degenerate leading to pain on movement and at rest. The cause of pain in OA due to the chemical mediators that sensitize the free nerve endings present in and around the joints. As the disease is due to an accelerated natural process, there has been an increasing interest in the use of growth factors (GFs) provided by alpha granules of autologous platelets. Many GFs have been identified to take part in the regulation of intra articular cartilage metabolism. Transforming growth factor (TGF β) in particular is the one which is most important as it is involved in the process of cartilage regeneration and hence pain relief⁷. The antinociceptive effect of BoNT-A Clostridium botulinum neurotoxins are due to direct effects on noncholinergic neurons such as pain fibers (via blockade of neurotransmitter release), effects on autonomic function, muscle spindles (via cholinergic gamma motor neurons), and central nervous system plasticity (decreased central sensitization and wind-up)⁸.

Although there are many studies on the use of intraarticular injection of PRP and Botulinum toxin A, we could not find a study comparing the effects of the two in terms of pain relief and functional improvement. The present study was performed on 30 patients of either sex in the age group of 40-70 years presenting with pain of OA knee treated with intra articular injection of either Platelet rich Plasma (PRP) or Botulinum toxin type A (BoNT/A). The patients were followed up for 6 months. The pain relief as documented by VAS in both the study groups was statistically significant from the base line pre treatment values. However patients in the PRP group showed better subjective pain relief and functional status as shown by lower oxford knee score in the PRP group. VAS scores however were better statistically in Botox group. **Kon et al**⁹ studied the use of Intra articular PRP and reported a statistically significant improvement at 2 and 6 months of follow up. **Gobi et al**¹⁰ reported a statistically significant improvement in clinical outcome using Intra articular PRP at 6 month and 12 months interval similar to the observations made in the present study. **Patel et al**¹¹ observed better results in OA patients treated with intra articular platelet rich plasma injection (2 doses three weeks apart) in pain relief in terms of clinical outcome and subjective pain relief similar to this study results. However, in this study single dose of intra articular PRP injection was administered. **Lin-Fen-Hsieh et al**¹² reported that the intra articular BoNT/A injection for knee OA considerably reduced the knee pain and improved the knee function with 42.6% pain relief at 1 week post treatment and 34.9% pain relief at 6 months post treatment. In an open-label study of patients with severe chronic arthritis pain who were unresponsive to Intra articular corticosteroid injections, **Mahowald et al**¹³ observed that intra articular BoNT/A injections reduced pain in the joints of the lower extremities (knee and ankle) by 55% and in the shoulder by 71%. Moreover, improvement of 36%, 67% and 42% was observed in the lower limb function, active shoulder flexion, and active shoulder abduction, respectively (19). Our results are consistent with those of Mahowald's study.

CONCLUSION:

The present study compares the pain relieving effects of a single intra articular injection of autologous PRP with 100 IU of Botulinum toxin for a period of 6 months and we observed that both PRP and botox A relieved pain of osteoarthritis significantly upto 6 months. However patients were more satisfied with PRP treatment as was shown by an improved functional status of patients in PRP group.

Table 1. AGE DISTRIBUTION IN THE TWO GROUPS

GROUP	AGE (Mean \pm SD)	f-value	p-value
GROUP I (n=15)	53.47 \pm 6.896	0.174	0.841
GROUP II (n=15)	53.27 \pm 6.660		

TABLE 2: COMPARISON OF VAS SCORE

TIME INTERVAL	GROUP I	GROUP II	f-value	p-value
Prett	7.80 \pm 0.414	7.93 \pm 0.594	0.364	0.697
1month	3.60 \pm 0.632	3.53 \pm 0.516	0.214	0.808
3month	3.40 \pm 0.507	3.40 \pm 0.507	0.089	0.915
6month	4.07 \pm 0.594	3.60 \pm 0.737	7.937	0.001

TABLE 3: COMPARISON OF CHANGE IN VAS SCORE FROM PRE-TREATMENT LEVEL

TIME INTERVAL	GROUP I	p-value	GROUP II	p-value
1month	3.60 \pm 0.632	<0.001	3.53 \pm 0.516	<0.001
3month	3.40 \pm 0.507	<0.001	3.40 \pm 0.507	<0.001
6month	4.07 \pm 0.594	<0.001	3.60 \pm 0.737	<0.001

Table 4 COMPARISON OF SUBJECTIVE PAIN RELIEF AT 6 MONTH INTERVAL

Month 6	Group I		Group II	
	No.	PERCENTAGE	No.	PERCENTAGE
Excellent	7	46.6	1	6.6
Good	5	33.3	2	13.3
Satisfactory	1	6.6	6	40
Unsatisfactory	2	13.3	6	40
Total	15	100	15	100

$$\chi^2=11.35; p=0.0099$$

REFERENCES:

- Lawrence RC, Felson DT, Helmick CG, National Arthritis Data Workgroup. Estimates of prevalence of arthritis and other rheumatic conditions in the United States Part II. *Arthritis Rheum.* 2008; 58(1): 23-6.
- Kon E. Non surgical management of early knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc.* 2012; 20(3):436-49.
- De La Mata J. Platelet rich plasma: a new treatment tool for the rheumatologist; *Rheumatol Clin.* 2013; 9(3):166-71.
- Mc Arthur BA, Dy CJ, Fabricant PD, Gonzalez DVA. Long term safety, efficacy, and patient acceptability of hyaluronic acid in patients with painful osteoarthritis of knee. *Patient Prefer Adherence.* 2012; 6:905-10.
- Hunter DJ, McDougall JJ, Keefe FJ. The symptoms of OA and the genesis of pain. *Rheum Dis Clin North Am.* 2008 August; 34(3): 623-643.
- Rayegani SR. Does intra articular platelet rich plasma injection improve function, pain and quality of life in patients with osteoarthritis of knee; A randomized clinical trial. *Orthop Rev.* 2014; 6(5405):112-7.
- Evans HC, Virginia B. Kraus VB, Setton LA. Progress in intra-articular therapy. *Nat Rev Rheumatol.* 2014 January; 10(1): 11-22
- Rowland LP: Stroke, spasticity and botulinum toxin. *N Engl J Med.* 2002; 347:382-3.
- Kon E, Mandelbaum B, Buda R et al. Platelet rich plasma intra articular injection versus hyaluronic acid visco supplementation as treatments for cartilage pathology: from early degeneration to osteoarthritis. *Arthroscopy.* 2011; 27(11):1490-501.
- Gobbi A, Karnatzikos G, Mahajan V, Machira S. Platelet rich plasma treatment in symptomatic patients with knee osteoarthritis: preliminary results in a group of active patients. *Sports Health.* 2012; 4(2):162-72.
- Patel S, Dhillion MS, Aggarwal S, Marwaha N, Jain A. Treatment With Platelet-Rich Plasma Is More Effective Than Placebo for Knee Osteoarthritis : A Prospective, Double-Blind, Randomized Trial. *Am J Sports Med* 2013; 41: 356
- Hsieh LF, Wu CW, Chou CC et al. Effects of botulinum toxin landmark guided intra articular injections in subjects with knee osteoarthritis. *PM&R.* 2016; 8(12):1127-35
- Mahowald ML, Singh JA, Dykstra D. Long term effects of intra articular botulinum toxin A for refractory joint pain. *Neurotox Res.* 2006; 9:179-188