Original Research Article

A randomized open label comparative study on efficacy of ultrasonography guided vis a vis anatomical landmark guided genicular nerve block in knee osteoarthritis in a tertiary care hospital in Eastern India

Nabarun Gupta[1], Sabnam Ara Begum[2], Arunava Biswas[3*], Debajyoti Saha[4], Vasundhara Ghosal[5], Rathindra Nath Haldar[6], Sukanta Sen[7]

[1]Medical Superintendent, Katwa Sub-divisional Hospital, Purba Burdwan, West Bengal 713130, India
[2]Assistant Professor, Department of Pharmacology, R G Kar Medical College & Hospital, Khudiram Bose Sarani, Kolkata, West Bengal 700004, India
[3]Associate Professor, Department of Pharmacology, Coochbehar Government Medical College & Hospital & MJN Hospital, Coochbehar, West Bengal 736101, India
[4]Senior Resident, Egra Superspeciality Hospital, Hospital Road, Katranka, Purba Medinipur, West Bengal 721454, India
[5]Assistant Professor, Department of Physical Medicine & Rehabilitation, IPGME&R, SSKM Hospital, 244 A.J.C. Bose Road, Kolkata, West Bengal 700 020, India
[6]Ex-Professor, Department of Physical Medicine & Rehabilitation, IPGME&R, SSKM Hospital, 244 A.J.C. Bose Road, Kolkata, West Bengal 700 020, India
[7]Professor & Head, Department of Pharmacology, ICARE Institute of Medical Sciences and Research, Banbishnupur, Purba Medinipur, Haldia, West Bengal 721645, India

Received: 23-08-2020 / Revised: 12-10-2020 / Accepted: 29-10-2020

Abstract

Introduction: Osteoarthritis is a widespread health problem throughout the world, with 20%-30% of patients aged over 65 years reported as symptomatic**.** This painful condition often unmanageable with conservative management.
Objective: To compare the efficacy and safety of USG guided genicular nerve block and by anatomical landmark guided blind procedure in patients with OA knee.**Materials & Methods**: A parallel group open level randomized prospective study was conducted on patients suffering osteoarthritis of knee divided into ultrasound guided genicular nerve block (n=44) and anatomical landmark guided blind method (n=45) at a tertiary care hospital and followed up over a period of 12 weeks with assessment of pain, stiffness and function measured by visual analogue scale (VAS) and Western Ontorio and McMaster Universities Osteoarthritis (WOMAC) at regular interval.**Results:** A significant improvement in pain, stiffness and function ($p<0.001$) observed at 4and 12 weeks of interval in both the study group. Ultra sound guided group showed a better result ($p<0.05$) when compared to anatomical landmark guided **b**lind group at 4th and 12th weeks interval with lesser complication like bleeding.**Conclusion:** Genicular nerve block (both Ultrasound guided and anatomical landmark guided blind) are both effective method for pain and stiffness reduction in osteoarthritis of knee with less adverse effects. Long term pain control was significantly greater in ultrasound aided block nerve.

Key Words: Ultrasonography, anatomical landmark based, genicular nerve, osteoarthritis, visual analogue scale (VAS), Western Ontorio and McMaster Universities Osteoarthritis (WOMAC)

Introduction

Knee osteoarthritis (OA) is a main cause of pain in the elderly and it affects their quality of life and activities of daily living [1]. Owing to its anatomic characteristics and location, the knee joints are mostly exposed to repetitive trauma and are directly affected by factors including weight gain, injuries, and accidents. This may result in painful conditions that are

**Correspondence*
Dr. Arunava Biswas
Associate Professor, Department of Pharmacology, Coochbehar Government Medical College & Hospital & MJN Hospital, Coochbehar, West Bengal, India
E-mail: drabiswas@gmail.com

often refractory to conservative therapeutic options. Pain, joint stiffness and decreased muscle strength can be seen, and cause poor quality of life and poor functional capacity [2].Pharmacologic management with agents such as non-steroidal anti-inflammatory drugs and opioids has significant limitations of long-term analgesic relief with addition to adverse effects. In the past few decades, the treatment algorithm for intractable knee pain has included intra-articular injections of steroids or hyaluronic acid, despite limited evidence of their long-term results. In severe cases, total knee replacement may be seen as the major treatment option to achieve positive result however, total knee arthroplasty can't be performed on all patients because some patients have comorbidities and the risk of surgery complications [3] . Wylde et al. reported the risk of chronic postsurgical knee pain with 44% prevalence of persistent pain 3 to 4 years after total knee replacement and 15% of patients complaining of extremely severe pain [4]. It is unclear if the development of a postsurgical pain state is related to preexisting conditions, lower pain threshold, and/or the result of postsurgical complications.Understanding the knee's sensory innervation has gained significant importance in the last few years as a potential target for radiofrequency denervation/nerve block. The description of the "genicular nerves" by Choi et al in 2011 [5], has been used to refer to the sensory nerves innervating the knee joint. The location of these nerves, their anatomical relationship with surrounding tissues, and their origin and termination become better understood through cadaveric studies; therefore, it is possible to target, identify and perform genicular nerve block (GNB) without imaging [6, 7]. Therefore, the genicular nerve block has come up as a method of control of pain in cases of advanced osteoarthritis of knee joint [5, 8]. This procedure aims to provide pain relief by inhibiting the major nerve fibers that innervate the knee joint for patients who are not willing or are medically unfit for surgical procedures such as total knee replacement. It has been found that interventional management of pain is good enough to keep the patients in pain free state. Nowadays, musculoskeletal ultrasound is a very good tool to localize the genicular nerves precisely. So, ultrasound guided (USG) genicular nerve block can be an accurate and effective method of pain management. Till date there is scarcity of data regarding the comparative efficacy between ultrasound guided and blind procedures of genicular nerve block. Hence, this study was attempted to compare the efficacy of USG guided genicular nerve block and by blind procedure in patients with OA knee in terms of pain, stiffness and function measured by visual analogue scale (VAS) [9] and Western Ontario and McMaster Universities Osteoarthritis (WOMAC) [10] index and compare the relative safety of the two therapies.

Materials and methods

A parallel group open label prospective randomized controlled study was conducted in the Department of Physical Medicine and Rehabilitation (PMR), Institute of Post Graduate Medical Education & Research (IPGMER), Seth Sukhlal Karnani Memorial Hospital (SSKM), Kolkata for a period of 18 months after prior approval from the institutional ethics committee on patients presenting with knee pain in grade III and IV OA of knee joint attending the PMR OPD. Sample size for this study was based on the difference in WOMAC function score as the primary outcome measure. It was estimated that 35 number of subjects will be required in each group in order to detect a difference of 10 in this parameter with 80% power and 5% probability of type-I error. This calculation assumes a standard deviation of 15 for WOMAC function score in both the groups and two-sided testing. Allowing for a dropout rate of 20% the recruitment target has been kept at 45 subjects per group. Sample size calculation has been done using nMaster-2.0 (Department of Biostatistics Christian Medical College, Vellore, 2011) software.Written informed consent was obtained from (n=90) patients of either sex of any age presenting with grade III & IV OA of knee, unfit and unwilling for Total Knee Replacement (TKR) operation with Visual analogue scale (VAS>7). Patients with allergic to depo-methyl prednisolone, lignocaine, bupivacaine, history of intra-articular knee injection of corticosteroid 3 months prior, uncontrolled diabetes mellitus, uncontrolled hypertension, bleeding diathesis, skin infections adjacent to knee joint, fever of any duration were excluded from the study. Following screening, patients those enrolled based on inclusion/exclusion criteria were randomized in two groups by distribution of sealed envelope in which the method of intervention is written into Group I receiving ultrasonography (USG) guided and Group II land mark based blind method genicular nerve block [Figure 1]. Routine blood parameters like complete blood count, fasting blood glucose, creatinine, bleeding time, clotting time, INR etc. were done and VAS & WOMAC osteoarthritis index were determined as baseline data. All data related to response to therapy and adverse effects (if any) were recorded in a pre-designed data collection form. Follow up of patients done with VAS and

WOMAC at 0, 4 & 12th weeks after genicular nerve block.

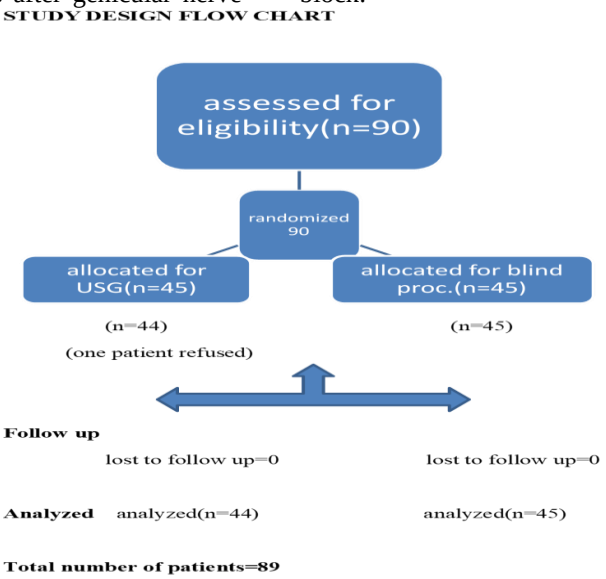

Fig 1: Study design flow chart

No pre-medications or sedatives were administered to either study group. For group 1 patients (n = 44) ultra sound machine was used with musculoskeletal probe (Samsung/ Model PT60A/Musculoskeletal probe 12MHz) to identify genicular nerve which was confirmed by color doppler. Next the needle was inserted in the plane of the ultrasound probe in the long-axis view. After confirmation of the position of the needle-tip next to a genicular artery, a gentle aspiration was done to check any accidental vessel prick and then a total 6 ml i.e. 2 ml each of lidocaine (2%) plus bupivacaine (0.5%) and methyl prednisolone (80mg) was injected with a 10ml syringe with 22G needle at 3 separate target sites: the superior lateral, superior medial, and inferior medial genicular nerves respectively [Figure 2].

Fig 2: USG guided intervention

In Group 2 patients (n=45) they received the same medication as mentioned above by anatomical landmark based blind method where after proper positioning of the patients the bony landmarks of medial and lateral femoral condyles and medial tibial condyle were identified and injection administered just proximal to the femoral and distal to the tibial condyles.[Figure 3] All the interventions in both the study groups was done by the same orthopedic surgeon.

Fig3: Injection for genicular nerve block

In the post intervention period patients of both groups were advised to avoid water contact for 24 hours, heavy exercises for 48 hours, oral acetaminophen 1gm on (if necessary) basis and continuation of orthotic support (if patient using previously prior to injection). Functional mobility & reduction of pain was measured by using WOMAC & VAS at prefixed time interval. All procedures and maneuvers were conducted by a single investigator to avoid bias.Data were summarized using Statistical version 6 [Tulsa, Oklahoma: Stat Soft Inc., 2001] and GraphPad Prism version 5 [San Diego, California: GraphPad Software Inc., 2007] by mean and standard deviation for numerical variables that were normally distributed, median and interquartile range for skewed numerical variables, counts and percentages for categorical variables. Fischer's exact test or Pearson's chi-square test were employed for inter-group comparison of categorical variables. Numerical variables were compared between groups by students' independent samples t-test, if normally distributed, or by Mann Whitney U test, if otherwise. Analysis of data was two-tailed and statistical significance level was set at $p < 0.05$ for all comparisons.

Results

A total of (n=89) patients assessed divided into two groups i.e. Group 1(USG guided) and Group 2(anatomical landmark guided) genicular nerve block respectively. One patient from the group 1 refused to participate further after group allocation and excluded from the study. The baseline parameters were comparable and the male: female distribution found was 50:39 altogether. In **[Table 1]** the WOMAC scores at different time interval in group 1 patients has been depicted where a very significant change ($p<0.001$) has been observed between 0 - 4 weeks, 0 - 12weeks and 4 - 12 weeks interval respectively.

Table 1: Comparison of WOMAC score at different time intervals in Group 1: USG guided genicular nerve block [n = 44]

Tukey's Multiple Comparison Test	Mean difference	q	P value	95% CI of difference
WOMAC 0 vs 4 weeks	15.455	28.091	< 0.001	13.595 to 17.314
WOMAC 0 vs 12 weeks	9.6591	17.557	< 0.001	7.7994 to 11.519
WOMAC 4 vs 12 weeks	-5.7955	10.534	< 0.001	-7.6552 to 3.9357

In **[Table 2]** the VAS scores at different time interval in group 1 patients were compared and a very significant change ($p<0.001$) was found between 0 - 4 weeks, 0 – 12 weeks and a $p<0.01$ during 4 - 12 weeks interval respectively.

Table 2: Comparison of VAS score at different time intervals in Group 1: USG guided genicular nerve block [n = 44]

Dunn's Multiple Comparison Test	Difference in rank sum	P value
VAS 0 vs 4 weeks	80.500	< 0.001
VAS 0 vs 12 weeks	50.000	< 0.001
VAS 4 vs 12 weeks	-30.500	< 0.01

In **[Table 3]** the WOMAC scores at different time interval in group 2 patients has been depicted where a very significant change ($p<0.001$) has been observed between 0 - 4 weeks, 0 - 12weeks and 4 - 12 weeks interval respectively.

Table 3: Comparison of WOMAC score at different time intervals in Group 2: anatomical landmark guided blind genicular nerve block [n = 45]

Tukey's Multiple Comparison Test	Mean difference	q	P value	95% CI of difference
WOMAC 0 vs 4 weeks	12.422	26.620	< 0.001	10.845 to 13.999
WOMAC 0 vs 12 weeks	6.6444	14.238	< 0.001	5.0677 to 8.2212
WOMAC 4 vs 12 weeks	-5.7778	12.381	< 0.001	-7.3546 to -4.2010

In **[Table 4]** the VAS scores at different time interval in group 2 patients were compared and a very significant change ($p<0.001$) was found between 0 - 4 weeks, 0 - 12weeks and during 4 - 12 weeks interval respectively.

Table 4: Comparison of VAS score at different time intervals in Group 2: anatomical landmark guided blind genicular nerve block [n = 45]

Dunn's Multiple Comparison Test	Difference in rank sum	P value
VAS 0 vs 4 weeks	84.000	< 0.001
VAS 0 vs 12 weeks	37.500	< 0.001
VAS 4 vs 12 weeks	-46.500	< 0.001

When the two study groups were compared in terms of WOMAC sub scoring of pain then a significant difference ($p<0.05$) in Group 1 at 4^{th} and 12^{th} weeks interval as compared to Group 2. Similarly, WOMAC sub score for stiffness when compared was found to be statistically significant change in Group 1 as compared to Group 2 during 4^{th} and 12^{th} weeks interval. But the WOMAC sub score for functionality was found to be statistically insignificant between the two groups **[Table 5].**

Table 5: Comparisons of different assessment parameters between Group 1 and Group 2 at various time intervals

Parameters	Group 1 USG (n=44)	Group 2 Blind (n=45)	P value
Age	66.11± 7.527	63.51±6.861	0.092
WOMAC P 0 weeks*	16.61± 1.146	16.47±1.160	0.549
WOMAC P 4 weeks*	10.93±1.690	11.73±1.763	**0.031**
WOMAC P 12 weeks*	12.91±1.927	13.89±1.682	**0.012**
WOMAC S 0 weeks*	6.32±0.800	6.58±0.723	0.112
WOMAC S 4 weeks*	4.61±1.316	5.07±0.986	**0.069**
WOMAC S 12 weeks*	5.30±1.133	5.89±0.959	**0.009**
WOMAC F 0 weeks*	46.27±7.478	44.51±4.551	0.182
WOMAC F 4 weeks*	38.14±8.045	37.84±5.950	0.846
WOMAC F 12 weeks*	41.20±8.569	40.60±6.206	0.704
VAS 0 weeks #	1742.0	2263.0	0.051
VAS 4 weeks#	1685.0	2320.0	**0.015**
VAS 12 weeks#	1507.0	2498.0	**< 0.001**

* Mean ± SD # Rank sum score, P= pain, S = stiffness, F = function

USG guided intervention showed no incidences of adverse effects while anatomical landmark guided blind procedures showed 6 cases of adverse effect e.g. bleeding from the injection site which is 13% of the population and is having statistical significance ($p<0.05$).

Discussion

A randomized open label control study was conducted at the Department of Physical Medicine and Rehabilitation at IPGMER, Kolkata over the period of 18 months and consisting of (n=89) patients who fulfilled the inclusion/exclusion criteria with a gender wise distribution of female patients more than male patients (51:38).In this study the two groups which were selected randomly from PMR OPD by sealed envelopes, group-1 (n=44) underwent USG guided intervention and the other group -2 (n=45) underwent blind (anatomical landmark) guided intervention. Patients from both the group underwent significant reduction of pain ($p<0.001$) which was evident from reduction of WOMAC score and VAS at the time of follow-up during 4 and 12 weeks. Comparison of skewed numerical variables between Groups 1 and 2 – Mann-Whitney U test showed that significant reduction of VAS and WOMAC ($p<0.001$) were there during the

follow up period of 4 weeks and 12 weeks. Almost similar kind of observation was found earlier in the study of Alahmari K et al [9]. Comparison of VAS and WOMAC during 0, 4 and 12th weeks showed significant amount of reduction ($p<0.05$) of those scores during 0-4 weeks, 0-12 weeks and 4 -12 weeks intervals respectively comparable with previous study of Kim H et al.[11] where they found significant pain and stiff reduction by both techniques in OA patients.The current study also revealed that as the duration of therapy progressed in the later part group 1 patients had significant reduction of pain as compared to group 2 which clearly signifies the superiority of USG guided GNB in comparison to the blind method. So far as the safety issue of both study procedures are concerned, it was observed that USG guided maneuver was statistically much safer ($p<0.05$) with lesser chances of bleeding which was again comparable with findings of studies conducted by Kim SY et al (2016) [11] and Strand N et al (2019) [12]. The study has few limitations like occupations where patients need to squat frequently or carry heavy weights not taken into account, biochemical alterations (if any) not assessed, small sample size, short duration of research work with shorter follow up sessions, conducted at a single study centre as it was a pilot study. Nevertheless, the findings of this study might help in building future plans in conduct of a robust multicentric study involving a good sample size which may validate the current findings firmly.

Conclusion

Genicular nerve block (both Ultrasound guided and anatomical landmark guided) is statistically effective method for pain and stiffness reduction in osteoarthritis of knee with less severe adverse effects. US guided procedure is safer and yield better result than the anatomical landmark guided blind method in the long term follow up of OA patients.

References

1. Dass RM, Kim E, Kim HK, Lee JY, Lee HJ, Rhee SJ. Alcohol neurolysis of genicular nerve for chronic knee pain. Korean J Pain 2019; 32: 223-7.
2. Kim DH, Lee MS, Lee S, Yoon SH, Shin JW, Choi SS. A prospective randomized comparison of the efficacy of ultrasound- vs fluoroscopy-guided genicular nerve block for chronic knee osteoarthritis. Pain Physician 2019; 22: 139-46
3. Santaguida PL, Hawker GA, Hudak PL, Glazier R, Mahomed NN, Kreder HJ, et al. Patient characteristics affecting the prognosis of total hip and knee joint arthroplasty: a systematic review. Can J Surg 2008; 51: 428-36.
4. Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. Pain. 2011 Mar;152(3):566-572.
5. Choi WJ, Hwang SJ, Song JG, Leem JG, Kang YU, Park PH, Shin JW. Radiofrequency treatment relieves chronic knee osteoarthritis pain: A double-blind randomized controlled trial. Pain 2011; 152:481-487
6. Yasar E, Kesikburun S, Kılıç C, Güzelküçük Ü, Yazar F, Tan AK. Accuracy of ultrasound-guided genicular nerve block: a cadaveric study. Pain Physician 2015; 18: E899-904.
7. Sutaria RG, Lee SW, Kim SY, Howe R, Downie SA. Localization of the lateral retinacular nerve for diagnostic and therapeutic nerve block for lateral knee pain: a cadaveric study.PM R 2017; 9: 149-53.
8. Kesikburun S, Yaşar E, Uran A, Adigüzel E, Yilmaz B. Ultrasound-guided genicular nerve pulsed radiofrequency treatment for painful knee osteoarthritis: a preliminary report.Pain Physician 2016; 19: E751-9.
9. Alahmari K, Silvian SP, Ahmad I, Reddy RS, Kakaraparthi VN. Subjective and objective evaluation of pain for older adults with knee osteoarthritis in Saudi Arabia: A reliability study. Niger J Clin Pract. 2020 Jul;23(7):934-943.
10. Sathiyanarayanan S, Shankar S, Padmini SK. Usefulness of WOMAC index as a screening tool for knee osteoarthritis among patients attending a rural health care center in Tamil Nadu. Int J Community Med Public Health 2017; 4:4290-4295.
11. Kim SY, Le PU, Kosharskyy B, Kaye AD, Shaparin N, Downie SA. Is genicular nerve radiofrequency ablation safe? A literature review and anatomical study. Pain Physician. 2016;19(5): E697-705.
12. Strand N, Jorge P, Freeman J, D'Souza RS. A rare complication of knee hematoma after genicular nerve radiofrequency ablation. Pain Rep. 2019;4(3): e736.

Source of Support:Nil
Conflict of Interest: Nil