Randomized Controlled Trial

A Randomized Controlled Trial Comparing the Effect of Two-Time Durations of Balloon Compression During Percutaneous Balloon Compression in Resistant Trigeminal Neuralgia

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Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 06-13-2023
Revised manuscript received: 08-17-2023
Accepted for publication: 08-29-2023

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Background: Percutaneous balloon compression of the trigeminal nerve's gasserian ganglion for the treatment of trigeminal neuralgia is an interventional pain procedure with results comparable to microvascular decompression surgery. The procedure is safe in experienced hands and has less morbidity associated with it. However, there is a lack of clear-cut guidelines about the details of the technique like balloon shape, inflation pressure, and duration of inflation. So, keeping the inflation pressure and shape of the balloon constant, we studied the effect of the duration of inflation of the balloon and its effect on pain relief in refractory trigeminal neuralgia cases.

Objectives: To study the outcome with 2 different durations of balloon inflation times in terms of pain relief and complications after percutaneous balloon compression.

Study Design: Prospective parallel design randomized, controlled trial.

Setting: The study was conducted in a tertiary care hospital in North Eastern India after obtaining approval from the Institutes' ethics committee (Dean/2018/EC/449). The study was also registered with the Clinical Trials Registry of India (CTRI no. CTRI/2019/03/018166). All patients referred to a pain clinic for unilateral facial pain were screened for the study over 2 years from April 2019 to March 2021.

Methods: Forty patients who met the diagnosis of trigeminal neuralgia and who did not respond satisfactorily to medications were included in the study. They underwent routine blood investigations and a magnetic resonance image of the brain to rule out any medical or surgical conditions. Percutaneous balloon compression was conducted under C-arm guidance using a 12 gauge cannula and a 4 Fr Fogarty balloon was used for compressing the gasserian rootlets.

Results: Patients who underwent 90 seconds as well as 120 seconds showed good pain relief. The 2 groups did not show any significant difference in pain relief based on the duration of compression. Visual analog scale scores were reduced from 7-8 to 0-3. Masseter muscle weakness was present in 47.5% of patients post-procedure and recovered in all except one patient.

Limitations: We have followed up with our patients for a short period of 6 months only. We could not measure the intra-luminal compression pressure of the balloon.

Conclusion: There is no difference in the pain relief obtained by the 2 different durations of compressions. A longer duration of compression, however, has more incidence of side effects.

Key words: Idiopathic trigeminal neuralgia, percutaneous balloon compression, time duration, shape of balloon, masseter muscle weakness, facial numbness, corneal dysesthesia

Pain Physician 2024: 27:21-26

Trigeminal neuralgia is defined as the unilateral, recurrent, shock-like, brief facial pain that is abrupt in onset and termination, triggered by innocuous stimuli, and occurs in one or more divisions of the trigeminal nerve. Recently, a concomitant continuous pain with moderate intensity within the distribution of the affected nerve territory is also included in the definition (1).

The etiology of the disease is dysmyelination or demyelination at the root entry zone (2) where the change in the quality of myelin sheath type (from peripheral to central) takes place. This process may be either primary- due to vascular compression (classical) or unknown cause (idiopathic), or secondary- due to some tumor or systemic diseases like multiple sclerosis.

The diagnosis is made mainly by history as there is no significant finding on physical examination. Some cases may show mild hyperalgesia in the affected area. Magnetic resonance imaging of the brain and brainstem has been shown to help differentiate the primary and secondary trigeminal neuralgias and also between classical and idiopathic neuralgia (3). The initial management of pain is by antiepileptic drugs. Carbamazepine and oxcarbazepine are the first line, followed by lamotrigine (4).

Percutaneous interventions for trigeminal neuralgia have a definite role in the management of cases with inadequate pain control with pharmacological methods. They are especially useful in an idiopathic variety of primary trigeminal neuralgia cases where no cause can be determined for dysmyelination leading to ephaptic transmission.

Percutaneous balloon compression (PBC) is a method of interrupting abnormal nerve transmissions by using mechanical pressure at the root entry zone. This area is susceptible to pressure changes. The procedure involves percutaneous insertion and inflation of a balloon near the trigeminal gasserian ganglion to compress the sensory nerve rootlets before they enter the pons. Although considered a standard treatment for refractory trigeminal neuralgia with results comparable to microvascular decompression (3), clear-cut guidelines regarding the duration of compression, the shape of the balloon, and the inflation pressures are lacking. Most studies have been done with a compression duration of one (60 seconds) minute to 5 minutes (300 seconds) (5-7). The standard practice in our institution was to do 90 seconds of balloon compression, and so to study the effect of the increase in the duration of compression on pain relief and complication rate, we increased the duration of the gasserian ganglion compression, by 30 seconds in the test group. Thus, we conducted a randomized, controlled study to determine the efficacy of 2 durations of compression (90 seconds vs 120 seconds) of the balloon to the effectiveness of pain relief.

Methods

Study Design

Prospective parallel design randomized, controlled trial with an allocation ratio of one.

Patient Selection

The study was conducted in the Pain Division of the Department of Anesthesiology, Institute of Medical Sciences after obtaining approval from the Institutes' ethics committee (Dean/2018/EC/449). The study was also registered with the Clinical Trials Registry of India (CTRI no. CTRI/2019/03/018166). All patients referred to a pain clinic for unilateral facial pain were screened for the study over 2 years from April 2019 to March 2021. Severe paroxysmal facial pain (visual analog scale [VAS] score > 6) of spontaneous onset characterized by brief electric shock-like pains in the distribution of second and third division of trigeminal nerve with pain-free intervals in between and who were unresponsive to at least 6 months of medical treatment were included in the study (International classification of headache disorders 3 Beta criteria). Patients with sinusitis, involvement of all the divisions of the trigeminal nerve, temporomandibular joint involvement, local infection, uncontrolled hypertension or coronary artery disease, and age > 65 years were excluded from the study. A total of 40 patients could be included in the study. Patients selected were randomly allocated into 2 groups using odd/even technique. In group A, patients underwent balloon compression for 90 seconds and in group B patients underwent compression for 120 seconds.

Procedure

A written informed consent was obtained from all patients. Patients were admitted a day before and were kept fasting for 6-8 hours before the procedure. All patients were advised to avoid the morning dose of analgesics. VAS and masseter muscle strength were assessed before the procedure. Intravenous access was secured and prophylactic antibiotic injection. Ceftriaxone was administered one hour before the procedure. Pulse oximetry, noninvasive blood pressure, and con-

tinuous electrocardiography monitoring were done in all. Patients were placed in a supine position on the operation table with the neck slightly extended and a pillow below the shoulders. The perioral region and puncture site were painted and draped. Skin entry site was marked on the cheek 2-3 cm lateral to the angle of the mouth on the affected side. Midazolam, propofol, and fentanyl were used for sedation. Using biplanar fluoroscopy, the foramen ovale was visualized, medial to angle to the angle of the mandible in a modified submental view (Fig. 1). A small size K wire was inserted through the foramen ovale. Then a 14-G blunt obturator was railroaded over the K wire till it reached the margins of the foramen ovale. The K wire was removed from the obturator and aspiration was performed to ensure that there was no cerebrospinal fluid or blood. Fogarty balloon catheter of size 4 was checked for patency of the balloon. The balloon catheter was advanced until 10 to 15 mm of the catheter was beyond the needle tip. The balloon was inflated with 0.75 to 1 mL water-soluble contrast dye. The shape of the balloon was noted (Fig. 2). The balloon was inflated for 90 seconds in group A and for 120 seconds in group B.

Intraoperative bleeding and hemodynamic stability were recorded. After the compression, the balloon was deflated, and the catheter and the cannula were removed together to avoid tethering or tearing of the balloon. After removing the cannula, the cheek was compressed against the maxilla for 5 minutes to stop any bleeding. The entry point was sealed with a sterile bandage and patients were transferred to post-anesthesia care unit. After the procedure, when patients regained full consciousness, they were tested for ipsilateral corneal sensations by cotton bud, masseter muscle weakness, and loss of /abnormal sensations on the face. VAS was noted during pretreatment, immediately post-operatively, and at day one, one week, one month, 3 months, and 6 months follow-up. VAS was assessed by asking the patients to put a mark on a 10 cm line where they feel that the maximum intensity of their pain is. The strength of the masseter muscle was assessed clinically by asking the patient to clench his teeth and comparing the muscle strength on both sides of the face, by palpation of the muscle belly before and after the procedure. If the muscle was flaccid compared to the opposite side, it was considered weak.

The demographic profiles of age, gender, height, weight, and comorbidities for the patients were noted (Table 1). The primary outcome was a VAS assessment between 2 groups based on the shape of the balloon, whether pear or nonpear shape. The secondary outcomes were the assessment of complications, such as masseter muscle weakness, corneal sensations, and sensation over the face in the trigeminal nerve territory that was present or absent (Table 2).

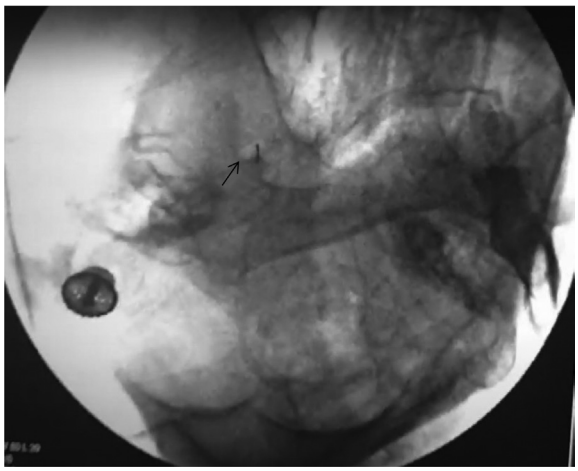

Fig. 1. *The location of foramen ovale in modified submental view under fluoroscopy. The foramen ovale is shown by the black arrow between the maxilla and mandibular ramus.*

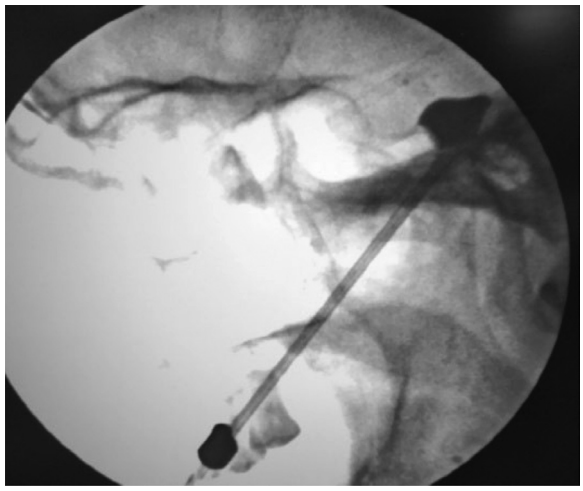

Fig. 2. *Shows the inflated balloon in the Meckel's cave taking the pear shaped.*

Statistics

For sample size calculation purposes, we considered this trial to be an equivalence trial (the new treatment is no better or worse than the existing treatment). Using a sealed envelope online power calcula-

Table 1. *Demographic profile and baseline vital parameters of the study patients.*

		Group 90 s (n = 20)	Group 120 s (n = 20)	*P* value
1.	Age	49.507 ± 7.66	48.431 ± 8.05	0.646
2.	Gender men	7	8	
3.	women	13	12	
4.	Height	163.05 ± 4.95	161.45 ± 4.58	0.295
5.	Weight	59.85 ± 7.45	57.95 ± 7.99	0.724
6.	Heart rate	78.5 ± 8.86	76.55 ± 6.62	0.230
7.	Mean Blood Pressure	73.35 ± 6.32	76.7 ± 8.86	0.170
8.	SPO_2	99.3 ± 0.57	98.9 ± 0.85	0.991
9.	Respiratory Rate	14.5 ± 1.05	14.95 ± 0.05	0.183
10.	VAS score	7.95 ± 0.99	8.00 ± 0.79	0.515

Table 2. *Comparison of Complications between the 2 groups.*

	Complication	90 s (n = 20)	120s (n = 20)	Significance (*P* value)
1	Masseter Muscle weakness			
	Immediate post procedure	7	12	0.048
	1 week	4	12	0.01
	1 month	4	7	0.288
	3 months	2	5	0.212
	6 months	0	1	0.311
2	Corneal sensations absent (from post-procedure to 6 months)	1	2	0.548
3	Facial Dysesthesia/ anesthesia (from immediate post-procedure period to 6 months)	16	8	0.01

tor (8), considering an alpha error of 5%, a power of 80%, considered a 99% success in both groups, and an equivalence limit of 9, the sample size of 42 patients was found adequate. However, data could be collected for 40 patients only during the given time.

The data was entered in a Microsoft Excel spreadsheet and an analysis was done using Statistical Package for Social Sciences (SPSS) version 16.0. Categorical variables were presented in number and continuous variables were presented as mean ± SD. Statistical tests were applied. A *P* value of 0.05 was considered statistically significant. Quantitative variables were compared using an unpaired t-test/ Mann-Whitney U Test (when the data sets were not normally distributed) between the 2 groups. Qualitative variables were correlated using the chi-square test/ Fisher's exact test.

Results

The 2 study groups were comparable in their demographic profile (age, gender, weight, height) as well as pre-procedure vital parameters (heart rate, blood pressure, respiratory rate, oxygen saturation, and pain). Each group had 20 patients with women being preponderance. The pre-treatment mean VAS in the 90 second group was 7.95 ± 0.998 and in the 120 second group was 8 ± 0.794. Immediate post-procedure comparison of mean VAS in group 90 second was 1.7 ± 1.301 and in group 120 second was 1.35 ± 0.988 (Fig. 3). The difference was statistically insignificant. The pain relief was maintained at one week (1.55 ± 1.39; 1.8 ± 1.005) and one month (1.85 ± 1.34; 2.4 ± 0.75) follow-up. This relief was sustained throughout the study period of 6 months and all patients had significant relief from pre-procedure VAS scores at the completion of the study period. However, the difference between the 2 groups was statistically insignificant.

All patients were observed for intraoperative and postoperative complications. Intraoperative bradycardia was observed in 11 patients in group A and 14 patients in group B. This difference was also not significant (*P* = 0.325). A satisfactory shape of the inflated balloon could be achieved in all patients. It was pear-shaped in 33 patients (17 vs 16) whereas dumbbell shaped in 7 patients (3 vs 4).

The corneal sensations, masseter muscle weakness, and facial numbness were evaluated in the post-operative and follow-up period. Immediately after the procedure, 7 patients in the 90 second group and 12 patients in the 120 second group developed masseter weakness. This weakness persisted for one month after the procedure and gradually improved over the study period and only one patient had masseter muscle weakness at the end of 6 months. Corneal sensations were lost in one patient in the 90 second group and 2 patients in the 120 second group. Facial numbness was found in 4 patients in the 90 second group and 12 patients in the 120s group (*P* = 0.010). The facial numbness and loss of corneal sensations were detected in the post-procedure period and persisted till 6 months of the study period.

Discussion

The present study was conducted on patients with refractory idiopathic trigeminal neuralgia. The pain

relief obtained by 2 different durations of mechanical balloon compression of the ipsilateral gasserian ganglion were compared. In half of the patients, the duration was 90 seconds, and in the other half, it was 120 seconds. We did not aim for higher compression durations of more than 120 seconds as that would increase the risk of severe bradycardia, due to trigeminocardiac reflex, especially when we lacked the pressure monitoring manometer in our equipment.

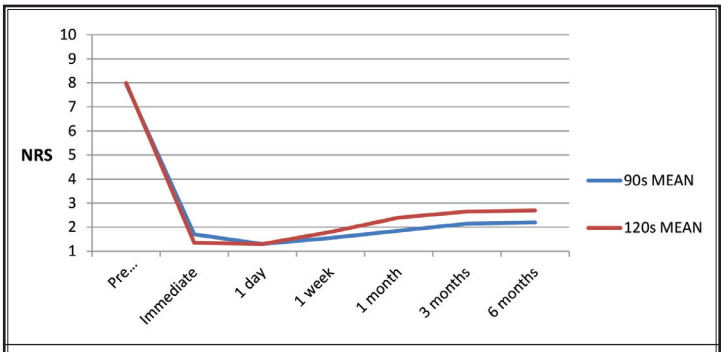

Fig. 3. *Comparison of VAS during the study period.*

The primary objective was to compare the reduction in the VAS score in the 2 groups. The secondary objective was to detect and compare complications and side effects related to the procedure in the 2 groups. Our study found that there was no significant difference in the pain relief obtained with 2 the different durations of compression. Both groups showed good pain relief (more than 50% from baseline) up till the completion of the study period. Preoperative VAS reduced from 7-8 to 0-3 during the 6-month follow-up study period.

Balloon compression at the root entry zone results in transient hypoxia and an increase in vascular endothelial growth factor expression in the compressed nerves (6,9,10). This leads to neovascularization that alleviates the chronic microvascular ischemia, which is the cause of demyelination. Lee et al (7) compared the effect of 60 seconds and 180 seconds of balloon compression and found good immediate pain relief in all patients. He observed a higher recurrence with shorter compression and a higher complication rate with longer duration.

Compression pressure measurement as a measure of the efficacy of the procedure has been evaluated previously (11,12), but we did not do it in our patients due to unavailability of equipment. However, we fixed the volume of dye used for inflation to be 1 mL of iohexol, assuming that it shall exert a similar pressure in all cases. We considered the pear and dumbbell shapes of the balloon to be markers of the efficacy of the procedure. Trojnik et al (5) studied PBC outcomes in 27 patients and used a variable duration of compression from one minute to 5 minutes based on the duration of the disease. They did not find any correlation between the length of balloon inflation and duration of pain relief, but observed that the pear shape of the balloon correlated with better pain outcomes, and this was a finding in our study too. The shape of the inflated balloon helps ascertain the degree of compression of the rootlets and hence has a direct relation to the extent of pain relief. It has been shown in the work of Sun et al (13) that if the balloon is positioned correctly in the Meckel's cave, it can assume certain shapes only. The average amount of dye required is 0.4 mL in place of a standard 0.75 to 1 mL in the Mullan and Lichtor study (14). We however used 1 mL as the standard volume. The maximum volume of the 4 Fr Fogarty catheter is 1 mL, so we used it to obtain the pear/dumbbell shape. In 0.4 mL volume, this shape could not be appreciated and the shape of the balloon was our only way to ascertain the correct placement of the needle as in our setup, we lack the manometer device to measure the compression pressure.

Kouzounias K et al (15) also found the pear shape to be the best marker of the outcome. Masseter muscle weakness post-PBC is a result of focal demyelination and resolves in around one month to 6 months (16). It was the most common side effect, present in 19/40 (47.5%) of our patients. It resolved completely by one month in all patients except one patient, whom the weakness persisted even at 6 months. This patient belonged to the 120 second compression group with a dumbbell balloon shape. Even though the V3 motor nerve lies outside the Meckel's cave and joins the V3 sensory division just outside the foramen ovale to form the mandibular nerve, entry of trocar and balloon inflation inadvertently presses on the motor fibers to cause motor weakness.

We found facial numbness in 16 (40%) of our patients post-PBC. Du et al (17) reported facial numbness in almost all their patients (97.1%) perhaps due to a longer compression time (mean time 6.2 minutes) and older age of their patients and proposed that post-operative hypoesthesia can be considered as a prognostic factor to good compression. This numbness may be well tolerated by most patients (18).

Limitations

Our study, however, had several limitations. We have followed up with our patients for a short period of only 6 months. We could not measure the intra-luminal compression pressure of the balloon as we did not have the manometer and we had to rely on the shape of the balloon for correct placement and effective compression. Our sample size was small by 2. Studies with larger sample sizes and longer duration of follow-up are needed to further validate the results of our study. Single trigeminal nerve branch-affected patients were excluded from the assessment. Despite all the limitations, the strength of our study is that it emphasizes the point that the duration of compression is not as important as the shape of the balloon. As percutaneous balloon compression treatment has comparable efficacy to microvascular decompression surgery, we recommend this treatment in elderly patients more than 65 years of age who are not fit for surgery with a long life expectancy as it is less invasive, cost-effective, requires a shorter hospital stay, and has a lower complication rate as well. As it is the most efficacious procedure among the percutaneous procedures, it may be tried in young adults, not willing to undergo surgery.

Conclusion

To conclude, our study points out that there is no difference in the pain relief obtained by the 2 different durations of compressions. Longer durations of compression, however, have more incidence of side effects without any significant benefit in pain relief.

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