ORIGINAL RESEARCH

Role of Platelet-rich Plasma in the Healing of Impacted Third Molar Socket: A Comparative Study on Central India Population

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Abstract

Aim: The aim of the study was to compare the healing and osseous regeneration of mandibular third molar extraction sockets with and without platelet-rich plasma (PRP) with the evaluation of clinical objectives such as pain, swelling, trismus, soft tissue healing, pocket depth distal to second molar and radiological evaluation of the bony density in the postextracted third molar socket.

Materials and methods: In this prospective study, 100 patients were selected by the random sampling method from the outpatient department of oral and maxillofacial surgery in the year 2016–2017. Patients were equally allocated into intervention (transalveolar extraction followed by PRP placement) and nonintervention (transalveolar extraction without PRP placement) group as group I and group II, respectively, and evaluation parameters were considered accordingly. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 (IBM, USA) statistical analysis software.

Results: The pain score of patients of group I (non-PRP) was found to be higher as compared to group II (with PRP). Mean trismus of patients of group II was found to be higher than that of group I at postoperative day 7, but this difference was not found to be statistically significant. Swelling at T-Sn (Tragus-Subnasale) and T-Pog (Tragus-Pogonion) was higher among patients of group I as compared to group II. Healing in group II was two to three times faster than group I. Healing among patients of group I and group II was found to be statistically significant. The mean pocket depth of patients of group I was found to be significantly higher than that of group II at follow-up of 1 and 2 months. The bone density of patients of group II was found to be significantly higher than that of group I at 3 months and 6 months follow-up.

Conclusion: The procedure of PRP preparation is simple and cost-effective, and can be prepared at the point of care. It had a significant impact on the postoperative healing of the third molar socket.

Clinical significance: The use of PRP application increases the bone density, healing process, and improvement in the pain and swelling, and there was a definite reduction in trismus and periodontal probing depth after the impacted mandibular wisdom teeth extraction.

Keywords: Platelet-rich plasma, Third molar, Tooth-impacted, Trismus, Wisdom teeth.

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Introduction

It is a well-known fact that there is a series of interactions initiated after the transalveolar extraction of the impacted third molar. Freeze-dried bone allograft in combination with PRP enhances bone healing and also provides a viable therapeutic alternative in surgery such as impaction of the third molar, ridge augmentation, sinus grafting, any osseous surgical defect, and implant. Platelet-rich plasma is an autologous concentrate of platelets in the plasma prepared by differential centrifugation having a platelet concentration above the baseline and enables the delivery of growth factors in surgical sites to enhance wound healing.[1,2] Growth factors act in an autocrine, paracrine, or endocrine manner and deposit in the extracellular matrix and are then released during the matrix degradation. They interact with surface receptors on the target cells and activate an intracellular signaling pathway that induces the transcription of the messenger RNA and proteins needed for its generative process.[3] The platelets play a central role in homeostasis and healing. It increases the radiographic maturation rate by 1.6–2.16 times.[4]

PRP was first introduced by Whitman et al. in 1997, and it became popular in the oral and maxillofacial surgery after a landmark article by Marx et al. in 1998 which stated that PRP is not osteoinductive, and the bone regeneration process starts with the release of platelet-derived growth factor (PDGF) and TGF-β through the degranulation of the platelet.[5–7]

PRP is usually prepared by centrifuging patients' blood. PRP when activated to form gel causes degranulation of α-granules in the platelets and releases enriched growth factors.[5]

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The extraction of mandibular wisdom tooth is one of the most common surgical procedures performed globally in oral and maxillofacial surgery. Pain, swelling, trismus, delayed healing, and food lodgment distal to second molar are the commonly associated with complications. We have, therefore, conducted the study to evaluate promising outcomes of PRP in the oral and maxillofacial surgery procedures.

The aim of the study was to evaluate the role of PRP in the healing of mandibular third molar extraction. The clinical evaluation objectives were pain, swelling, trismus, soft tissue healing, pocket depth distal to second molar and radiological evaluation of bony density in the postextracted third molar socket.

Materials and Methods

This prospective, split-mouth, comparative study was conducted after taking written informed consent and ethical clearance (251516/OMFS/EC/SPPGIDMS-2016) from the institutional ethical committee in the Outpatient Department of Oral and Maxillofacial Surgery, Sardar Patel Post Graduate Institute of Dental and Medical Sciences, Lucknow, Uttar Pradesh, India, for 1 year (2016–2017). Hundred patients were included by a simple randomization method to the study and divided into two groups, i.e., control group (nonintervention: group I) and (PRP: group II).

All procedures performed in the study were following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. An age group of 18–35, bilateral Class I, Position A or B, mesioangular impacted third molars, and required transalveolar extraction were included in the study. Patients with a history of smoking, alcohol drinking, uncontrolled diabetes mellitus, any immunologic diseases, ongoing chemotherapy, and postradiotherapy were excluded from the study. Each patient was assessed radiographically by orthopantomogram (OPG) [PaxI3D Smart machine (Vatech Co. Ltd., Hwaseong-si, Gyeonggi-do, Korea) 74 kVp/12 mA/10 seconds] and intraoral periapical radiograph (IOPA) [Kodak 2200 Intraoral X-ray machine at 60 kV, 7 mA, and 0.25 second]. An evaluation was done in terms of depth, pattern, and angulation of the impacted mandibular third molar (Pell and Gregory/Winter's classification). The case history was taken with a standard questionnaire. Routine blood investigations [(CBC (Including Platelets Count), RBS, Viral Markers (HIV, HCV, HbsAg)] were carried out for all patients.

Under all aseptic techniques, 5 mL of venous blood was collected from the antecubital region, stored in 4 mL CPDA (citrate phosphate dextrose adenine) anticoagulant solution tube, and placed in a centrifuge machine. The first centrifuge cycle was done at 2,000 rpm for 15 minutes, and the blood column was separated into a lower red blood cell and upper straw-colored plasma. This plasma contains a relatively low concentration of platelets called platelet-poor plasma (PPP) in the uppermost region, and a higher concentration of platelets and white blood cells in the boundary layer is often called "Buffy coat." With a micropipette, the PPP and the buffy coat layer including 1 mm below the boundary layer were collected in a sterile test tube and centrifuged at 3,000 rpm for 10 minutes. After the second centrifuge, the upper half was discarded and the lower half was used as PRP.

A surgical removal of the impacted mandibular third molar was done under local anesthesia (2% lignocaine with 1:20,0000 adrenaline) on both sides in the same sitting (split-mouth design) by the same surgeon every time, and one of the extraction sockets was randomly chosen for the PRP placement. PRP was taken into the sterile stainless steel bowl, and 0.5 mL of $CaCl_2$ ($CaCl_2$ directly activates platelets, which then facilitate clot formation independently and in cooperation with the coagulation pathway) was mixed to obtain the PRP gel, which was placed into the selected extraction socket and a primary closure was done with 3-0 black braided silk-interrupted suture. Pressure pack was given. The postoperative instructions were given along with medications [Tablet: diclofenac sodium (50 mg) and TDS and amoxicillin (500 mg) with clavulanic acid (125 mg) for 3 days]. In both the groups, the patients were recalled on the third day, seventh day, and fifteenth day postoperatively to assess pain, trismus, and soft tissue healing of the wound.

The clinical evaluation included the measurement of the probing depth distal to the second molar preoperatively as well as after the first month and second month postoperatively.

IOPA and OPG were advised preoperatively and postoperatively after the first month and the second month to assess the alveolar bone height distal to the second molar and sixth month postoperatively to assess the bone density.

Evaluation Criteria

- The pain was measured using the VAS scale on postoperative days 1, 3, and 7, respectively.
- The swelling was investigated by measuring the distance between Tragus-Pogonion (T-Pog) and Tragus-Subnasale (T-Sn) on the criteria given by Pöllmann[8] on postoperative days 1, 3 and 7, respectively.
- Trismus (assessment was based on the interincisal distance measured between the incisal edge of maxillary central incisor and the incisal edge of mandibular central incisor) measured on postoperative days 1, 3, and 7, respectively.
- Soft tissue healing was assessed based on the criteria given by Landry et al.[9] on postoperative days 1, 7, and 15, respectively.
- Healing Index 1: Very poor; Healing Index 2: Poor; Healing Index 3: Good; Healing Index 4: Very good; Healing Index 5: Excellent
- Probing depth was measured in millimeters by a periodontal probe (UNC-15).
- For the bone density measurements, all the OPG and IOPA images were scanned and digitalized. The mean gray level histogram values of the scanned IOPA images of the extraction sockets were obtained through Adobe Photoshop CS6–Grayscale histogram (SPPGIDMS, Lucknow, UP, India).

Statistical Analysis

Mean, standard deviation, Wilcoxon's signed rank test, Mann–Whitney *U* test, Student's *t*-test, Paired *t*-test, and Chi-square test were used. A multivariate analysis was done for all the variables. Results with $p < 0.05$ were considered statistically significant for the study. The statistical analysis was done using the SPSS (Statistical Package for Social Sciences), Version 15.0 (IBM, USA) statistical analysis software.

Results

A majority of the patients were aged up to 30 years (71.0%) and the rest were aged >30 years. The most common age group was 21–30 years (61.0%) followed by 31–40 years (25.0%), while the least common age group was 41–50 years (4.0%) followed by up to 20 years (10.0%); Of 100 patients, 68 (68.0%) were males and the rest 32 (32.0%) were females. The male-to-female ratio was 2.13:1. The pain score of patients of group I was found to be higher as compared to group II, and the difference in the pain score of patients of group I

and group II was found to be statistically significant ($p < 0.001$). In both the groups, a decline in the baseline pain was observed on postoperative day 3 and day 7, and a change in the baseline pain was found to be statistically significant ($p < 0.001$) in both the groups at day 3 and at day 7 as shown in Tables 1 and 2.

Swelling at T-Sn (Tragus-Subnasale) and T-Pog (Tragus-Pogonion) was higher among patients of group I as compared to group II on postoperative day 2 as shown in Table 3.

The difference in trismus among patients of group I and group II was not found to be statistically significant ($p = 0.304$). Mean trismus of patients of group II was found to be significantly higher ($p < 0.001$) than that of group I at postoperative day 1 and postoperative day 3. Mean trismus of patients of group II was found to be higher than that of group I at postoperative day 7, but this difference was not found to be statistically significant, and intragroup change in preoperative trismus at different postoperative periods was shown by Paired *t*-test in Tables 4 and 5.

The mean of soft-tissue healing at postoperative day 3, day 7, and day 15 of patients of group II was found to be higher than that of group I, and a difference in soft-tissue healing among patients of group I and group II was found to be statistically significant at day 7 and 15. An intragroup change in the baseline soft tissue healing at different periods showed statistically significant as shown in Tables 6 and 7.

The difference in preoperative pocket depth among patients of group I and group II was not found to be statistically significant, and the mean pocket depth of patients of group I was found to be significantly higher than that of group II at 1 month and 2

Table 1: Comparison of pain at different postoperative periods between both groups

	Group I (non-PRP)		*Group II (with PRP)*		*Mann–Whitney U test*	
	Mean	*SD*	*Mean*	*SD*	*z*	*p*
Postoperative day 1 (baseline)	4.14	0.88	2.78	0.69	10.048	<0.001
Postoperative day 3	2.46	0.77	2.00	1.63	7.015	<0.001
Postoperative day 7	1.29	0.77	0.46	0.66	7.188	<0.001

SD, standard deviation; *p*, probability value

Table 2: Intragroup change in baseline pain at different postoperative periods (Wilcoxon's signed rank test)

	Group I					*Group II*				
	Mean Ch	*SD*	*% Ch.*	*z*	*p*	*Mean Ch*	*SD*	*% Ch.*	*z*	*p*
Day 3	−1.68	0.65	−40.58	8.835	<0.001	−1.15	0.74	−41.37	8.211	<0.001
Day 7	−2.85	0.94	−68.84	8.823	<0.001	−2.32	0.76	−83.45	8.848	<0.001

SD, standard deviation; Ch, change; *p*, probability value

Table 3: Comparison of swelling at different postoperative periods in both groups

		Group I		*Group II*		*Student t test*	
Location		*Mean*	*SD*	*Mean*	*SD*	*t*	*p*
T-Sn (Tragus-Subnasale)	Day 2	12.19	3.32	10.92	3.28	2.721	0.007
	Day 7	1.49	0.70	0.50	0.66	10.270	<0.001
T-Pog (Tragus-Pogonion)	Day 2	11.84	3.17	10.56	3.21	2.835	0.005
	Day 7	1.60	1.16	0.46	1.31	6.540	<0.001

SD, standard deviation; *p*, probability value

Table 4: Comparison of trismus at different postoperative periods in both groups

	Group I		*Group II*		*Student t test*	
	Mean	*SD*	*Mean*	*SD*	*t*	*p*
Preoperatively	40.70	3.40	40.19	3.59	1.031	0.304
Postoperative day 1	26.66	3.43	31.32	2.16	−11.505	<0.001
Postoperative day 3	31.74	3.87	35.75	3.32	−7.864	<0.001
Postoperative day 7	38.66	3.11	39.03	3.71	−0.764	0.446

SD, standard deviation; *p*, probability value

Table 5: Intragroup change in the preoperative trismus at different postoperative periods

	Group I					*Group II*				
	Mean	*SD*	*% Ch.*	*t*	*p*	*Mean*	*SD*	*% Ch.*	*t*	*p*
Postoperative day 1	−14.04	2.20	−34.50	−63.906	<0.001	−8.87	1.75	−22.07	−50.675	<0.001
Postoperative day 3	−8.96	1.22	−22.01	−73.321	<0.001	−4.44	1.51	−11.05	−29.345	<0.001
Postoperative day 7	−2.04	0.91	−5.01	−22.437	<0.001	−1.16	0.93	−2.89	−12.487	<0.001

SD, standard deviation; Ch, change; *p*, probability value

Table 6: Comparison of the softtissue healing at different postoperative periods in both groups

	Group I		*Group II*		*Mann–Whitney U test*	
	Mean	*SD*	*Mean*	*SD*	*z*	*p*
Postoperative day 3 (baseline)	2.92	0.69	3.04	0.70	1.222	0.222
Postoperative day 7	3.64	0.61	3.86	0.71	2.471	0.013
Postoperative day 15	4.49	0.60	4.78	0.42	3.715	<0.001

SD, standard deviation; *p*, probability value

Table 7: Intragroup change in the baseline soft tissue healing at different time periods (Wilcoxon's Signed Rank Test)

	Group I					*Group II*				
	Mean	*SD*	*% Ch.*	*z*	*p*	*Mean*	*SD*	*% Ch.*	*z*	*p*
Day 7	0.72	0.73	24.66	9.919	<0.001	0.82	0.76	26.97	10.830	<0.001
Day 15	1.57	0.76	53.77	20.780	<0.001	1.74	0.75	57.24	23.294	<0.001

SD, standard deviation; Ch, change; *p*, probability value

Table 8: Comparison of pocket depth (mm) at preoperative and postoperative different periods between both groups

	Group I		*Group II*		*Student t test*	
	Mean	*SD*	*Mean*	*SD*	*t*	*p*
Preoperative	6.58	0.99	6.55	0.74	0.219	0.827
Postoperative 1 month	5.89	0.95	5.48	0.76	3.380	<0.001
Postoperative 2 month	5.34	0.89	4.59	0.80	6.225	<0.001

SD, standard deviation; *p*, probability value

Table 9: Intragroup change in preoperative pocket depth at different time periods (paired *t* test)

	Group I					*Group II*				
	Mean Ch	*SD*	*% Ch.*	*t*	*p*	*Mean Ch*	*SD*	*% Ch.*	*t*	*p*
Month1	−0.69	0.22	−10.49	−31.110	<0.001	−1.08	0.32	−16.41	−33.155	<0.001
Month2	−1.24	0.36	−18.88	−34.809	<0.001	−1.96	0.42	−29.95	−46.250	<0.001

SD, standard deviation; Ch, change; *p*, probability value

months, postoperatively. A decline in the preoperative pocket depth (baseline) was observed in both the groups at 1 month and 2 months postoperatively and was found to be statistically significant in both the groups as shown in Tables 8 and 9.

The bone density was measured using the grayscale value. As gray scale value increases, the density decreases. Bone density of patients of group I was found to be significantly higher than that of group II at 3 months postoperatively and 6 months postoperatively.

Discussion

This study examined the effect of PRP on postoperative pain, swelling, and trismus as well as healing and bone regeneration potential on third molar extraction sockets.[8]

In the present study, the pain was evaluated for both groups (with PRP and without PRP) on 1st, 3rd, and 7th postoperative day. The mean postoperative pain score (VAS) was lower for the PRP group at all time points when compared with the control, and this was statistically significant ($p > 0.001$) (Tables 1 and 2). This result was supported by Ogundipe et al.[10] and Das et al.,[11] and they indicate the reduction of pain in the test group. In contrary, Kaur et al.[12] stated in their study that the severity of pain was equal in both the groups.

Swelling is also a common complaint caused by edema associated with surgical trauma. In the present study, maximum swelling scores were observed on the second postoperative day in both the groups, but no significant differences were found between the groups. The swelling was measured preoperatively and on 2nd and 7th postoperative day using the suture material (3-0 mersilk) and Vernier caliper scale. This was statistically insignificant (Table 3). Thus, PRP did not have any statistical significance on swelling on the test side. Barona-Dorado[13] and Ogundipe[10] findings also supported our study and found that there was a significant difference between mean values percentage of swelling in the control and study group at 2nd and 7th postoperative day, suggesting that percentage of the facial swelling in the non-PRP group is higher than that of PRP group. Ogundipe et al.,[10] Nathani et al.,[14] and Del Fabbro et al.[15] also concluded that the postoperative swelling was lower at all time in PRP group when compared with the non-PRP group which was not significant ($p < 0.001$).

Third molar extraction results in trismus due to either of inflammation to the muscles of mastication or direct trauma to the temporomandibular joint (TMJ) and secondarily to pain and swelling. In the present study, trismus was evaluated for both groups (with PRP and without PRP) on 1st, 3rd, and 7th postoperative day using the Vernier caliper. The difference in preoperative trismus among patients of group I and group II was not found to be statistically significant ($p = 0.304$). The man trismus of patients of group II was found to be higher (better) than that of group I, but this difference was not found to be

statistically significant. In both the groups, trismus was found to be significantly lower than its baseline levels at day 1, day 3, and day 7 of the surgery (Tables 4 and 5). The result of the study of Ogundipe et al.[10] and Kumar et al.[16] was similar in terms of mouth opening.

Healing in surgical sites with PRP showed two to three times faster than that without PRP as it hastens wound maturity and epithelialization, and inhibit cytokine release, hence decreased scar formation. Platelet-derived growth factor and epidermal growth factor (EGF) were the main growth factors involved in fibroblast migration, proliferation, and collagen synthesis, and that was the reason behind the hastened soft-tissue wound healing.[17] In our study, the assessment of the soft-tissue healing was based on the criteria set by Landry et al.[9] The mean value of the healing assessment was done in the 3rd postoperative day and was found to be 2.92 in the control side and 3.04 in the test side ($p = 0.222$). On the 7th postoperative day, the mean was 3.64 for the control side and 3.86 for the test side ($p = 0.13$). One the 15th day postoperatively, it was seen that the mean for the test side was 4.78 while that for the control side was 4.49 ($p < 0.001$) (Tables 6 and 7). Though the test group exhibited better soft-tissue healing, it was statistically insignificant which was similar to the study conducted by Das et al.[11] This was probably due to the small sample size.

Dutta et al.[18] showed results similar to our study, although the result was statistically significant. The findings of Nathani et al.[14] and Yelamali et al.[19] showed significant differences in the mean scores of the soft-tissue healing in the PRP group as compared to the non-PRP group.

In the present study, the periodontal pocket depth was recorded 1 and 2 months preoperatively. It might be difficult to judge the probing depth appropriately when there is a close association between the second and third molars. The mean pocket depth distal to the second molar of patients of group I was found to be significantly higher than that of group II at 1 month and 2 months postoperatively. The difference in the preoperative pocket depth among patients of group I and group II was not found to be statistically significant ($p = 0.827$) (Tables 8 and 9). A similar result was found in the study of Sammartino et al.[20] and Kumar et al.[16]

Platelet-derived growth factor and TGF-β in PRP can influence periodontal regeneration, although it is not yet completely acknowledged. Some *in vitro* studies have suggested that PDGF acts principally on osteoblastic proliferation. This suggests that TGF-β could favor the differentiation of osteoblasts and cementoblasts and the production of fibronectin, which involved in the adhesion of fibroblasts and the angiogenic process. Fibrin content, in PRP gel, permits stabilized coagulation of the blood and advocates regeneration of the osseous defect.[21]

In our study, the bone density of patients of group II was found to be significantly higher than that of group I at 3 months and 6 months postoperatively. The bone density was measured using grayscale values. As the grayscale value increases, the density decreases. As grayscale value increases, density decreases as shown in Figure 1 to 143.99 showing less grayvalue histogram than as shown in Figure 2 which is 150.83 denoting more bone density on the right side where PRP was placed. Our study was supported by a study done by Das et al.[11] who assessed the gray-value scale using the Adobe Photoshop software.

There was a significant difference in the mean value of gray scale in the histogram at 3rd and 6th month postoperatively. However, our findings were supported by Mancuso et al.[22] who reported more dense radiographic bone healing. Anitua[23] also reported improved epithelization and bone density when PRP was placed in the extraction socket.

In contrast, Gurbuzer et al.[24] concluded that the application of PRP alone into the soft tissue-impacted mandibular third molar extraction sockets failed to increase the osteoblastic activity in postsurgical weeks 1 and 4 in comparison to non-PRP-treated sockets. They investigated the early effect of PRP on the osteoblastic activity during the healing process of soft tissue-impacted mandibular third molar extraction sockets.

PRP has beneficial effects on the improvement of reduction of pain, pocket depth distal to second molar, better soft-tissue healing, and bone density after mandibular third molar impaction surgery. In contrary, in our study, we did not find any statistically significant benefit of PRP on the prevention of reduction of swelling and trismus postoperatively. The present study was done on 100 patients with a follow-up of 6 months; further clinical trials with bigger sample size and longer duration of follow-up should be done to get more informative and conclusive results.

Conclusion

The procedure of PRP preparation is simple and cost-effective and can be prepared at the point of care. PRP and its application increase the bone density and healing process, and there was a definite reduction in trismus and periodontal probing depth. So, this study highlights the use of PRP and its inducing and accelerating effect on the soft- and hard-tissue regeneration. The limitation of this study was that a long-term follow-up is required along with a histological study of the bone for the assessment of the efficacy of PRP.

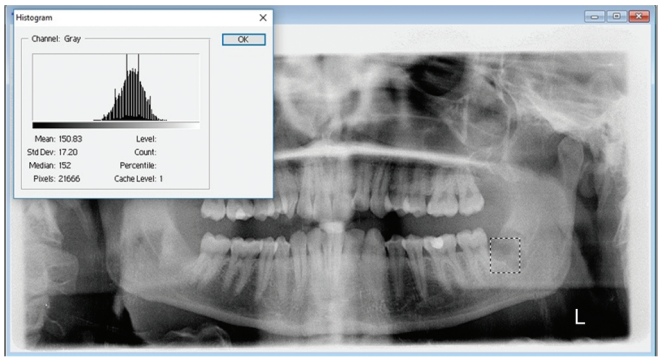

Fig. 1: Gray scale histogram of group II (6 months postoperative with PRP)

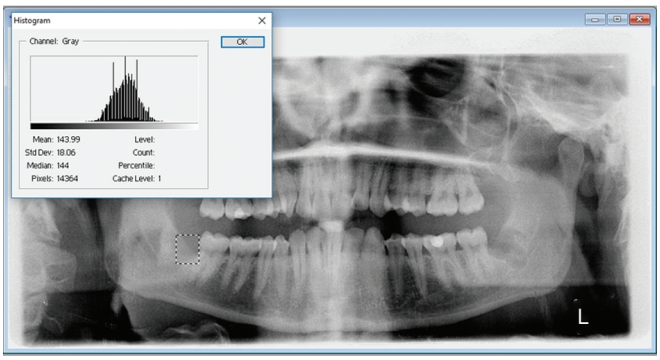

Fig. 2: Gray scale histogram of group I (6 months postoperative without PRP)

Patient Declaration of Consent

Informed written consent was obtained for participation in the study and publication of the data for research and educational purposes. Participants were given the freedom to withdraw from the trial at any point. Regular care was ensured to the participant in the case of withdrawal.

Data Availability Statement

The data set used in the current study is available on request from the data set that can be made available after the embargo period due to commercial restrictions.

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