Section : Research Paper
ISSN 2063-5346

Intranasal Photo-biomodulation: A novel aid for behavior management in pediatric dentistry?

[1]Dr. Tanaya Kulkarni, [2]Dr. Anil Patil, [3]Prof. Chandrashekar Yavagal, [4]Dr. Sachin B Mangalekar, [5]Dr. Sandhyarani B, [6]Dr. Sujatha Paranna

[1]Postgraduate student, [2]Professor and Head of the Department, Department of Pediatric and Preventive Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Sangli, Maharashtra, India
[3]Director and Head of Laser Dentistry and Photomedicine, MMNGH Institute of Dental Sciences, Belgaum, Karnataka, India
[4]Professor and Head of the Department, Department of Periodontology, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Sangli, Maharashtra, India
[5,6]Associate Professor, Department of Pediatric and Preventive Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Sangli, Maharashtra, India

Corresponding author: Dr. Tanaya Kulkarni, Postgraduate student, Department of Pediatric and Preventive Dentistry, Bharati Vidyapeeth (Deemed to be University) Dental College and Hospital, Sangli, Maharashtra, India **Email:** tanukul09@gmail.com

ABSTRACT

Background- Intranasal photobiomodulation is an innovative technology having numerous applications in medicine. This technique has been identified as having therapeutic applications in treating many symptoms related to central nervous system disorders. It has also been used for treating clinical anxiety and depression in adults.

Aim- To observe the effect of intranasal photobiomodulation (IPBM) on anxiety levels of pediatric dental patients.

Materials and methodology- Thirty children were selected for the study. They were divided equally into two groups [Group 1: (n=15) Placebo group, Group 2: (n=15) Intranasal PBM group]. The children received dental treatment according to a pre-planned schedule for standardization and received IPBM (Group 1) or placebo (Group 2) according to their allotted treatment group. The baseline, 4 week, 8 week and 3 month readings of Raghavendra, Madhuri, and Sujata Pictorial Scale (RMS-PS) readings, Wright's modification of Frankl's behavior rating scale (FBRS), Oxygen saturation and pulse rate were obtained.

Results- There was a significant reduction in RMS-PS score, Wright's modification of FBRS, and pulse rate within group 1 and group 2 from initial assessment to last follow-up period. The overall change in FBRS score within group 2 from initial assessment to last follow-up showed significant improvement. Intergroup comparison showed that difference RMS-PS score between two groups was significant after 4 weeks with group 2 showing significantly lesser score.

Conclusion- The present study displays positive results for use of IPBM in reducing anxiety and modulating the behavior of pediatric dental patients. Further long term clinical studies are required to explore the applications of IPBM in detail.

Keywords: Dental anxiety, Pediatric dental patient, photobiomodulation.

INTRODUCTION

Photobiomodulation (PBM) is the application of low levels of red or near-infrared (NIR) light to either stimulate or inhibit biological cells and tissues involving photochemical mechanisms.[1] It was first discovered by Endre Mesterin1967, when he observed that low powered laser treatment promoted hair regrowth in rats.[2] This observation persuaded many researchers to use low level lasers and light emitting diodes (LEDs) for therapeutic purposes. It was collectively termed as 'low level light therapy' (LLLT). In 2015, a global initiative was taken by researchers in this field to standardize the term to 'photobiomodulation'.

Photobiomodulation therapy (PBMT) is widely used to treat a variety of medical conditions such as wound healing, diabetic ulcers, blood disorders, as well as tissue repair and regeneration. Moreover, PBMT has attracted increasing interest for many applications to the brain, ranging from neurotrauma, neurodegeneration, and neuropsychiatric disorders to improve brain functions in healthy individuals.[3]

Transcranial PBM (tPBM), targets delivery of light energy to the brain and is associated with increased cerebral blood flow, oxygenation, adenosine triphophosphate (ATP) production, and mitochondrial activity.[4]Also,tPBM has been recognized as a treatment modality for neurological and neurodegenerative conditions.[5]

The broad clinical impact of PBMT is because of its ability to stimulate healing in both soft tissues such as mucosa and skin as well as mineralized tissues such as bone and teeth. Hence, this treatment modality is widely used in the field of Dentistry. In the recent years, use of lasers for endodontic therapy, soft tissue surgery, etc has increased in pediatric dental patients. A major limitation with these groups of patients is related to the anxiety and fear of dentistry, especially with special needs. Hence, novel non-invasive technologies that can alleviate pain and anxiety and facilitate improved relationship between dentist and the patient, should be explored.[6]

MATERIALS AND METHODS

Ethical approval: The institutional ethics committee of Bharati Vidyapeeth (Deemed to be University) medical college and hospital, Sangli (BV(DU)MC & H/Sangli/ IEC/D-77-22) has approved the present study.

Thirty children in the age group of 5 to 10 years who reported to the department of Pediatric and Preventive dentistry for their first dental visit were selected for the study. Children having history of systemic or psychiatric disorder and children having definitely negative Frankl's behavior scale rating were excluded from the study.

Baseline RMS-PS readings (for subjective anxiety assessment), Wright's modification of FBRS readings (for objective anxiety assessment), oxygen saturation and pulse rate of all the test subjects were recorded before any treatment.[7]The children were allotted into two groups [Group 1: (n=15) Placebo group, Group 2: (n=15) Intranasal PBM group] by a different evaluator who did not participate in the treatment or in the statistical analysis of the results. Simple random sampling was done by coin toss method.

The intranasal PBM group received 5-minute procedure administrations across a four-week period: two procedures per week. The placebo group (without activating the intranasal PBM device) received 5-minuteprocedure administrations across a four-week period: two procedures per week.[8]Bio Quant LED Intranasal PBM device was used for the study. Parameters were as follows- 660nm, five minutes, 5mW, continuous mode (Program P1)

RMS-PS readings, Wright's modification of FBRS, Oxygen saturation and pulse rate of all the test subjects will be recorded at end-point (4 weeks of LLLT treatment), 8 weeks and after 3 months of treatment. [8]

The following dental treatment protocol was followed for all the subjects in both groups-

1. **First week-**

a. First visit- Oral health check- up + IPBM

↓ 3 days

b. Second visit- only IPBM

↓ 3 days

2. **Second week-**

a. Third visit-only IPBM

↓ 3 days

b. Fourth visit- Fluoride application + IPBM

↓ 3 days

3. **Third week-**

a. Fifth visit- only IPBM

↓ 3 days

b. Sixth visit- Restoration + IPBM

↓ 3 days

4. **Fourth week-**

a. Seventh visit- only IPBM

↓ 3 days

b. Eighth visit- Extraction under LA + IPBM

Where, IPBM= Intranasal Photobiomodulation

LA= Local anaesthesia

RESULT

Statistical analyses were performed using the SPSS version 23 software. Analysis of variance (ANOVA) followed by the Tukey's post hoc test was applied to compare the four groups during the four visits. Intragroup comparison was done using repeated measure

ANOVA test for pulse rate, oxygen saturation and RMS-PS readings and that for Frankl's behavior rating scale was done using Friedman test. Comparison of RMS-PS score and pulse rate between two groups was done using Independent t test and that for Frankl's behavior rating scale was done using Mann whitney test.
There was a significant reduction in RMS-PS score within group 1 and group 2 from initial assessment to last follow-up period (table 1). There was a significant reduction in pulse rate within group 1 and group 2 from initial assessment to last follow-up period.
The overall change in FBRS score within group 1from initial assessment to last follow-up showed non-significant difference (table 2).The overall change in FBRS score within group 2 from initial assessment to last follow-up showed significant improvement.
Intergroup comparison showed that difference RMS-PS score between two groups (table 4) was significant after 4 weeks with group 2 showing significantly lesser score.
There was no difference in FBRS score between two groups before the treatment and 4weeks, 8weeks and 3 months after the treatment (table 5).

Table 1: Comparison of change in RMS-PS score and pulse rate within each group

Variable	Group	Initial	4 week	8 week	3 months	p value
RMS-PS	1	4.00 ± 0.85	3.73 ± 0.59	3.27 ± 0.70	2.67 ± 0.72	0.001*
	2	3.67 ± 0.98	3.13 ± 0.92	2.87 ± 0.92	2.40 ± 0.83	0.001*
Pulse rate	1	99.47 ± 8.50	99.87 ± 8.63	99.07 ± 9.10	97.07 ± 8.71	0.001*
	2	101.07 ± 9.00	99.20 ± 8.38	99.87 ± 8.23	98.53 ± 8.47	0.015*

Repeated measure ANOVA test; * indicates significant difference at $p \leq 0.05$

Table 2: Comparison of change in Frankl's behavior rating scale score within each group

Groups	FBRS score	Initial	4 week	8 week	3 months	p value
1	-	5 (33.3)	5 (33.3)	6 (40)	0	0.065
	+	5 (33.3)	7 (46.7)	9 (60)	12 (80)	
	++	5 (33.3)	3 (20)	0	3 (20)	
2	-	5 (33.3)	6 (40)	3 (20)	0	0.003*
	+	5 (33.3)	7 (46.7)	11 (73.3)	9 (60)	
	++	5 (33.3)	2 (13.3)	1 (6.7)	6 (40)	

Friedman test; * indicates significant difference at $p \leq 0.05$

Table 3: Pairwise comparison of RMS-PS score, FBRS score and pulse rate within each group

Pair	RMS-PS		Pulse rate		FBRS	
	1	2	1	2	1	2
Initial vs 4 week	0.983	0.089	1.000	0.473	0.480	0.1057
Initial vs 8 weeks	0.063	0.001*	1.000	0.865	0.130	0.480
Initial vs 3 months	0.001*	0.010*	0.001*	0.039*	0.405	0.058
4 week vs 8 week	0.021*	0.623	0.986	1.000	0.206	0.414
4 week vs 3 months	0.001*	0.001*	0.001*	1.000	0.166	0.002*
8 week vs 3 months	0.003*	0.021*	0.017*	0.115	0.003*	0.005*

Adjustments for multiple comparisons: Bonferroni test; Wilcoxon signed rank test; * indicates significant difference at $p \leq 0.05$

ISSN 2063-5346

Table 4: Comparison of RMS-PS score and pulse rate between two groups

Variable		Initial	4 week	8 week	3 months
RMS-PS	**Gr 1**	4.00 ± 0.85	3.73 ± 0.59	3.27 ± 0.70	2.67 ± 0.72
	Gr 2	3.67 ± 0.98	3.13 ± 0.92	2.87 ± 0.92	2.40 ± 0.83
	p value	0.326	0.042*	0.190	0.356
Pulse rate	**Gr 1**	99.47 ± 8.50	99.87 ± 8.63	99.07 ± 9.10	97.07 ± 8.71
	Gr 2	101.07 ± 9.00	99.20 ± 8.38	99.87 ± 8.23	98.53 ± 8.47
	p value	0.621	0.832	0.802	0.644

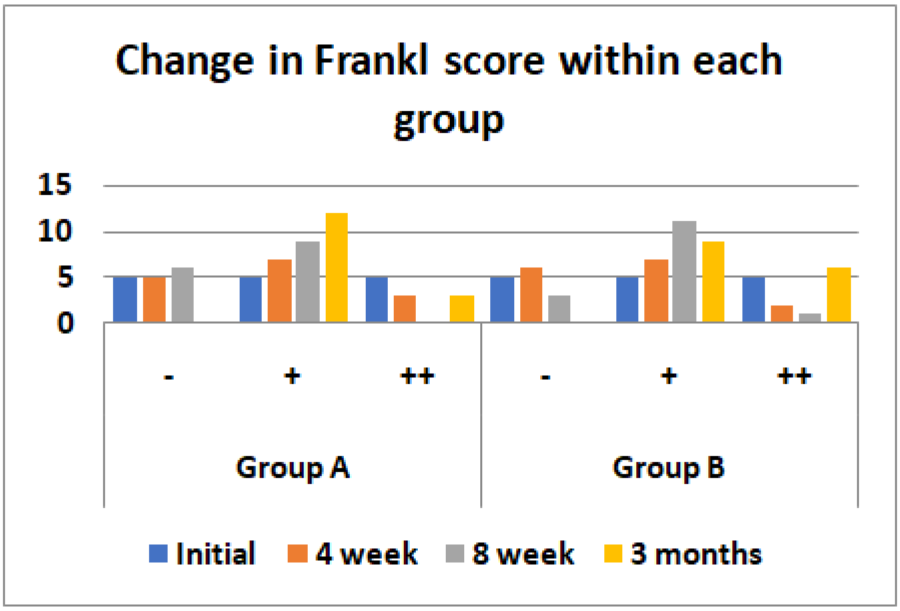
Independent t test; * indicates significant difference at $p \leq 0.05$

Table 5: Comparison of FBRS score between two groups

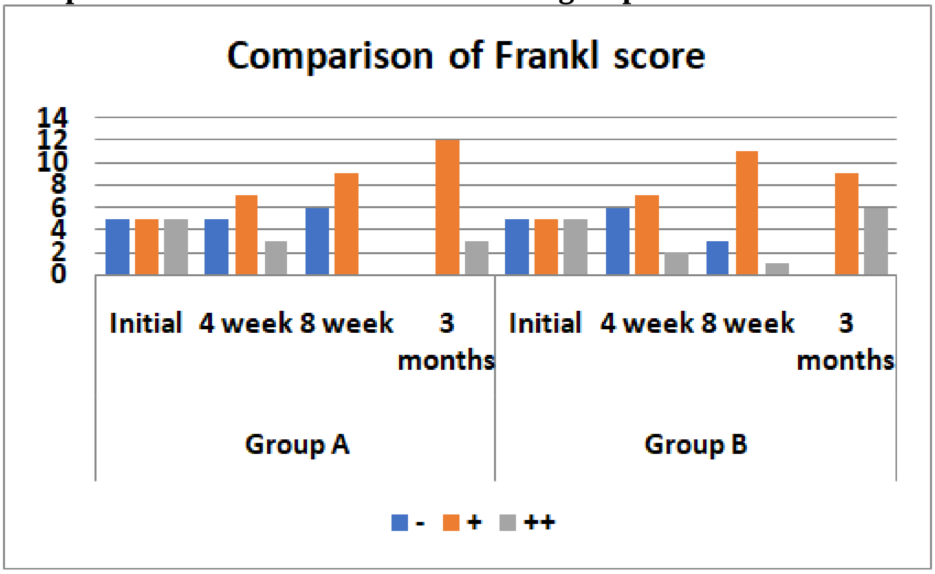
Interval	**Group 1**			**Group 2**			**p value**
	-	+	++	-	+	++	
Initial	5 (33.3)	5 (33.3)	5 (33.3)	5 (33.3)	5 (33.3)	5 (33.3)	1.00
4 week	5 (33.3)	7 (46.7)	3 (20)	6 (40)	7 (46.7)	2 (13.3)	0.653
8 week	6 (40)	9 (60)	0	3 (20)	11 (73.3)	1 (6.7)	0.267
3 months	0	12 (80)	3 (20)	0	9 (60)	6 (40)	0.367

Mann whitney test

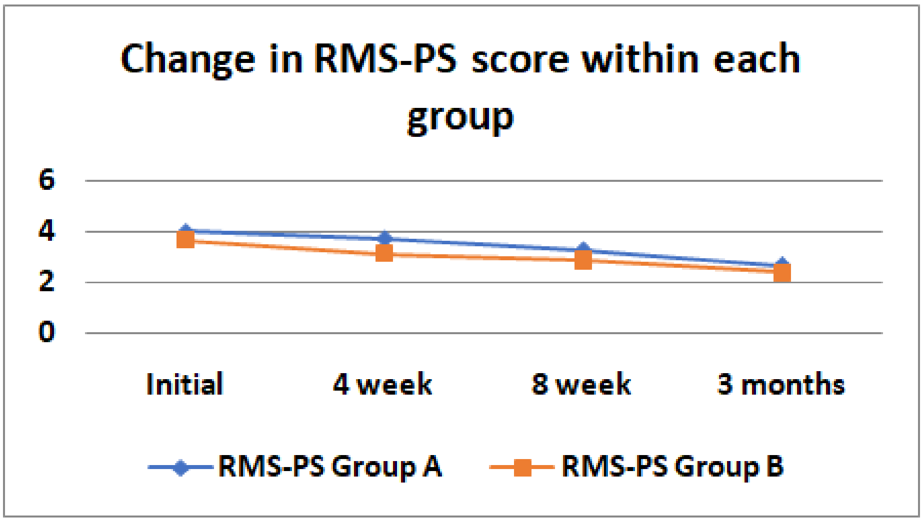
Graph 1: Comparison of change in Frankl's behavior rating scale score within each group



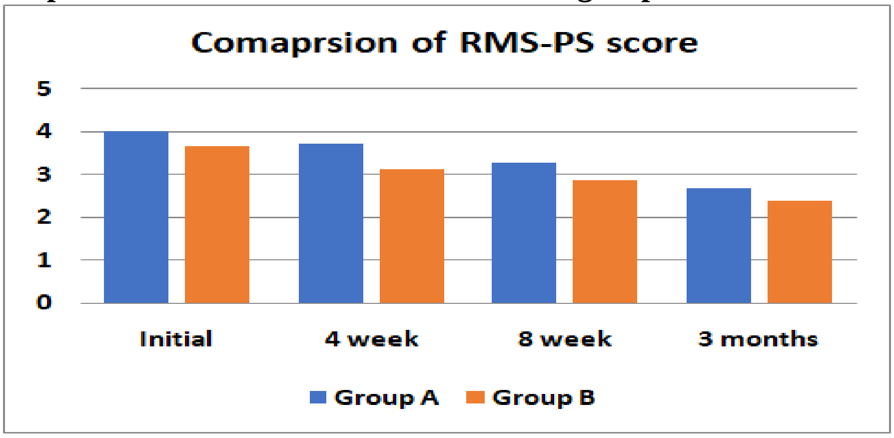
Graph 2: Comparison of FBRS score between two groups



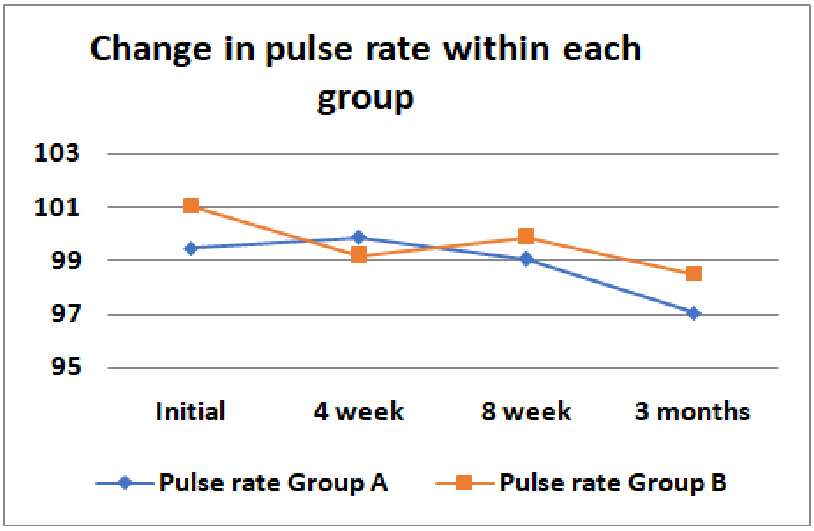
Graph 3: Comparison of change in RMS-PS score within each group



Graph 4: Comparison of RMS-PS score between two groups



Graph 5: Comparison of change in pulse rate within each group



Graph 6: Comparison of pulse rate between two groups

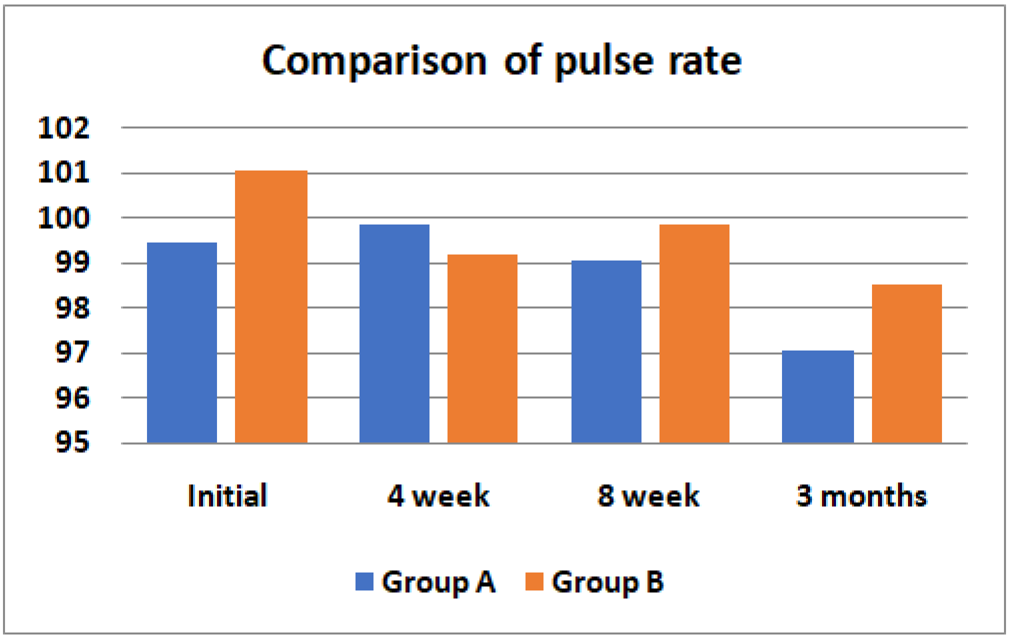


Figure 1. Armamentarium

Section : Research Paper
ISSN 2063-5346

Figure 2. A. Recording baseline pulse rate and oxygen saturation of the child. B. Recording RMS-PS reading of the child. C. Administration of intranasal photobiomodulation to the child.

A B C

DISCUSSION

Children in the age group of 5–10 years were selected in the present study as children may have difficult behavior in this age group and are tougher to manage. The RMS-PS is a newer anxiety assessment scale. The validity of the RMS-PS in the assessment of a child's dental anxiety in the dental setting was supported by its strong correlation with the Venham picture test scores in the study performed by Khandelwal et al in 2019.[7]It offers a simple, quick, efficient evaluation of anxiety for a pediatric dental patient. A pulse oximeter is a universally accepted method for measuring the physiological changes because, it gives continuous percentage measurements of the patient's arterial haemoglobin oxygenation and the pulse rate. Hence, RMS-PS, FBRS, pulse rate, and oxygen saturation were used for the assessment of anxiety in this study.

The observations from this study indicated that there was a significant reduction in RMS-PS score and pulse rate within both the groups from initial assessment to last follow-up period. This indicated a positive outcome of the use of IPBM in the physiological as well as subjective anxiety parameters in the test subjects. The overall change in Frankl's behavior score within group 1 from initial assessment to last follow-up showed a non-significant difference (0.065). Whereas, the overall change in FBRS within group 2 from initial assessment to last follow-up showed significant improvement. There was no statistically significant difference in FBRS between two groups before the treatment and 4weeks, 8weeks and 3 months after the treatment. However, the intergroup comparison showed that difference RMS-PS score between two groups was significant after 4 weeks with group 2 showing significantly lesser score.

PBMT can achieve a therapeutic effect by using nonionizing light, including lasers, light-emitting diodes or broadband light in the visible red (600-700 nm) and near-infrared (780-1100 nm) spectra.[9] It has been demonstrated that, PBMT promotes cell and neuronal repair and brain network rearrangement in some neurologic disorders. PBMT can fast track wound-healing as mitochondria respond to light in the red and near infrared (NIR) spectra.[9] Reports are emerging that PBMT can significantly increase the secretion of brain-derived neurotrophic factor (BDNF) which is associated with dendritic sprouting and brain connectivity. Hence, nerve cells may seem to thrive and grown in the presence of low energy light.[10]

Sufficient evidence exists in literature on the ability of LLLT to penetrate the skull in diagnostic and therapeutic applications. Low energy laser systems apply the quantum optical

induced transparency (QIT)-effect. This effect controls optical properties of dense media and enhances transparency contrast by a factor of five. Thus, the skull or spine can be penetrated even with moderate intensity light. By virtue of this effect, the radiation can reach deep tissue layers in muscles, connective tissue and bone, enabling non-invasive transcranial treatment.[10]
Photo biomodulation using LLLT has been demonstrated to be a safe and effective technique in improving the mood, memory and attention in patients with chronic traumatic brain injury.[10]
The results presented in the study performed by C Machado et al showed clinical improvement of the key evaluable behaviours which are characteristic of autism disorder in children and adolescents. The improvement in symptoms was seen for up to 6 months after transcranial LLLT treatment completion. This might have been observed because, LLLT progressively rearranges anatomical, functional and effective connectivity, modifying those neuronal networks which are related to the complex symptoms in autistics.[8]
The ease-of-use of tPBM, along with its seemingly advantageous tolerability profile, makes it an appealing, non-invasive brain stimulation (NIBS) method[11], especially in children.
According to Hamblin, red light has a short wavelength and high frequency to penetrate into the tissue to elicit changes in physiology without causing harmful effects. The olfactory bulb is a direct line to the brain, present superior to the nasal cavity and inferior to the frontal lobe. Photons from the PBMT can directly reach the fibers of the olfactory nerve and the prefrontal cortex, which is connected to the thalamus and hypothalamus. Therefore, the effects on the brain are mediated by circulating mitochondria from direct irradiation of blood within the nasal capillaries. Moreover, light may reach sensory terminations of the olfactory nerve and indirectly affect the limbic system as the light cannot penetrate deeper at the low power and wavelength used. At low level, i.e., less energy/time of fluency, there is an increase in membrane activity, while the effects decrease at a higher fluence.[12] The limbic system controls many functions such as, emotion, behavior, motivation, long-term memory and olfaction. For this reason, it is also known as the emotional nervous system. Hence, it is suggested that, IPBM stimulates the positive neural circuits of parts of the limbic system and brings about a general improvement in the mood of that individual.
According to Alba Guti´errez-Men´endez, PBM achieves enough brain penetration to produce beneficial effects in **healthy subjects and subjects with multiple pathologies**. **LED devices** have reported **higher safety and versatility than lasers**, despite their lower penetration, and pulsed emission is more effective than continuous emission. Likewise, wavelengths of 810 nm and 1064 nm achieve the best results in depression treatment and cognitive enhancement. [13]
Thus, it is important for the treating doctor to advise treatment with PBM by properly specifying the doses, as high doses may cause adverse effects, but within lower parameters may lead to great benefit.

CONCLUSION

Intranasal photobiomodulation is an under-explored non-invasive technology having vast applications in medicine. The present study displays encouraging results for use of IPBM in reducing anxiety and modulating the behavior of pediatric dental patients. More clinical trials and case reports having larger sample size and longer follow up period will be necessary in the future, to further explore the efficacy of IPBM in pediatric dentistry for behavior management.

CONFLICT OF INTEREST

None

SOURCE OF FUNDING
Nil
All participants provided informed consent and the consent was in written format.

REFERENCES
1. Hamblin M. R. Photobiomodulation or low-level laser therapy. Journal ofBiophotonics.2016;9: 1122–1124.
2. Mester E., Ludany G., Sellyei M.,Szende B. On the biologic effect of laser rays. Bulletin de la Societe internatioanale de chirurgie. 1968;27: 68–73.
3. Salehpour F, Gholipour-Khalili S, Farajdokht F, Kamari F, Walski T, Hamblin M.R. Therapeutic potential of intranasal photobiomodulation therapy for neurological and neuropsychiatric disorders: a narrative review. Rev Neuroscience. 2020; 31(3): 269–286
4. Hamblin M. R. Shining light on the head: Photobiomodulation for brain disorders. BBA Clinical. 2016;6: 113–124.
5. Naeser M. A., Saltmarche A., Krengel, M. H., Hamblin M. R., Knight J. A. Improved cognitive function after transcranial, light emitting diode treatments in chronic, traumatic brain injury: two case reports. Photomedicine and Laser Surgery. 2016;29: 351–358.
6. Fornaini C, Praveen Arany, Jean-Paul Rocca, Elisabetta Merigo. Photobiomodulation in Pediatric Dentistry: A Current State-of-the-Art. Photobiomodulation, Photomedicine, and Laser Surgery. 2019;37(12):798–813.
7. Khandelwal M, Shetty R, Rath S. Effectiveness of Distraction Techniques in Managing Pediatric Dental Patients International Journal of Clinical Pediatric Dentistry. 2019; 12 (1): 19-24.
8. Machado C, Machado Y, Chinchilla M, Machado Y. *Follow-Up Assessment Of Autistic Children 6 Months After Finishing Low Lever Laser Therapy*. The Internet Journal of Neurology. 2019;21(1):1-8.
9. deFreitas L. F., Hamblin M.R. Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. Institute of Electrical and Electronics Engineering Journal of selected topics in Quantum Electronics.2016;22(3):1-37.
10. Hamblin, M. R. Photobiomodulation for traumatic brain injury and stroke. Journal of Neuroscience Research. 2018; 96: 731-43.
11. Zomorrodi R, Loheswaran G, Pushparaj A, Lim L. Pulsed Near Infrared transcranial and Intranasal photobiomodulation Significantly Modulates Neural oscillations: a pilot exploratory study. Scientific reports.2019; 9:6309.
12. Hamper M, Cassano P, Lombard J. Treatment of Kleine-Levin Syndrome With Intranasal Photobiomodulation and Methylene Blue. Cureus. 2021;13(10):1-6.
13. Guti´errez-Men´endez A, Marcos-Nistal M, M´endez M, Arias J. L. Photobiomodulation as a promising new tool in the management of psychological disorders: A systematic review. Neuroscience and Bio-behavioral Reviews. 2020;119:242–254.