



ORIGINAL ARTICLE

A survey on awareness and knowledge among dentist practicing regenerative endodontics towards current regenerative endodontic protocols and the scaffolds used in regenerative dentistry



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Received 12 December 2022; revised 2 May 2023; accepted 14 May 2023

Available online 20 May 2023

KEYWORDS

American Academy of Endodontics;
Plasma Rich Fibrin;
Regenerative Endodontics;
Regenerative Endodontic Protocols;
Stem cells of Apical Papillae

Abstract There are many inconsistencies in the protocols followed for Regenerative Endodontic Procedures (REP's). This study was formulated with an aim to conduct a survey among Pediatric Dentists, Endodontists and General Practitioners treating Necrotic young permanent teeth to examine their awareness and Knowledge on Current Regenerative Endodontic Protocols and Scaffolds used in regenerative dentistry.

Methods: A Cross-Sectional Survey was carried out amongst 100 Pediatric dentists, 100 Endodontists and 100 General Practitioners. It was web-based survey and the questionnaire was formulated and all the items in the questionnaire were tested for reliability and validity before circulation of the questionnaire for the purpose of the study.

Results: The results of the study indicated that all the three groups were unaware that failure of cases should be reported to AEE (American Academy of Endodontics) REP Database and only 20.2, 20.1 and 0.3 % of Pediatric dentists, Endodontists and General Dentists preferred Regenerative Dentistry as a clinical protocol for REP. With respect to knowledge regarding irrigation and disinfection procedures all three groups were lacking in the knowledge regarding intracanal medicament for disinfection and the irrigation solutions.

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Peer review under responsibility of King Saud University. Production and hosting by Elsevier.



Conclusion: There is a lack of homogeneity in protocols followed for REP among those practicing Regenerative Endodontics as a protocol. Since it's an evolving science there is a need to bring about a uniformity in practices to increase the evidences to support the causal effect relation of regenerative endodontics.

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1. Introduction

Regenerative endodontics has caught the attention of clinicians and researchers alike as a new emerging treatment protocol for necrotic immature permanent teeth (Shah et al., 2016). Regenerative endodontics uses the concept of tissue engineering to restore the root canals to a healthy state, allowing for continued development of the root and surrounding tissue. (Pulyodan et al., 2020).

There is a paradigm shift in treatment of immature necrotic teeth with regenerative endodontic protocol replacing traditional apexification procedures. Introduced by Nygard Ostby in 1960 (Thomson and Kahler, 2010), the rationale behind this procedure is that it has now been shown that the tissue in periapical region of nonvital teeth has potential to regenerate, contributing to qualitative and quantitative increase in root dimensions, thus fracture of teeth associated with traditional procedures can be prevented. (Namour and Theys, 2014).

The three components that determine the success of this procedure are stem cells that are capable of hard tissue formation, signalling molecules for cellular stimulation, proliferation, and differentiation and finally, a 3-dimensional physical scaffold that can fortify cell growth and differentiation. (Sharma and Mittal, 2016).

Since the cases are diverse in etiology as well as in treatment protocols followed in the published REP's cases it is difficult to predict which of these protocols have led to a successful outcome. AAE (American Academy of Endodontics) has recently come out with the revised regenerative endodontic treatment protocol in 2016 based on the best currently available evidences. (Galler et al., 2015) Despite the lack of higher levels of evidence such as randomized controlled trials and the little information available regarding the clinical protocols in failed REP cases the use of guidelines such as the "AAE Clinical Considerations for a Regenerative Procedure" might help maximize successful outcomes. (American Association of Endodontists, 2017).

Epelman et al. survey on the attitude of the dental practitioners towards this new procedure for treatment of young permanent tooth. (Epelman et al., 2009) Various other surveys were also conducted across the globe to understand the attitude of dental practitioners towards regenerative endodontics and most of them focus upon stem cell research (Shah et al., 2016). Scaffolds are an indispensable part of regenerative endodontics, as they provide structural support for cells to proliferate and differentiate. Though they are available in synthetic and natural forms there is limited usage and research of these biomaterials. (Sharma and Mittal, 2016).

There are speculations of unparalleled advances awaiting us in the field of regenerative endodontics in the coming decades. However, there is a need for translation of this novel therapy

into day today practice. For the same to occur, detailed knowledge of current regenerative endodontic protocols, adequate skill development and training of dental professionals is a must. (Shah et al., 2016).

Hence, it is important to understand the level of knowledge and attitude among the Endodontist, Pedodontist and General Practitioners treating young permanent teeth towards the current clinical regenerative endodontic protocols and the scaffolds used in regenerative dentistry. This will give us an insight into how and what clinical protocols and scaffolds are used in clinical practice in treating an immature young permanent tooth, which would further help us in increasing the scope of adequate skill development and training of dental professionals in the field of regenerative endodontics to increase the number of successful outcomes in treating an immature young permanent teeth. This would also help us in gathering the information and thus using it for further research in this area of innovation in regenerative endodontics.

2. Materials and methods

A Cross Sectional questionnaire based survey was carried out among Pedodontists, Endodontists and General Practitioners. The questionnaire was sent through electronic media. Ethical approval was obtained from the Institutional Ethical Board from Bapuji Dental College and Hospital Davangere (Ref. No. BDC/Exam/290/2018–19). Informed Consent was taken from the participants and the data procured was kept confidential. The questionnaire excluding the demographic details had a total of 22 questions (3 questions were formulated to assess the knowledge regarding Regenerative Endodontics, 10 questions were regarding current Regenerative Endodontic protocols and 9 questions regarding the Scaffold systems used in regenerative endodontics) which were developed after reviewing the existing literature. The questionnaire was tested for reliability and validity. The Cronbach's Alpha for the questionnaire ranged from 0.7 to 0.83. After face validity the questions were distributed to subject experts for content validity. Waltz and Basel formula (Yaghmaie, 2003) for used where in the professionals ranked the items of the questionnaire as compatible or full compatible for each criterion (relevancy, clarity, and simplicity). The average value of three criteria was used as the total CVI (Content Validity Index) for each item. Minimal required amount of CVI for each item was 0.79. The items which had less than this was modified or excluded from the study. The total CVI score for the questionnaire as a whole was 93.32%.

Survey proforma contains demographic details of the participants along with questionnaires about the knowledge and practice related to current regenerative protocols and the scaffold

Table 1 Descriptive statistics regarding Knowledge of Regenerative Endodontics.

	Pedodontist	Endodontist	General Practitioners	P value
Percentage of cases in your practice involves the treatment of immature young permanent teeth				0.0001*
< 10%	28.1%	48.7%	25.6%	
11–25%	70.8%	23.5%	29.8%	
26–50%	0.54%	0.83%	10.3%	
more than 50%	0.39%	0.1%	7.5%	
What is the source of your clinical protocol for Regenerative endodontic procedures (REPs)? (could choose more than one option)				0.0001*
Self study /literature search				
	73.7	82.6	30.5	
CDE programs	30.5	40.7	10.2	
Protocols taught in residency	39	38.6	0.03	
Others-specify	5.1	0.3	0.05	
Preferred Clinical Protocol				0.0001*
Calcium hydroxide apexification	15.2	10.4	47.6	
MTA apical plug followed by filling of an obturation material	64.6	69.5	51.8	
Regenerative endodontics	20.2	20.1	0.3	
Reporting of REP success/failures				0.0001*
American academy of endodontics	39.3	41.7	28.4	
European society of endodontology	49.4	52.5	25.7	
Indian endodontic society	10.6	10	15	
Other	0.7	0.8	0.2	

P value < 0.0001* is considered highly significant.

folds used in regenerative endodontic treatment of young permanent teeth.

The sample size was calculated with the following assumptions of type 1 error of 5%, desired power of 80% and moderate differences in between the groups $d = 0.35$. The sample size was calculated as 300 with 20% non-response rate ie 100 for each group.

The questionnaire was distributed among 100 Pedodontists, 100 Endodontists and 100 General Practitioners who were treating necrotic immature young permanent tooth out of which we got 86 responses atleast from each group separately.

Scoring Criteria:

- The questionnaire data will be analyzed by a number of responses as a percentage of total responses to gain insight into the majority opinions of the participants for each question.
- Each question will be individually scored and the participants overall knowledge was categorized using modified Blooms criteria ie a score more than 80% was considered good, 50–79% was considered as moderate in the present study it was considered as adequate and a score of < 50% was considered as poor or inadequate. (Alzahrani et al., 2022)
- The questions after individual scoring will be grouped into three; Group 1: knowledge regarding Regenerative Endodontics; Group 2: containing questions regarding the current regenerative endodontic procedures and Group 3: containing the scaffold systems used in regenerative endodontics respectively.

3. Results

• Profile of Participants

All the participants were in the age group of 25–35 years. (55%) of the respondents were females and (40%) were males. Chi-Square inferential statistical analysis was done to understand the difference of opinions between groups.

• Knowledge And Opinion of Regenerative Endodontics among Pedodontists, Endodontists and General Practitioners

On statistical analysis there was a highly significant statistical difference noted (p value of 0.0001*) between all three groups with respect to percentage of cases of necrotic young immature permanent teeth (NYIPT) they encounter in their practice, source of knowledge of REPs, preferred clinical protocol and reporting of success or failure of REPs to clinical databases. (Table 1).

• Knowledge, Attitude And Opinion Regarding Current Regenerative Endodontic Protocols for irrigation and intracanal medicament use among Pedodontists, Endodontists and General Practitioners.

On statistical analysis there was found to be a highly significant statistical difference noted (p value of 0.0001*) between the groups with respect to case selection, procedures of

Table 2 Descriptive statistics regarding Protocols to be Followed in Regenerative Endodontic Procedure.

Case Selection	Pedodontists	Endodontists	General Practitioner	P value
In what cases would you consider performing a regenerative endodontic procedure?				0.0001*
Preoperative radiograph showing incomplete root formation, wide apical foramen-apex > = 1mm with thin dentinal walls.	88.5	87.4	70.8	
Grossly decayed or fractured young permanent teeth that require post and core as final restoration	0.3	0.2	0.8	
Presence of draining sinus and presence of periodontal pockets.	4.6	3.3	12.6	
Presence of periapical radiolucency more than 10 mm.	3.8	4.4	16.7	
Presence of external and internal root resorption	2.8	4.7	8.4	
Do you mechanically instrument the dentinal walls?	18.7	15.4	51.7	0.0001*
Yes				
No	88.9	84.8	44.6	
Role of Growth Factors				0.0001*
Yes	89.6	90.6	79.5	
No	0.8	0.9	1.2	
May be	9.6	8.5	19.3	
Which stem cells are the most important in guiding regeneration?SCAP (Stem Cells of Apical Papilla)				0.0001*
DPSC (Dental Pulp Stem Cell)	65.5	69.5	50.7	
SHED(Stem Cells from Human Deciduous teeth)	27.6	28.2	45.7	
	6.9	2.3	3.6	
What do you use for disinfection irrigation for the 1st appointment? (select all that apply)				0.0001*
NaOCl concentration > 3.0%				
	11	12	27	
NaOCl concentration 1.6%–3.0%	30.5	25.8	23	
NaOCl concentration 1.5%	28.8	29	19	
NaOCl concentration < 1.5%	11	13.4	12.3	
Chlorhexidine 0.12%	8.5	5.6	2.6	
Chlorhexidine 2%	19.5	0.4	1.6	
EDTA	27.1	40.2	10.5	
Sterile water	7.6	2.3	0.3	
Sterile saline	59	34	29	
Other	0.8	0.4	0.8	
Which type of intracanal medicament do you use?				0.0001*
No intracanal medicament	0.2	0.6	10	
Triple antibiotic paste	53.4	65.3	67.7	
Double antibiotic paste	5.6	6.9	16.6	
Calcium hydroxide	39	25.2	5.3	
Other	1.8	2	0.2	
When do you call the patient back for the second visit?				0.0001*
1 week				
	33.1	35.3	47.2	
2 weeks	31.4	40.2	25.6	
3 weeks	24.6	18.7	15.8	
> 4 weeks	11	5.8	11.4	
If there are signs/symptoms of persistent infection, what would you do?				0.01*
Reapply the same intracanal medicament and follow-up				
	55.1	57.9	58.9	
Apply a different intracanal medicament and follow-up	21.2	34.3	25.4	
Cease the REP	23.3	7.1	10.4	
Other _____	0.4	0.7	5.3	
Which of these is the primary goal of regenerative endodontic procedure?				0.0001*
Increased root wall thickness and increased root length				
	33.1	40.4	35.3	
Complete closure of apex	40.7	37.5	54.3	
Positive vitality test	26.3	22.1	10.4	

Table 2 (continued)

Case Selection	Pedodontists	Endodontists	General Practitioner	P value
Which of the following irrigation solution is recommended to be used at the end disinfection irrigation in the current regenerative endodontic protocol to increase the adhesion, proliferation and differentiation of scaffold?				0.0001*
Chlorohexidine				
MTAD	29.5	27.4	40.5	
17% EDTA	18.7	19.3	10.6	
	51.8	53.3	48.9	

P value < 0.0001* is considered highly significant.

mechanical instrumentation of root canal, role and importance of growth factors, the disinfection protocols for REPs ie the use of root canal irrigating solutions and intracanal medication and goals of regenerative endodontics.(Table 2).

- Knowledge, Attitude And Opinion Regarding Scaffolds Used in Regenerative Endodontic practice among Pedodontists, Endodontists and General Practitioners

On statistical analysis with respect to scaffolds used in REPs there was a highly significant statistical difference in KAP noted (p value of 0.0001*) with respect to ideal properties of scaffold, material used as coronal barrier, advantages of synthetic scaffold and their know-how and scaffolds used in regenerative endodontics while there was statistically no significant difference noted between groups with a (p value 0.064) with respect to use of vasoconstrictor.(Table 3).

4. Discussion

Management of necrotic immature young permanent teeth poses a significant challenge due to a lack of natural apical constriction and thin dentinal walls, which makes endodontic treatment consisting of chemomechanical preparation and obturation to achieve a hermetic seal arduous. (Carmen et al., 2017) The earlier methods of calcium hydroxide apexification and single-visit apexification with MTA had the disadvantages of not reinforcing the teeth in question, not maintaining the proper crown root ratio, and failing to restore the functional properties of the pulp. Regenerative endodontics, on the other hand, aims at increasing the root length and dentin thickness because of its potential to repair and regenerate the root canal apex by stimulating the stem cells of the apical papilla and re-restoring the pulp's vitality. (Kahler et al., 2017).

The array of case reports since the introduction of regenerative endodontics have used varying protocols in those cases. Since a treatment rendered should always be evidence-based, the American Academy of Endodontists did react to ongoing inconsistencies and brought about a statement of protocols for regenerative endodontics, which it revised every three years. (American Association of Endodontists, 2017; Galler, 2016) The present survey was designed to assess knowledge,

attitude, and opinion regarding the current regenerative protocols. In the present study, both pedodontists and endodontists did receive at least 10–15% of cases of NIYPT, in which 60.7% of respondents dealt with 10% of NIYPT in their practice, and most of them had procured their know-how about regenerative endodontics from self-study. The preferred treatment protocol that they all used the most was MTA apexification and they were lacking in knowledge that the failure and success of regenerative endodontics should be reported to the American Academy of Endodontics as it can help in establishing a proper causal effect relationship. (American Association of Endodontists, 2017).

With respect to the protocols used in regenerative endodontics, the pedodontists (88.5%), endodontists (87.4%), and general practitioners (70.8%) were seen to have adequate awareness with respect to case selection, the importance of growth factors, and stem cells of the apical papilla (SCAP). The three most important procedures that determine the fate of regenerative endodontic procedures are minimal instrumentation, irrigation and disinfection, and scaffold placement. The pedodontists (88.9%) and endodontists (84.8%) had adequate knowledge regarding the minimal instrumentation of canals in REPs, whereas the general dentists were found to be lacking in knowledge regarding the minimal instrumentation of canals, as minimal instrumentation is required to remove the microbiota biofilm while at the same time preserving the fragility of dentin and cells of the apical papilla. (Lin et al., 2014) Regarding irrigation protocols in REPs, pedodontists, endodontists, and general practitioners were not aware of the percentage of sodium hypochlorite used in REPs; a percentage greater than 1.5% was shown to be toxic to SCAP. Martin et al., concluded in his study on different concentrations of NaOCl that 1.5% NaOCl maintained the vitality of SCAP, was adequate as a disinfectant, and did not depart from its primary objective of root canal debridement. (Martin et al., 2014) There was adequate knowledge regarding the last irrigation solution to be used at the end of the procedure among pedodontists (51.8%) and endodontists (53.3%), but it was inadequate among general dentists (48.9%), as EDTA has been shown to enhance proliferation and adhesion of SCAP. Zeng et al., also in their study to investigate the release of growth factors into the root canal space after the irrigation procedure following the current American Association of Endodontists (AAE)

Table 3 Descriptive Statistics regarding Scaffolds used in the Regenerative Dentistry.

	PEDODONTIST	ENDODONTIST	PRACTIONER	P value
What are the ideal properties that a scaffold should possess? (select all that apply)				0.0001*
Biocompatible with the host tissues	75.3	77.5	60.3	
Should be porous	50.3	56.4	52.2	
Rapid rate of biodegradability	67.2	69.2	51.6	
Rich in signaling molecule	59.4	60.1	57.3	
What kind of local anaesthetic do you use at the scaffold formation appointment?				0.064
Anaesthetic with vasoconstrictor	45.4	46.3	56.3	
Anaesthetic without vasoconstrictor	63.2	53.7	43.7	
What is the material that you place directly over the blood clot (coronal barrier)?				0.0001*
MTA	85.2	90	81	
Glass ionomer	0.3	0.1	0.7	
Biodentine	9.1	9.1	10.3	
Endosequence Root Repair Material	5.4	0.8	8	
What are the advantages of synthetic scaffold (select all that apply)				0.0001*
Easy placement				
	67.8	70.6	55.4	
Mechanical stiffness	28.4	29.4	55.3	
Biocompatibility	38.4	30.1	23.3	
Economical	15.7	20.6	10.5	
Which of these have a sustained slow release of growth factor over time?				0.0001*
Platelet rich fibrin				
	20.4	20.9	36	
Platelet rich plasma	52.4	50.5	49.3	
Blood clot	27.2	28.6	14.7	
Do you consider that the process of drawing of blood in children for preparation of Platelet rich fibrin and Platelet rich plasma increases the anxiety and fear related behaviour in children that may hamper the process of rendering treatment?				0.0001*
Yes				
	90.3	90.2	93.2	
No	9.7	9.8	6.8	
Which among these synthetic scaffolds have you come across in your practice, journals or conferences?PLA (Polylactic Acid)				0.0001*
Collagen	28.7	19.7.3	10.5	
PGLA (Poly-Lactic-Co-Glycolic Acid)	57.7	60.6	76.5	
	13.6	19.7	13	
Which of these synthetic materials have high resemblance with extracellular matrix?				0.0001*
Collagen				
	76.9	69.3	60.4	
PLGA (Poly-Lactic-Co-Glycolic Acid)	12.5	20.6	23.3	
PLA (Polylactic Acid)	10.6	10.11	15.3	
Which of the following scaffolds do you use?				0.0001*
Blood clot				
	36.3	35.5	50.5	
Collagen	0.4	0.2	0.0.2	
PRF(Platelet Rich Fibrin)	30.6	33.6	34.7	
PRP(Platelet Rich Plasma)	32.4	30.5	14.6	
PGLA(Poly-Lactic-Co-Glycolic Acid)	0.5	0.2	0.1	

P value < 0.0001* is considered highly significant.

regenerative endodontic protocol, concluded in their study that NaOCl, when followed by EDTA, enhanced the release of TGF- β_1 and the canal space had a concentration of 2–90 ng/ml of TGF- β_1 was capable of inducing cell migration as it acts as chemokine and a growth factor, which helps in the binding of SCAP to dentin matrix, thereby enhancing regenerative endodontic success by cell homing procedure. (Zeng et al., 2016) The awareness of the use of irrigants was greater than the awareness of respondents in the study conducted by Ariwala et al. (Ariwala et al., 2020) With respect to intracanal medicaments used in REPs, most of the pedodontists, endodontists, and general practitioners were of the opinion that Triple Antibiotic Paste should be used, but the in-vitro studies by Ruparel et al. have already shown that TAP when used in clinical concentration is lethal to SCAP, (Ruparel et al., 2012) the results were similar to a study done by Assiry A A et al., where the majority of the participants chose TAP as an intracanal medicament. (Assiry et al., 2022) The pedodontists (53.4%) endodontists (65.3%), and general practitioners (67.7%) were unaware of the toxic effects of TAP on SCAP.

The role of the apical papilla in root formation has been discussed previously by Huang et al. SCAP is capable of self-renewal and can give rise to progenitor cells that eventually differentiate into specialized cells. Since regenerative endodontics relies on cell homing strategies, it's important to preserve the stem cell niche, a concept proposed by Schofield as a specialized microenvironment that regulates the fate of stem cell progeny. One of the critical factors during irrigation and disinfection procedures in regenerative endodontics is to retain the viability of SCAP. (Kim et al., 2012).

The pedodontists (33.1%), endodontists (40.4%), and general dentists (35.3%) were found to be lacking in knowledge regarding the primary goals of regenerative endodontics. The degree of success of regenerative endodontic procedures is evaluated by the goals achieved, i.e., the primary goal, which is the elimination of symptoms and evidence of bone healing, secondary goal, which is increased root wall thickness and increased root length, which is desirable; and the tertiary goal, which is positive vitality testing, which if achieved could prove the organisation of pulp tissue. (American Association of Endodontists, 2017).

Scaffold placement plays a major role in the success of regenerative endodontics. Even though all three groups had shown adequate knowledge regarding most of the ideal properties (Kahler et al., 2017; Gathani and Raghavendra, 2016) they were not well aware of some specific properties like the porous size of the scaffold (pedodontists- 50.3%, endodontists- 56.4%, general practitioners- 52.2%) and the rate of degradation, most of them were of the opinion that it was ideal for scaffolds to degrade fast (pedodontists: 67.2%, endodontists: 69.2, general dentists- 51.6%) whereas with respect to biodegradability, it should be able to sustain over a long period in order to be capable of regenerative activity. (Kahler et al., 2017) Regarding sustained release of growth factors over time, knowledge was found to be lacking, as in all three groups the majority of them believed that it was PRP that had sustained release, whereas on the contrary, it was PRF that had sustained release of growth factors for 28 days. (Dohan Ehrenfest et al., 2009) The prognosis of regenerative endodontics also depends on the adhesion, proliferation and

differentiation of stem cells; hence, it is important that the rate of degradation of the scaffold be slow so that the growth factors present in the scaffold can act as a signalling cascade for cell homing to take place. (Kahler et al., 2017).

The awareness regarding the other artificial scaffolds was also found to be lower. Most of the pedodontists (Blood Clot –36.3%, PRF-32.4%) and endodontists (Blood Clot –35.5%, PRF-30.5%) preferred using Blood Clot and PRF as the scaffold Blood Clot and PRF as the scaffold, whereas general practitioners (Blood Clot –50.5%, preferred using Blood Clot and PRF as the scaffold, and only (PRF-14.26%) considered using PRF as the scaffold. According to the majority of them (pedodontists –90.3%, endodontists –90.2% and general practitioners – 93.2%), the process of drawing blood for PRF /PRP increases anxiety and fear related behaviour.

The pedodontists (85.2%), endodontists (90%) and general practitioners (81%) were of the opinion that MTA should be used as a coronal barrier when compared to Biodentin, but the literature already states that Biodentin has improved physical qualities and handling, including its other wide range of applications like endodontic repair and pulp capping. (Kaur et al., 2017).

The findings of this study are in correlation with the study done by Lee et al. (Lee et al., 2018) The results of the present study do indicate that there needs to be an increase in awareness regarding regenerative endodontic procedures among general dentists. The present study was a web-based survey, hence the limitations of online surveys like response bias, non-respondent characteristics, maintenance of confidentiality, and ethical issues. (Mudavath and Narayan, 2019) There is an urgent need to fill the knowledge lacunae among pedodontists and endodontists regarding irrigation protocols, intracanal medicaments, and scaffolds by making it an essential part of their training programmes in colleges. Since regenerative endodontics is an emerging treatment in endodontics, there are fewer clinical trials; hence, the level of evidence for this proper treatment protocol is very low. So, it is also our responsibility as practising academicians and clinicians to increase the knowledge base by reporting cases of failure to the American Academy of Endodontics.

More such surveys should be conducted across the globe for REPs to bring about increased awareness regarding the REPs (Shah et al., 2016) and also to expand the guidelines governing the success of REPs in addition to those given by AAE.

5. Conclusion

The present study could conclude that there is a lacunae existing in knowledge and awareness regarding irrigation protocols, intracanal medicament use, and scaffold systems used in regenerative endodontics among pedodontists, endodontists, and general practitioners treating NIYPPT.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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