Original Research Article

DENTAL STEM CELL THERAPY: AWARENESS AND PERSPECTIVE AMONG INDIAN ORTHODONTISTS

ABSTRACT:

AIM: To assess the awareness of stem cells among Orthodontists in India.

Materials and Methods: A cross-sectional, self-modified, validated questionnaire-based, nationwide survey was conducted among practicing Orthodontists and postgraduate students belonging to various colleges in India. A total of 502 participants completed the questionnaire. Google Form link was generated and circulated. Data were imported in Microsoft Excel (Version 2016) format. The data was analyzed using **SPSS** Statistics for Windows, version 25.0 (**SPSS** Inc., Chicago, Ill., USA). Inferential statistics were performed using the Chi-square test. Categorical variables were described using frequency and percentages.

Results: The awareness of the participants about stem cells was assessed. Statistically significant differences were obtained in comparing both the groups ($p<0.0001$)

Conclusion: This is a nationwide survey to assess the levels of awareness of the Postgraduate students and the Orthodontists towards dental stem cell therapy. It has been seen that there are a variety of responses across the zones among the groups. Overall comparisons have suggested that there is equitable knowledge among all the participants towards stem cell applications. Comparatively lesser scores have been reported by the postgraduates in the knowledge and awareness domains.

Keywords: Orthodontists, stem cells, knowledge, awareness, emerging trends

INTRODUCTION

In a major breakthrough in 1908, Russian histologist Alexander Maksimov proposed the term “stem cell” for scientific usage[1]. Stem cells are defined as clonogenic cells capable of both self-renewal and multi-lineage differentiation. The breakthrough in dental history was achieved in 2000 when Gronthos et al. identified and isolated odontogenic progenitor population in the adult dental pulp. [2] These cells were referred to as dental pulp stem cells (DPSCs). Since this discovery, several researchers have reported varieties of dental stem cells, which include: DPSCs (Dental pulp stem cells)

- SHED (stem cells from human exfoliated deciduous teeth)
- SCAP (Stem cells from apical papilla)
- PDLSCs (Periodontal ligament stem cells) [3]

Most researches are directed toward the regeneration of damaged dentin, pulp, resorbed root, periodontal regeneration, and to repair perforations. Whole tooth regeneration to replace the traditional dental implants is also in pipeline. [4] Stem cells (SCs) have been extracted from various organs including muscle, dermis, bone marrow, adipose tissue, periosteum, blood, umbilical cord, synovial membrane, and teeth [5, 6]. Research evidence states the application of stem cells in Orthodontics and cranio-facial Orthopedics. The applications are common towards correcting dentofacial anomalies, regeneration of hard (alveolar cleft) and soft tissues (hemifacial microsomia) [7].. As the extraction of primary teeth or permanent premolar or wisdom teeth are common intervention in Orthodontic treatment of malocclusions, SCs sources from the teeth could be gained without extra morbidity[8]

Future application of SCs in Orthodontics could involve accelerating tooth movement, regenerating resorbed roots, and expanding tooth movement limitations [9, 10, and 11]. Unfortunately, evidences on the knowledge of the Orthodontists and post graduate students about these have been reported to be weak. [12] This hinders the practice of adopting stem cell for treating the problems using these technologies. Hence, there is a need to educate the Orthodontists and post graduates about the applications of SCs in the field of Orthodontics. This could only be possible if we know the existing levels of knowledge, attitude and practices of the Orthodontists and post graduates.

Thus, the focus of our survey was to assess knowledge, awareness and perception about stem cell therapy among Orthodontists and by doing so we intend to establish a rationale behind its use. We have also explicated as to why Orthodontists despite being intrigued have dithered the use of stem cell therapy in their practice.

METHODOLOGY

A cross-sectional, self-modified, validated questionnaire-based, web-based nationwide survey was conducted among the practicing Orthodontists and postgraduate students nationwide. A proportionate random sampling technique was chosen. Sample size was calculated using the following formula: ($n= Z^2 P(1-P)/D2$) and minimum sample size calculated was 368.

$$(n= Z^2 P(1-P)/D^2)= 3.8416*0.6*0.4/(0.05)^2$$

India was segregated into five zone: East, West, North, South, and Central. Based on the proportion of dental colleges present and the availability of Orthodontic subjects, sample selection was made. College selection was done randomly and the approach was made through social media groups, email conversations, text messages mentioning the link, and also the DCI College list. The sample size was calculated based on the empirical data by using G Power software (Version 3.1.9.7). A total of 502 practicing Orthodontists and postgraduate students participated in the study. The Institutional Ethics Board (147/IRB-IBSEC/SIS) clearance was obtained and the study follows Helsinki Ethics Code 2014.

A pilot survey (n=40) was conducted before the commencement of the main survey to check for the face validation, feasibility, and accessibility of the study. The questionnaire was made based on previous research reports. Content validation was done by a panel of experts. Cronbach's α value was 0.74; which inferred moderate reliability. A Google Form link was generated and circulated through known contacts, considered to be the state representative for data collection among the colleges or Orthodontists of those

states. The questionnaire contained 26 questions which included both close-ended and self-administered questions. Data were exported in Microsoft Excel (Version 2016) format and analyzed using **SPSS** Statistics for Windows, version 25.0 (**SPSS** Inc., Chicago, Ill., USA). Inferential statistics were performed using the Chi-square test. Categorical variables were described using frequency and percentages. Chi-square test was used for measuring the association between two independent groups. Intergroup comparison of various domain scores at different follow up points was done using Mann Whitney U test. The confidence interval was kept at 95%. The level of statistical significance was set at 0.05.

RESULTS:

A total of 502 participants completed the questionnaire**.** Maximum participants belonged to southern India (36.1%). The majority of the participants had an experience of 0-5 years (39.0%) and pursued private practice (27.3%). The gender distribution was almost at par with 49.8% males and 50.2% females.

The source of knowledge was internet for 72% and 49% obtained from books and journals. The postgraduates predominantly resorted to internet for information. Most Orthodontists (63.7%) and postgraduates (91.2%) reported that they did not attend any conferences related to stem cell applications in Orthodontics. It was seen that 70.6% of the Orthodontists and 37.7% of the postgraduates knew the characteristics of the stem cells. It was reported that 69.6% of Orthodontists and 43.9% of postgraduates were aware that dental stem cells could be a second chance for those who did not bank their cord stem cells. It was reported by 66.8% of

Orthodontists and 37.7% of postgraduates that they knew that dental stem cells can be used for the regeneration of tooth, root, bone, and PDL. Orthodontists (37.6%) and postgraduates (34.2%) reported knowing that stem cell therapy produces autoimmune reactions even if it's from your own body. Most of the postgraduates (14.4%) and Orthodontists (24.6%) reported that the ideal source of obtaining stem cells was primary molars and wisdom tooth. It was seen that Orthodontists (70.1%) and postgraduates (43.0%) reported that dental stem cells can be derived from periodontal ligaments, dental ligament, pulpal tissues etc. Significant differences were observed between both groups for the entire variable (Table 1). The knowledge scores were classified according to the degree of goo67.0% felt that dental stem cells had a wide array of applications in the field of Orthodontics. Postgraduates (55.3%) and Orthodontists (65.2%) were aware of the existing literature. Orthodontists (50.5%) were much more aware of the use of Stem cells in Distraction osteogenesis. It was seen that 45.1% of the Orthodontists and 28.9% of the postgraduates were aware that stem cells can be bioengineered for TMJ replacement and treating temporomandibular joint disorders. Postgraduates (35.1%) had comparatively less knowledge towards literature showing dental stem cell application in shortening treatment duration and retention period in the palatal suture. Awareness was comparatively better among Orthodontists (46.1%) towards stem cell therapy helps to solve external root resorption in Orthodontics. Statistically significant differences were observed about the awareness towards distraction osteogenesis. Mann-Whitney U test was used to compare both the groups. (Table 2)

Awareness related to ICMR Dental stem cells guidelines was reported by 32.2% of Orthodontists and 14.0% of Postgraduates. The responses were at par for preserving the stem cells for both the postgraduates (41.2%) and the Orthodontists (38.1%). When asked about recommending to patients, the postgraduates ranked higher (95.6%) than that of Orthodontists (88.4%). Statistically significant

differences were observed with regard to advising patients regarding stem cell and the various obstacles faced. Mann Whitney U test has been used to find the differences between the groups (Table 3).

DISCUSSION:

Stem cells have been used for correcting various craniofacial abnormalities, in distraction osteogenesis, and also in correcting temporomandibular joint anomalies. Recently, it has gained an enormous momentum and hence the need arises to report the level of awareness among various groups of Dentists throughout the Indian subcontinent. The present study aimed to assess the knowledge, awareness, and recommendations of the practicing Orthodontists and postgraduates about application in the field of Orthodontics, stem cell isolation and preservation. A positive interest has been cultivated among dentists which highlight the need to improve the stem cell-related knowledge among the post-graduate students and the practicing orthodontists which would improve their practice and benefit the patients in the long run. There is a paucity of data towards the assessment of knowledge, awareness, and attitude of Orthodontists directing the need for researching this area of interest.

The level of knowledge appertain to application of stem cells in Orthodontics in the present study was found to be (57%) among postgraduates and (65%) among Orthodontists. In a study conducted by Goswami et al (2019) the level of knowledge was 72%. In the present study, the years of experience were recorded and it was seen that increased years of experience was related to the improvement

in knowledge domain scores and post graduates showed a fair knowledge score compared to good knowledge score in that of the Orthodontist. For the Orthodontists, the source of information included conferences, books, and journals while the main source of information was the internet and curriculum books for the post-graduate students. Thus it could be substantiated that postgraduates would only have higher knowledge if it is inculcated in their curriculum and Orthodontists have exposure to varied journal proceedings, conferences, and also clinical experiences that improve their knowledge.

Isolation and potential harvesting of the dental stem cells are evident from primary (SHED) and permanent pulpal tissues and also from those of impacted and therapeutically extracted teeth. [13, 15]. The cells from the periodontal ligament, apical papilla of erupted permanent teeth, developing dental follicle also serve as sources of dental stem cells. [12] The overall awareness scores ranked higher. Comparisons were made with other studies where it was reported that the majority of the respondents were aware of the potential sources of the stem cells; (81%) in the study conducted by Goswami et al., 69.6% and 60.3% as reported by Goyal (2015). [12, 16] Age-wise comparisons were made among the study population and it was seen that with an increase in age the positive response increased.

Banking of stem cells involves extraction, processing, and storage of dental stem cells for future endeavors. Various storage methods are being used. Education of dental stem cells would not only involve the sources, it should also involve the stem cell harvesting methods along with the techniques of identification.

The current study showed that the postgraduates were more towards adapting newer techniques as compared to the practicing Orthodontists. Hence, this positive attitude should be encouraged through conferences, CDE programs on stem cells, and academic inclusions to benefit a majority of the population.

The constraints of our study is that it's solely based on the responses of the participants, and it could be subjected to response bias. A clinical intervention to improve the validation of the responses would have been a better alternative.

CONCLUSION:

This is a nationwide survey to determine the knowledge, attitude, and practice of Postgraduates and Orthodontists towards application of stem cells in treating Dental, craniofacial anomalies and to facilitate Orthodontic interventions. A varied response was noted among the Orthodontists and post graduates throughout the country. Results suggest that there is equitable knowledge among all the participants towards stem cell applications recommending the need to educate them about the applications of stem cell in the field of Orthodontics. Comparatively lesser scores have been reported by the postgraduates in the knowledge and awareness domains. The present study recommends the need to incorporate the stem cell topic into the academic curriculum for better clinical performance of the dental specialists this would encourage more of in vivo studies to improve the efficaciousness of treatment rendered to the patients and in turn improve their quality of living.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCES:

1.Igor EK. The Man behind the Unitarian Theory of Hematopoiesis. Perspect Biol Med. 2000;43:269–76.

2.Safari S, Mahdian A, Motamedian SR. Applications of stem cells in orthodontics and dentofacial orthopedics: Current trends and future perspectives. World Journal of Stem Cells. 2018 Jun 26;10(6):66.

3.Mohanty P, Prasad NK, Sahoo N, Kumar G, Mohanty D, Sah S. Reforming craniofacial orthodontics via stem cells. Journal of International Society of Preventive & Community Dentistry. 2015 Jan;5(1):13.

4.Dr. Mohammadi Begum, M. D. T. A. P. M. (2016). Role of stem cells in Orthodontics - A review. Indian Journal of Medical Research and Pharmaceutical Sciences, 3(9), 1–7. http://doi.org/10.5281/zenodo.61773

5. Tania SM, George AM. Extending the envelope of regenerative medicine in orthodontics by stem cells. International Journal of Orthodontic Rehabilitation. 2019 Apr 1;10(2):82.

6.Gul Amuk N, Kurt G, Karsli E, Ozcan S, Acar MB, Amuk M, Lekesizcan A, Gurgan CA. Effects of mesenchymal stem cell transfer on Orthodontically induced root resorption and Orthodontic tooth movement during orthodontic arch expansion protocols: an experimental study in rats. European journal of orthodontics. 2020 Jun 23;42(3):305-16.

7. Huang H, Yang R, Zhou YH. Mechanobiology of periodontal ligament stem cells in Orthodontic tooth movement. Stem cells international. 2018 Jan 1;2018.

8.Shanbhag S, Suliman S, Pandis N, Stavropoulos A, Sanz M, Mustafa K. Cell therapy for orofacial bone regeneration: A systematic review and meta-analysis. Journal of clinical periodontology. 2019 Jun;46:162-82.

9. Rickert D, Sauerbier S, Nagursky H, Menne D, Vissink A, Raghoebar GM. Maxillary sinus floor elevation with bovine bone mineral combined with either autogenous bone or autogenous stem cells: a prospective randomized clinical trial. Clinical oral implants research. 2011 Mar;22(3):251-8.

10.Paz AG, Maghaireh H, Mangano FG. Stem Cells in Dentistry: Types of Intra-and Extraoral Tissue-Derived Stem Cells and Clinical Applications. Stem Cells International. 2018 Jul 2;2018.

11. Aly LA. Stem cells: Sources, and regenerative therapies in dental research and practice. World journal of stem cells. 2015 Aug 26;7(7):1047.

12. Goswami M, Kumar G, Sharma S. "Dental Stem Cells": Awareness, knowledge, and attitude of dental professionals—A cross-sectional study. Special Care in Dentistry. 2020 Jan;40(1):90-6.

13. Chitroda PK, Katti G, Attar NM, Shahbaz S, Sreenivasarao G, Patil A. Stem cells in dentistry: a study regarding awareness of stem cells among dental professionals. *Indian J Dent Res*. 2017;28(6):711- 716.

14. Katge F, Shetty AJ, Rusawat B, Vamsi KC. Knowledge and attitude of Indian dentists regarding dental stem cells: a cross-sectionaldescriptive survey. *Indian J Dent Res*. 2017;28(4):367-374.

15. Sede MA, Audu O, Azodo CC. Stem cells in dentistry: knowledge and attitude of Nigerian dentists. *BMC Oral Health*. 2013;13(1):27.

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16. Goyal A. Knowledge, awareness and attitude regarding stem cells among dental practitioners in Udaipur city, Rajasthan. *Int J Adv Res*. 2015;3(2):677-684.

17. Ayna M, Gülses A, Wiltfang J, Açil Y. Mesenchymal Stem Cells for Optimizing Bone Volume at the Dental Implant Recipient Site. Mesenchymal Stem Cells: Isolation, Characterization and Applications. 2017 Nov 29:185.

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KNOWLEDGE RESPONSES		Postgraduates		Orthodontists		Z Score	P-value
		N	%	N	%		
Source of Information (internet=1 conference=2 books journal=3 ug training=4 pg train=5)	1;2	1	0.9	21	5.4	3.087	0.0001*
	1;2;3	0	0	58	14.9		
	1;2;3;4;	0	0	1	0.3		
	1;2;3;4;5	2	1.8	5	1.3		
	1;2;3;5	3	2.6	31	8.0		
	1;2;4	2	1.8				
	1;2;5	3	2.6	14	3.6		
	1;3	6	5.3	42	10.8		
	1;4	0	0	2	.5		
	1;3;4;5	1	0.9	0	0		
	1;3;5	7	6.1	19	4.9		
	1;4; 5	0	0	2	0.5		
	1;5	28	24.6	0	0		
	2;3	2	1.8	26	6.7		
	2;5	4	3.5	8	2.1		
	3;4	0	0	1	0.3		
	3;5	0	0	10	2.6		
	4;5	0	0	1	.3		
Attended any Conferences or CDE programs?	Yes	10	8.8	141	36.3	-5.637	0.0001*
	No	104	91.2	247	63.7		
Differences in the characteristics of	Yes	43	37.7	274	70.6	-0.814	0.416

Pluripotent cells, Multipotent cells, and Totipotent stem cells?	No	26	22.8	29	7.5		
	Heard of	45	39.5	85	21.9		
Second chance for those who did not bank their cord stem cells?	Yes	50	43.9	270	69.6	-0.426	0.670
	No	35	30.7	65	16.8		
	Heard of	29	25.4	53	13.7		
Dental stem cells can be used for the regeneration of tooth, root, bone, and PDL?	Yes	43	37.7	259	66.8	-1.322	0.186
	No	31	27.2	26	6.7		
	May be	40	35.1	103	26.5		
Stem cell therapy produces auto immune reaction even if it's from your own body?	Yes	39	34.2	146	37.6	-0.677	0.499
	No	33	28.9	94	24.2		
	Not sure	42	36.8	148	38.1		
Which is the ideal source for obtaining stem cells? (Don't know 0 Prim 1 perm 2 wisdom 3	1;0	1	.9	2	.5	4.32	0.0001*
	2;0	0	0	1	.3		
	3;0	0	0	2	.5		
	1;2	3	2.6	6	1.5		
	1;2;3	1	0.9	12	3.1		
	1;2;3;0	1	0.9	0	0		
	1;3	28	24.6	56	14.4		

unaware 4)	2;3	1	0.9	0	0		
Dental stem cells can be derived from dental pulp, follicle, apical papilla, and periodontal ligament?	Yes	49	43.0	272	70.1	-0.792	0.428
	No	27	23.7	47	12.1		
	Heard of	38	33.3	69	17.8		

*statistically significant

Table 1: Knowledge related responses of both the groups

ATTITUDE		Postgraduates		Orthodontists		Z Score	P-value
		N	%	N	%		
Dental stem cells have application in the field of Orthodontics	Yes	95	83.3	260	67.0	-1.326	0.185
	No	2	1.8	27	7.0		
	Heard Of	17	14.9	101	26.0		
Are you aware of the studies proving stem cells can enhance the treatment	Yes	63	55.3	253	65.2	-1.091	0.275
	No	20	17.5	62	16.0		

	Heard Of	31	27.2	73	18.8		
Are you aware of the use of Stem cells in Distraction osteogenesis?	Yes	34	29.8	196	50.5	-2.250	0.024*
	No	50	43.9	97	25.0		
	Heard Of	30	26.3	95	24.5		
Use of stem cells in bioengineered TMJ replacement and also to treat temporomandibular joint disorders?	Yes	33	28.9	175	45.1	-0.446	0.656
	No	45	39.5	116	29.9		
	Heard Of	36	31.6	97	25.0		
Shorten treatment time	Yes	40	35.1	174	44.8	-0.974	0.330
	No	40	35.1	134	34.5		
	Heard Of	34	29.8	80	20.6		
Are you aware that Stem Cell therapy helps in solving the complication of external apical root resorption in orthodontics?	Yes	41	36.0	179	46.1	-1.079	0.281
	No	37	32.5	124	32.0		
	Heard Of	36	31.6	85	21.9		

Table 2: Attitude related responses as compared between the groups

RECOMMENDATION AND PRACTICE		Postgraduates		Orthodontists		Z Score	P-value
		N	%	N	%		
Are you aware of the guidelines related to Dental stem cells by ICMR?	Yes	16	14.0	125	32.2	-0.837	0.403
	No	60	52.6	191	49.2		
	Heard Of	38	33.3	72	18.6		
How many years do you think dental stem cells can be preserved?	21	38	33.3	140	36.1	-1.506	0.132
	15	28	24.6	55	14.2		
	10	6	5.3	27	7.0		
	unaware	42	36.8	166	42.8		
Are you aware of the insurance policies which cover for stem cell banking and cryopreservation certificate?	Yes	47	41.2	148	38.1	-1.707	0.088
	No	42	36.8	175	45.1		

	Heard Of	25	21.9	65	16.8		
Will you advise your patients to bank their stem cells?	Yes	109	95.6	343	88.4	-2.258	0.024*
	No	5	4.4	45	11.6		
Obstacles faced	1;2	25	21.9	77	19.8	4.098	0.002*
	1;2;3	6	5.3	18	4.6		
Convincing patient=1	1;2;3;4	14	12.3	47	12.1		
cost factor=2	1;2;4	11	9.6	21	5.4		
laborious process=3	1;3	11	9.6	9	2.3		
ethical=4	1;3;4	3	2.6	1	.3		
	1;4	6	5.3	8	2.1		
	2;3	7	6.1	21	5.4		
	2;3;4	1	.9	9	2.3		
	2;4	4	3.5	22	5.7		
	3;4	0	0	6	1.5		
Do you like to upgrade your knowledge about stem cells?	Yes	114	100.0	382	98.5	-1.334	0.182
	No	0	0	6	1.5		

*Significant scores

Table 3: Practices related to stem cells responses as compared between the groups