

Knowledge and Attitude of Dental Students and Recent Dental Graduates Towards Dental Pulp Stem Cells in Iran

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Objectives Considering the growing knowledge about stem cells and the role of cell-based therapies in the future, dentists should have adequate knowledge about oral stem cell sources and their applications in dentistry. The present study assessed the knowledge and attitude of dental students and recent dental graduates towards dental pulp stem cells (DPSCs) in Iran.

Methods This descriptive cross-sectional study was performed in 2021 on 175 participants, including 86 dental students and 89 recent dental graduates from the Dental School of Rafsanjan University of Medical Sciences (RUMS), Rafsanjan, Iran and Dental School of Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran. A researcher-designed questionnaire was used to collect data. The validity and reliability of the questionnaire were assessed. The data were analyzed by SPSS version 21 using the Kolmogorov-Smirnov test, independent t-test, and ANOVA.

Results The mean knowledge and attitude scores of the participants were $66.16 \pm 8.51\%$ and $68.65 \pm 11.87\%$, respectively. The mean attitude score was significantly correlated with “interest in participating in the courses related to stem cells” and “scientific journal review rate”. The level of knowledge of the participants from SBMU was significantly higher than that of participants from RUMS ($P < 0.05$). Other variables did not have a significant effect on the mean score of knowledge or attitude ($P > 0.05$).

Conclusion Dental students had a positive attitude towards the application of stem cells; however, their knowledge was inadequate. Therefore, some appropriate measures must be adopted to enhance the knowledge of dental students about DPSCs, especially in universities with lower ranks.

Keywords Knowledge; Attitude; Dental Pulp; Stem Cells; Students, Dental

Introduction

Stem cells promise a brighter future in reconstructive medicine with their two main characteristics, namely self-renewal and differentiation into multiple lineages.¹ Stem cells are generally divided into two main categories of embryonic stem cells and adult stem cells. Embryonic stem cells can differentiate into all types of cells in the body, but adult stem cells have a limited ability to differentiate into certain lineages.² However, adult stem cells are a better option for regenerative treatments due to their significant advantages such as their presence in almost all mesenchymal and epithelial tissues of the body, less rigid ethical concerns, lower risk of rejection by the immune system, and less tumorigenesis.³

Different populations of adult stem cells have been identified in different dental tissues, which are generally called dental stem cells. Different populations of mesenchymal stem cells are present in the tooth.⁴ Mesenchymal stem cells, which are multipotent, were discovered by Friedenstein in the bone marrow, and have the ability to differentiate into different types of cells in different tissues.⁵ These cells are used to enhance the healing of various injured tissues, including the heart muscle, skin, bone, and cartilage, and to treat osteoarthritis, heart failure, myocardial ischemia, spinal cord injury, traumatic brain injury, etc.⁶

Depending on the location of mesenchymal cells in dental tissues, they are named dental pulp stem cells (DPSCs),

human deciduous tooth stem cells, periodontal ligament stem cells, human dental follicle stem cells, and stem cells of the apical papilla.⁴ Dental stem cells have many advantages, including better survival under freezing conditions, better interactions with growth factors and scaffolding, easier access, and fewer complications following cell collection. Furthermore, unlike the umbilical cord blood, they can be collected for many years after birth.⁷⁻⁹ These cells can be used for regenerative treatments in the oral cavity and other body tissues. Various studies have used dental stem cells in corneal reconstruction, neuronal differentiation for treatment of neurodegenerative diseases such as Parkinson's and Alzheimer's diseases, treatment of orthopedic lesions and spinal injuries, etc.^{3, 8-11} Many advances have been made in regeneration of dental tissues. Zhuang et al. demonstrated the potential of dentinogenesis of dental stem cells.¹² Treatment of apical periodontitis and root perforation has also been successful.¹³ Many attempts have been made to regenerate the dentin/pulp complex, and regeneration of dentin/pulp complex with dental stem cells has been observed in vitro, but various studies have indicated its future potential.¹⁴⁻¹⁷ Despite the numerous benefits of stem cell-based therapies, there are many controversies regarding stem cell use due to legal, ethical, spiritual, and philosophical issues. Ethical issues are as complex as legal issues, and there is no scale to determine how to resolve spiritual issues, and philosophy needs to analyze an action or a principle to determine whether it has benefits for the society.^{18, 19} The

key issues and concerns include the possibility of human cloning, abuse of embryo donors, and issues raised by new techniques used to obtain stem cells.²⁰

Dentists are no exception to this rule, and their attitude towards the use of dental stem cells is a crucial factor in development and expansion of stem cell-based therapies. On the other hand, due to the increasing knowledge about stem cells and the role of cell-based therapies in the future²¹, dentists should have enough knowledge about oral stem cell sources as well as their applications in dentistry. Therefore, the present study investigated the knowledge and attitude of dental students and recent dental graduates towards DPSCs in Iran to take a step forward to improve the educational curriculum and also shed more light on the applications of DPSCs.

Methods and Materials

This descriptive cross-sectional study was performed on 175 individuals, including 85 participants from the Dental School of Rafsanjan University of Medical Sciences (RUMS), Rafsanjan, Iran and 90 participants from the Dental school of Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran, in 2021, with the ethical approval code of IR.RUMS.REC.1400.068. The participants included undergraduate dental students in their final 2 years of education and recent dental graduates. Participants were selected by enumeration sampling method, and a researcher-designed questionnaire was used to collect data. The prepared questionnaire consisted of three parts. The first part included demographic information and had 5 questions about gender, educational status, academic year of education, history of participation in courses related to stem cells, and willingness to participate in such courses. The second part consisted of 29 questions that examined the dentists' knowledge about dental stem cells. The questions were selected from the exam taken at the end of the advanced course of Academy of Dental Therapeutics and Stomatology, which were included in the questionnaire after a few modifications.²¹

The third section included 14 questions that assessed the dentists' attitude towards dental stem cells. They were selected from a set of questions used in similar studies.²²⁻²⁶

The validity of the questionnaire, which included its content validity ratio and content validity index, was confirmed by the experts. The mean scores of these indices were 0.93 and 1 for the knowledge questions, and 0.9 and 1 for the attitude questions, respectively. The test-retest reliability of the questionnaire also showed Pearson correlation coefficients of 0.99 and 0.98 for attitude and knowledge questions, respectively. Reliability calculation using Cronbach's alpha method showed Cronbach's alpha index of 0.79 for attitude questions and 0.51 for knowledge questions. After removing questions 9, 15, 7, 12, and 5, the

values of 0.56, 0.60, 0.62, 0.65, and 0.67 were obtained, respectively.

The five-point Likert scale for knowledge questions included strongly agree, agree, disagree, and strongly disagree, which were given a score of 5 to 1, respectively, and the total score ranged from 0 to 100. Moreover, the knowledge questions had three answer choices of correct, I have no opinion, and wrong. After completing the questionnaire, the total score was calculated which ranged from 1 to 100, and the mean value was reported as the knowledge score.

To evaluate the goodness of fit of the model, the Chi-square index divided by the degree of freedom (CMIN/DF) and the RMSEA index are usually used. If the value of the CMIN/DF index is less than 3 and the RMSEA index is less than 0.08, it indicates that the model is well-fitted to the data. In this study, all goodness of fit indices were within the acceptable range.

Furthermore, the effect of each question on the total score of the questionnaire (attitude) was examined. The effect of each question on the attitude score was also examined, which was significant for all questions, except for questions 7, 9, and 14.

The Rasch model was used to evaluate the construct validity of the knowledge questionnaire. According to this theory, there was a hidden variable called knowledge, the value of which was different for each person, and the more knowledgeable a person was, the more likely he or she was to answer the questions correctly.

In the Rasch model, the difficulty of each question was estimated based on the responses given by the participants. In this study, question 9 was the most difficult and question 2 was the easiest question to answer.

To evaluate the appropriateness of the questions, two methods of fitting statistics and differential item functioning (DIF) were used. Two infit MNSQ and outfit MNSQ indices were used to check the fit of the questions. MNSQ is statistically a chi-square statistic divided by its degree of freedom. The distance 0.6-1.4 was suggested as the standard distance for MNSQ. In this study, this index was within the acceptable distance for all questions. The DIF analysis examines the same performance of questions in different groups.

For the participants in this study, the DIF analysis was performed for two important demographic characteristics, including gender (male and female) and status (final 2-year students and general dentists). The overall difficulty of the questions was assessed between the male and female groups, as well as between the final 2-year students and general dentists. Questions with a difference greater than 0.5 for at least one of these variables in the two groups were identified as DIF and had to be excluded in the subsequent analyses. The difference between the groups in each of the variables was less than 0.5.

Questionnaires were uploaded into the EPOLL system version 4.13.20 (Epoll, Tehran, Iran), and the link was sent to students via text message. The collected data were fed into SPSS software version 22 and analyzed. The hypothesis of normality of scores was examined using the Kolmogorov-Smirnov test. Then, independent t-test and ANOVA were used to investigate the relationship between different demographic variables and knowledge and attitude scores, depending on the type of variable. The structural validity of the questionnaire was also assessed.

Results

Among the 214 participants for whom the questionnaire was sent, 175 participants, 89 general dentists and 86 dental students, participated in this study. The frequency of responses to the knowledge and attitude questions is reported in Table 1.

Table 1- Frequency of participants' answers to each question

| Knowledge questions | N(%) | | |
|---|-----------|-----------|-----------|
| | Correct | Incorrect | No Idea |
| 1 Stem cells are undifferentiated cells. | 148(84.6) | 19(10.9) | 8(4.6) |
| 2 Some of the stem cell-based therapies have already been approved or reviewed by the Food and Drug Administrations of other countries. | 156(89.1) | 3(1.7) | 16(9.1) |
| 3 Some cardiovascular, oncological, and orthopedic patients are currently under treatment with stem cells. | 137(78.3) | 0 | 38(21.7) |
| 4 Xenogeneic stem cells are isolated from the patient being treated, while allogeneic stem cells are obtained from another person. | 116(66.3) | 28(16) | 31(17.7) |
| 5 It has not been accurately proven that allogeneic stem cells do not initiate an immune response. | 31(17.7) | 60(34.3) | 84(48) |
| 6 Autologous stem cells reduce the risk of transplant rejection. | 120(68.6) | 6(3.4) | 49(28) |
| 7 Multipotent stem cells can differentiate into any type of tissue. | 34(19.4) | 110(62.9) | 31(17.7) |
| 8 The two main forms of stem cells are primary and secondary stem cells. | 51(29.1) | 11(6.3) | 113(64.6) |
| 9 Embryonic stem cells can only be obtained from the embryo; therefore, they are associated with ethical issues. | 19(10.9) | 95(54.1) | 61(34.9) |
| 10 Stem cell sources include the umbilical cord, amniotic fluid, bone marrow, adipose tissue, brain, and teeth. | 123(70.3) | 14(8) | 38(21.7) |
| 11 Umbilical cord blood stem cells can only be collected at birth. | 105(60) | 21(12) | 49(28) |
| 12 Bone marrow-derived stem cells can also be isolated from saliva. | 27(15.4) | 42(24) | 106(60.6) |
| 13 Adipose-derived stem cells are usually isolated through liposuction and lipectomy. | 51(29.1) | 19(10.9) | 105(60) |
| 14 Stem cells can be created by inducing mature human skin cells. | 44(25.1) | 24(13.7) | 107(61.1) |
| 15 Dental stem cells can only be obtained from the pulp of deciduous and permanent teeth. | 68(38.9) | 37(21.1) | 70(40) |
| 16 Periodontal ligament-derived stem cells can regenerate a whole new tooth. | 42(24) | 35(20) | 98(56) |
| 17 Periodontal ligament-derived stem cells and stem cells of exfoliated or extracted deciduous teeth are superior to other teeth as a stem cell source. | 51(29.1) | 31(17.7) | 93(53.1) |
| 18 Dental pulp stem cells form secondary and tertiary dentin. | 83(47.4) | 26(14.9) | 66(37.7) |
| 19 Stem cell-derived osteoblasts and chondrocytes can regenerate TMJ. | 90(51.4) | 10(5.7) | 75(42.9) |
| 20 The use of stem cells is superior to autologous bone grafting because it does not require bone removal from the patient. | 117(66.9) | 11(6.3) | 47(26.9) |
| 21 Dental stem cells are a type of mesenchymal stem cell. | 95(54.3) | 11(6.3) | 69(39.4) |
| 22 In theory, dental stem cells can differentiate into neural cell lines. | 86(49.1) | 7(4) | 82(46.9) |
| 23 Patients have been treated with mesenchymal stem cells to regenerate heart muscle and improve the valve function. | 72(41.1) | 7(4) | 96(54.9) |
| 24 The potential for future use of dental stem cells includes regenerating a whole new tooth. | 120(68.6) | 11(6.3) | 44(25.1) |
| 25 Researchers have been able to reconstruct a whole new tooth in animal studies. | 50(28.6) | 15(8.6) | 110(62.9) |
| 26 Stem cells can be frozen and stored for a long time. | 119(68) | 4(2.3) | 52(29.7) |
| 27 Periodontal ligament-derived stem cells survive freezing. | 54(30.9) | 8(4.6) | 113(64.6) |
| 28 Collection and freezing of deciduous teeth for future use are currently underway. | 58(33.1) | 13(7.4) | 104(59.4) |
| 29 One of the side effects of cell therapy is turning into cancer cells. | 73(41.7) | 21(12) | 81(46.3) |

| Continue the table 1 | | | | | | |
|----------------------|---|----------|----------|----------|-------------------|---------|
| Attitude questions | N(%) | | | | | |
| | Strongly agree | Agree | unsure | Disagree | Strongly Disagree | |
| 1 | My relatives and I like to use umbilical cord stem cell banking. | 56(32) | 67(38.3) | 48(27.4) | 2(1.1) | 2(1.1) |
| 2 | Stem cell-based regeneration should be a part of dentistry. | 60(34.3) | 74(42.3) | 35(20) | 5(2.9) | 1(0.6) |
| 3 | Dental stem cell banking will be useful for regeneration of dental tissues. | 63(36) | 73(41.7) | 29(16.6) | 9(5.1) | 1(0.6) |
| 4 | Topics related to stem cells should be included in the undergraduate curriculum. | 55(31.4) | 62(35.4) | 37(21.1) | 14(8) | 7(4) |
| 5 | You want to save your teeth and dental tissue for future treatments. | 66(37.7) | 79(45.1) | 21(12) | 8(4.6) | 1(0.6) |
| 6 | Regenerative dental treatment will be a better treatment option than implant placement. | 63(36) | 66(37.7) | 33(18.9) | 10(5.7) | 3(1.7) |
| 7 | You are concerned about the potential health hazards regarding the use of stem cells as part of regenerative dentistry. | 2(1.1) | 33(18.9) | 61(34.9) | 62(35.4) | 17(9.7) |
| 8 | Stem cell clinics will offer dental treatments in the future. | 22(12.6) | 65(37.1) | 68(38.9) | 15(8.6) | 5(2.9) |
| 9 | You have ethical concerns regarding the use of stem cells in dentistry. | 30(17.1) | 60(34.4) | 49(28) | 28(16) | 8(4.6) |
| 10 | If there is any stem cell bank in the city, you advise the patients to store their dental stem cells and explain the vision to the patient. | 38(21.7) | 92(52.6) | 28(16) | 12(6.9) | 5(2.9) |
| 11 | The rules for the use of dental stem cells and dental regenerative treatments should be regulated by dental associations. | 47(26.9) | 86(49.1) | 26(14.9) | 14(8) | 2(1.1) |
| 12 | You will refer a patient for whom you cannot perform regenerative treatment to a specialist who can perform such treatment. | 57(32.6) | 85(49.1) | 22(12.6) | 7(4) | 3(1.7) |
| 13 | You are willing to deliver dental treatments that involve embryonic stem cells sourced from a human fetus. | 22(12.6) | 50(28.6) | 75(42.9) | 23(13.1) | 5(2.9) |
| 14 | The government should ban all research on embryonic-derived or aborted embryonic stem cells. | 37(21.1) | 58(33.1) | 58(33.1) | 14(8) | 8(4.6) |

The results showed that the participants' mean knowledge score was $66.16 \pm 8.51\%$, and their mean attitude score was $68.65 \pm 11.87\%$. The frequency of attitude and knowledge scores in terms of different variables is reported in Tables 2 and 3.

| Variable | Variable level | Number (%) | Mean score | Standard deviation | P-value |
|--|----------------|------------|------------|--------------------|---------|
| Dental School | RUMs | 85(48.6) | 67.94 | 12.41 | 0.444* |
| | SBMU | 90(51.4) | 69.32 | 11.38 | |
| Gender | Male | 72(41.1) | 67.63 | 12.98 | 0.344* |
| | Female | 103(58.9) | 69.37 | 11.05 | |
| Status | Undergraduate | 86(49.1) | 67.90 | 11.77 | 0.410* |
| | Graduate | 89(50.9) | 69.38 | 12.00 | |
| | Weekly | 25(14.3) | 70.36 | 8.02 | |
| | Monthly | 24(13.7) | 74.48 | 10.12 | |
| Scientific journal study | Rarely | 100(57.1) | 68.68 | 11.92 | 0.001** |
| | Never | 26(14.9) | 61.54 | 13.20 | |
| | Yes | 26(14.9) | 71.43 | 9.62 | |
| History of participation in a stem cell course | No | 149(85.1) | 68.17 | 12.19 | 0.197* |
| | Yes | 88(50.3) | 72.04 | 11.04 | |
| Willingness to participate in a stem cell-related course | Yes | 88(50.3) | 72.04 | 11.04 | <0.001* |
| | No | 87(49.7) | 65.23 | 11.76 | |

*Independent samples t-test, ** One-way ANOVA

The mean attitude score was significantly different between those interested in participating in a course related to stem cells and those who were not ($P=0.001$). Moreover, the mean scores of attitude were significantly different among different groups regarding scientific journal review ($P<0.001$). The level of knowledge of participants from

SBMU was significantly higher than that of participants from RUMS (Table 3), but the mean scores of knowledge and attitude did not show significant associations with other variables ($P>0.05$).

Table 3- Mean Knowledge score in terms of different variables

| Variable | Variable level | Number | Mean score | Standard deviation | P value |
|--|----------------|-----------|------------|--------------------|---------|
| Dental School | RUMs | 85(48.6) | 64.12 | 8.05 | 0.002* |
| | SBMU | 90(51.4) | 68.10 | 8.52 | |
| Gender | Male | 72(41.1) | 66.33 | 9.26 | 0.832* |
| | Female | 103(58.9) | 66.05 | 7.99 | |
| Status | Undergraduate | 86(49.1) | 65.22 | 8.80 | 0.147* |
| | Graduate | 89(50.9) | 67.09 | 8.16 | |
| | Weekly | 25(14.3) | 66.62 | 9.48 | |
| Scientific journal study | Monthly | 24(13.7) | 70.40 | 8.87 | 0.056** |
| | Rarely | 100(57.1) | 65.40 | 7.65 | |
| | Never | 26(14.9) | 64.79 | 9.60 | |
| History of participation in a stem cell course | Yes | 26(14.9) | 68.83 | 9.87 | 0.084* |
| | No | 149(85.1) | 65.70 | 8.20 | |
| Willingness to participate in a stem cell-related course | Yes | 88(50.3) | 67.07 | 8.36 | 0.161* |
| | No | 87(49.7) | 65.26 | 8.61 | |

*Independent samples t-test, ** One-way ANOVA

Discussion

Various dental and medical applications of dental stem cells and increasing awareness among the general population make it necessary for dental practitioners to have adequate knowledge about the many aspects of dental stem cells. Moreover, stem cell research is a rapidly growing field in medicine that has triggered enthusiasm for incorporation of regenerative medicine into dentistry, and growing demand for more courses to be added to the undergraduate curricula.²⁶ The present study aimed to assess the knowledge and attitude of undergraduate dental students and recent dental graduates towards DPSCs.

The questionnaire used in this study was similar to the one used in previous studies²²⁻²⁶ and was designed based on the Advanced Dental Technology and Research program. The validity and reliability of the questionnaire were assessed, and some items were modified based on the results of the assessments.

The percentage of participants who reported reviewing of scientific dental journals in the present study was lower than that in other studies.^{23, 27} Older participants and residents who participated in previous studies might be the reason for this difference. Most participants in the present study had not taken any educational courses on stem cells or regenerative treatments, which might be because they were still student or were recent graduates who had little chance to participate in such courses. These findings were in agreement with those of Manguno et al,²⁸ and Abedi et al.²³

Furthermore, in line with other studies, most participants (50.3%) were willing to attend workshops or training courses on stem cells, and obtained a higher score in attitude towards the application of DPSCs. Thus, it provides evidence on the acceptance of regenerative treatments in dentistry by the undergraduates and recent dental graduates.^{26, 28, 29} In line with the present study, Basson et al.²⁶ showed that 73% of participants were willing to attend additional training courses and lecture programs on stem cells.

In the present study, the majority of the participants were female general dentists who had not participated in any dental stem cell courses. Knowledge score was higher among participants who attended regenerative courses and reviewed scientific dental journals on a weekly and monthly basis, which was in agreement with the results of Basson et al,²⁶ and Ez-Abadi et al.²³ The attitude score was also higher among the participants who attended regenerative courses.

Most participants in the present study agreed/totally agreed with stem cell-based regenerative treatments as part of dental practice and curricula. They also mentioned that it would be beneficial to have dental stem cell banks for their patients (74.3%), confirming the results of previous studies.^{23, 28, 29} Since more evidence is needed to confirm the efficacy and safety of these modern treatments, research activities on dental stem cells and regenerative medicine are increasing.²⁶ In agreement with other studies,^{26, 29} most of the participants agreed/totally agreed that regenerative treatments are a better option than dental implant therapy; however, only 20.0% of participants were concerned about the health hazards of stem cell therapy. On the other hand, they did not consider many hazards imposed on patients, such as tumorigenesis of stem cells, risk of rejection of implanted cells or the scaffold used, and infection transmission^{30, 31}, which can be indicative of the participants' poor knowledge of the topic.

A previous study indicated that dental interns thought that the use of stem cells in dentistry contradicted ethical issues³²; however, participants in the present study were equally against and for the ethical concerns about the use of stem cells in dentistry.

One of the objectives of the present study was to compare the questionnaires between type one and type two medical universities; thus, SBMU and RUMS were chosen, which are categorized as type one and type two universities, respectively among all medical universities in Iran. The last but not least finding of the present study was the higher knowledge score of graduate and undergraduate students in SBMU than those in RUMS, indicating that the type and

ranking of university may affect the knowledge of students in different fields. Type one universities with several research centers and different curricula may provide their students with more up-to-date knowledge, which may justify these differences.

The major limitation of this study was self-report data collection through the questionnaire, which could have led to bias in responses of participants. Another limitation of the present study was the small sample size due to the low admission rate of students by dental schools in Iran.

Conclusion

In conclusion, progresses in regenerative dentistry and the positive attitude towards the application of dental stem cells may lead to increasing application of these cells in near future. It seems imperative for dental professionals to

be aware of the various aspects of dental stem cells. Therefore, appropriate methods must be adopted to increase the knowledge about dental stem cells, especially in universities with lower ranks. Moreover, curriculum modification based on up-to-date findings of dental stem cells is warranted.

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Conflict of Interest

No Conflict of Interest Declared ■

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