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TREATMENT OF GINGIVAL RECESSION DEFECT USING MESENCHYMAL STEM CELLS CULTURED PCL BASED BONE REGENERATING SCAFFOLD: A RANDOMIZED CONTROLLED CLINICAL STUDY

SHIVAJI KASHTE[1], ANSHUMAN DWIVEDI[2], SHRADDHA GAUTAM[3], R. K. SHARMA[4], SACHIN KADAM[1,3*]

[1]Department of Stem Cell and Regenerative Medicine, Centre For Interdisciplinary Research, D. Y. Patil Education Society (Institution Deemed To Be University), Kolhapur 416006, India, [2]Personal Dental Care, Noida, Uttar Pradesh 201301, India, [3]Advancells, Noida, Uttar Pradesh 201301, India, [4]D. Y. Patil Medical College, D. Y. Patil Education Society (Institution Deemed To Be University), Kolhapur 416006, India
Email: Kadamsachin@gmail.com

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ABSTRACT

Gingival recession defects generally give rise to functional as well as aesthetic problems. Basic periodontal treatment could only get rid of plaque and calculus to control inflammation, while the ultimate goal of periodontal treatment is to repair and reconstruct the periodontal lining using a gum grafting periodontal plastic surgery. So far, use of stem cells has proven to be effective for *in vivo* periodontal regeneration and repair of structural defects in case of Miller's classification class I. However, class II and class III required serious bone grafting to repair the defect.

In the present study, a patient of multiple gingival recession (Miller's class II) was treated using human Umbilical Cord Wharton's jelly derived mesenchymal stem cells (hUCMSCs) in combination with bone regeneration poly ε-caprolactone (PCL)-graphene oxide (GO)-*Cissus quadrangularis*(CQ)(PCL-GO-CQ) scaffold. The study was concluded with reference to clinical parameters including root coverage that was recorded at baseline, and at 2 months postoperative. The final analysis revealed significant reduction of gingival recession with over 70% of root coverage. Thus, the study proved the efficacy of bone regenerating scaffold to regenerate multiple tissue defects, when seeded with human Umbilical cord Wharton's jelly derived mesenchymal stem cells.

Keywords: Multiple Gingival Recession, Human Umbilical cord Wharton's jelly derived mesenchymal stem cells, PCL based bone regenerating scaffold

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INTRODUCTION

The multiple gingival recessions and their treatment with complete root coverage is a clinical challenge. There are functional as well as aesthetic challenges with gingival recession defects [1]. Primitive periodontal treatment could only get rid of plaque and calculus to constraint inflammation, while the ultimate aim of periodontal care is to heal the periodontal lining with the help of a gum grafting periodontal plastic surgery [2]. There are various periodontal plastic surgical procedures for the treatment of multiple gingival recessions, including coronally advanced flaps (CAF) as the gold standard treatment and modified coronally advanced tunnel technique [3]. But they have inadequacies such as morbidity and or limited supply of donor tissue. Also, there have been reports of wound healing to be compromised in multiple gingival recessions due to differences in recession depths and tooth position, especially due to the width of the avascular surface [2, 4].

The scaffolds, stem cells and growth factors have demonstrated to be of high potential in regenerative medicine. Various studies conducted for wound healing, restoration of periodontal ligament have mentioned the improved ability of 3D engineered stem cells in stimulating widespread gingival attachment, which can exclusively cover the exposed root surface [5].

In the current study, we have used human Umbilical cord Wharton's jelly-derived mesenchymal stem cells (hUCMSCs) in combination with poly ε-caprolactone (PCL)-graphene oxide (GO)-*Cissus quadrangularis* (CQ) (PCL-GO-CQ) scaffold for the treatment of multiple gingival recessions. PCL is a U. S. Food and Drug Administration (FDA) approved polymer which has been widely used in numerous tissue engineering applications. The entire credit for the same reportedly goes to its biocompatibility, biodegradability and its easy interaction with stem cells to promote cellular attachment, proliferation as well as differentiation into different lineages like. Osteoblasts, chondroblasts, and neurons [6]. The stem extract of CQ plant has immense medicinal potential with reported antimicrobial, antioxidant activity [7] and osteogenic activity [8].

CASE REPORT

A 35-year-old male patient with aesthetic concerns was selected for the study. The study participant reportedly neither had a positive medical record nor was provided with any medications that are able to hamper a soft tissue recovery. The patient had multiple gingival recession (Miller's class II 6 mm-8 mm defects on the mandibular central and lateral incisors, left mandibular canines). The clinical probing depths were ranged from 2-3 mm. The main points of the procedure were given to the patient and informed consent was obtained.

The patient was tutored to watch skilled oral cleanliness measures at the side of preliminary medical care enclosed dental scaling, polishing, and occlusal adjustment thirty days earlier to the surgery. The patient was tutored to use a non-traumatic brushing technique (roll technique) with a soft toothbrush.

Preparation of a PCL Based Bone regenerating scaffold: PCL was used for the fabrication of scaffold sheets by electro spinning. These PCL sheets were surface modified by the layer-by-layer technique to deposit alternative layers of graphene oxide (GO) and *Cissus quadrangularis* (CQ) callus culture extract. We have used CQ callus culture extract obtained from callus culture, a plant tissue culture technique used to propagate the plant *in vitro*. The prepared PCL-GO-CQ scaffold was EtOH sterilized. The hUCMSCs ($3X10^4$ cells/ml) were seeded on these scaffolds and the same was used further for the healing of multiple gingival recessions (fig. 1).

The procedure was meted out underneath local anesthesia. A sulcular incision was created close to the defect and cell-seeded scaffold was accustomed to cowl the defective region. The scaffold was then stabilized by sutures and the wound was closed. There was no usage of periodontic dressing. The patient was provided a chilly compress additional orally to decrease inflammation and blood loss. The patient was then given antibiotics, analgesics and mouthwash. Patient was educated against chewing or cleansing the surgical space for the primary

two weeks till once removal of sutures. Additional directions of oral hygiene and roll technique brushing were given. The patient was concerned with visits once every week throughout the primary month and twice a week during the second month to watch healing and plaque management.

The final analysis was meted out two months post-surgery. The analysis revealed good color melding of the doctored region with adjacent soft tissue. The root coverage was reportable to be within the span of 70%-80% for the mandibular anterior teeth, beside the sustained decline in sensitivity (fig. 2).

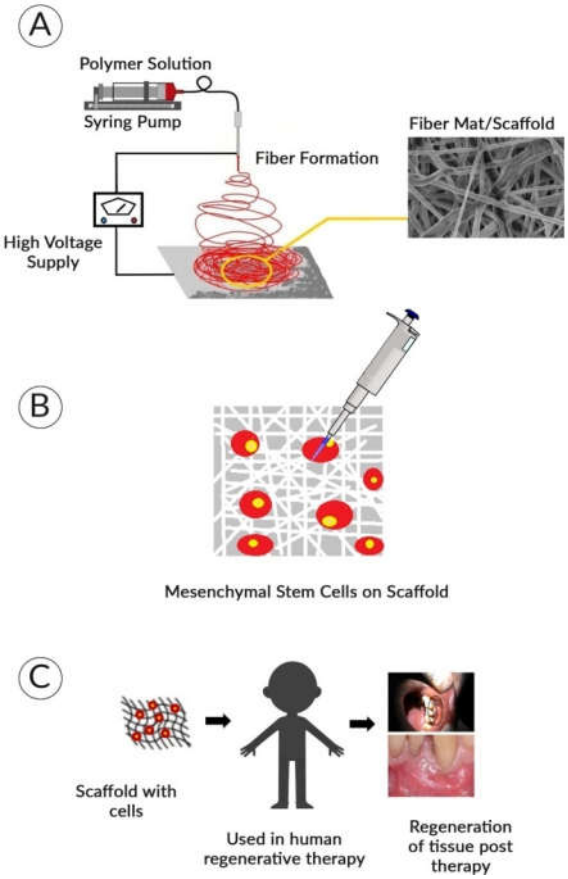

Fig. 1: Schematic representation of start to end procedure of regenerative medicine a: preparation of scaffold by electrospinning B: Seeding of cells on scaffold surface C: Cell seeded scaffold used for regenerative therapy

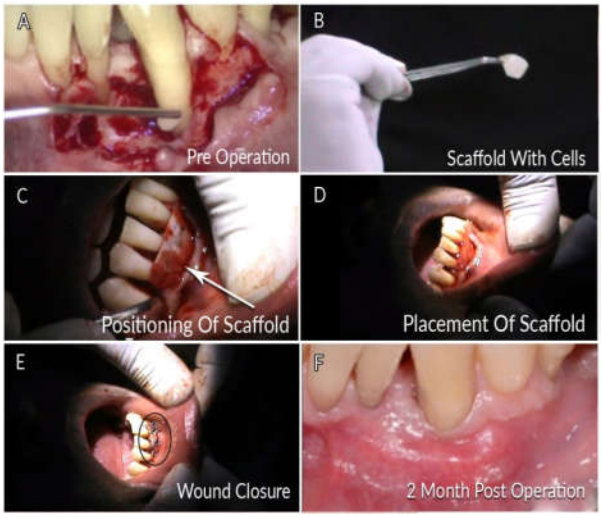

Fig. 2: A: Preoperative view of multiple gingival recessions. B: hUCMSCs seeded PCL based Scaffold. C: Positioning of scaffold. D: Placement of Scaffold. E: Scaffold transplanted in the recipient site and sutured. F: Post-operative root coverage at 2 mo

DISCUSSION

Although varied dental medicine approaches for the cure of gingival recession are presently applied, there is still a demand for a clinical trial, which might discover the foremost predictable dental material and aesthetic surgical approach for complete tissue restoration and reduction in dentin hypersensitivity and treatment of gingival recessions [4]. The goal of the current study was to assess the restorative capabilities of PCL based bone regenerating scaffold in multiple gingival recessions. The root coverage after 2 mo post-treatment was in the range of 70% to 80%. Previous studies have confirmed comparable results, with approximately 78% to 69% root coverage at 12th-month post-surgery, when gingival recessions were treated with CAF-Acellular dermal matrix (ADM)-Platelet-rich plasma and CAF-ADF [2]. The gingival recessions related with non-carious cervical lesions (NCCL) were treated with modified CAF in combination with connective tissue graft (CTG). The NCCL was restored earlier to surgery by nanofilled composite resin (NCR), resin-modified glass ionomer cement (RMGI) or giomer. When the gingival recessions were treated with CTG; there was root coverage of 71% for NCR+CTG, 71% for RMGI+CTG and 64% for giomer after one year of post-surgery [4]. There was 75% to 87% root coverage when multiple gingival recessions were treated with subepithelial, connective tissue graft (SCTG) after 90 d of treatment [9]. In point of fact, a few variations in the results can be justified with variable initial recession dimensions, different evaluation periods, variable sample size, procedural changes as well as a number of multiple adjacent teeth.

The root coverage techniques tent to vary with success and predictability. Success correlates to the average percentage of root coverage attained; however, predictability illustrates the percent of the treated teeth in which complete root coverage is attained [9]. The success rate of PCL based bone regenerating scaffolds was more than 80%. This study, within its limitations, showed effective results; still, more relevant case studies are required for further analysis of the periodontal parameters.

In the current case report, multiple teeth were treated simultaneously with a single PCL-based bone regenerating scaffold, with 80% success rate. However, the study also revealed the possibility of treating a single tooth recession with a superior success ratio.

The treated defect site revealed recovered root coverage with a decrease in dentin hypersensitivity lacking any probing defect or any other significant complications. The tissue restorations did not show any negative effect on the adjacent gingival tissues. The study results can finally be concluded to be compatible with other studies [4, 10].

CONCLUSION

The present study thus has successfully evaluated the periodontal potential of the PCL based scaffold. These scaffolds could be used for the treatment of multiple gingival recessions.

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AUTHORS CONTRIBUTIONS

S. Kashte has performed the experiments, interpreted the data and wrote the manuscript. A. Dwivedi has performed the experiments. S. Gautam has contributed to the interpretation of the data. R. K. Sharma has conceived the experiments. S. Kadam has conceived the experiments, contributed to the interpretation of the data and writing the manuscript.

CONFLICTING INTERESTS

The authors declare no conflict of interest and no competing financial interests exist.

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