



Protocol for Managing Antimicrobial Activity in the Patients with Maxillary Defect by Functionalization of Silicone Using Different Nanoparticles: A Randomized Control Trial

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Study Protocol

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ABSTRACT

Background: Patients with facial or intraoral defects are mostly reconstructed by prosthesis for which maxillofacial silicone considered as a material of choice for better aesthetics. Silicones are widely used medical materials. One of the major problems associated with the use of maxillofacial silicone material is microorganisms and fungal growth especially *Candida albicans*, which can result in chronic infection, inflammation and degradation of silicone material that's why the development of antimicrobial silicone elastomer became so important. So, a multiple study is performed trying to improve this property. Nanoparticle technology is rapidly advancing and is used for a wide range of applications in medicine. The potential of metal nanoparticles as antimicrobial agents is widely studied and is considered as an alternative approach to overcome the challenge posed by multidrug resistance in bacteria.

Objective: The present study aims at to evaluate compare the antimicrobial activity of different nanoparticles through functionalization of silicone in the patients with maxillary defect.

Methods: A prospective interventional study will be conducted for two years. The subjects in the

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study will be randomly selected comprising of 21 number of patients undergoing a surgical intervention of maxilla (developmental or acquired defect), after which obturators as a rehabilitation prosthesis is the treatment of choice. Relining of interim obturator incorporate with two different nanoparticles is planned and accordingly subjects will be divided in two interventional group and one control group. For control group, that means were prosthesis is fabricated in a conventional manner without any interventions, so in such patients swab will be taken from the intaglio surface of prosthesis after a specific intervals (after 2,6,12weeks). For interventional group in which prosthesis is relined with two different functionalized silicones, swab will be made again from defect site and from intaglio surface of obturator (after 2,6,12 weeks) with paper points to check microbial colonization growth after which comparative evaluation of antimicrobial activity will be performed.

Results: Descriptive and analytical statistics will be done. SPSS (Statistical package for social sciences) Version 20.1 will be used as statistical software. The statistical significance between control group and interventional group in particular intervals will be evaluated at $p < 0.05$ as P value is considered as level of significance.

Conclusion: Functionalized silicone prosthesis which will thus be given to a patient of maxillary defects to prevent further adhesion of microbial growth on surgical site and which ultimately helps in wound healing. Hypothesis of present study is antimicrobial property of functionalized silicone using Hybrid nanoparticle may be more effective as compared to that of Chitosan nanoparticles in the interim obturators.

Keywords: Nanoparticles; maxillary defects; interim obturators; maxillofacial silicone material.

1. INTRODUCTION

Background & Rationale: Maxillary defects are created by surgical treatment of benign or malignant neoplasms, congenital malformation and trauma. Patients with acquired maxillary defects differ from those with congenital defects due to the abrupt alteration in physiologic processes associated with surgical resection of the maxilla. The ensuing defect creates oronasal and oroantral communication leading to difficulties in mastication, hypernasal speech, fluid leakage and various degrees of cosmetic concerns [1]. The primary objective in each case is to construct a prosthesis, which will restore the defect, improve aesthetics and thereby benefit the morale and boost up the psychological impact of patient.

The maxillofacial prosthodontist, as a member of the surgical team, aids in the recovery of the patient by fabricating and placing obturator prosthesis. As name suggest "Obturator" means "to close or to shut off". According to the Glossary of Prosthodontic Terms-8, obturator is defined as prosthesis used to close a congenital or an acquired tissue opening, primarily of hard palate and or contiguous alveolar structures [2].

The obturators provided in the form of maxillofacial prosthesis are fabricated with silicone that is always in contact with soft tissues, saliva and nasal secretions. Constant exposure to these body fluids might further lead to

colonization of various pathogenic microorganisms over their surfaces causing elastomer degradation or infection which ultimately results in increased percentage of consumption of drugs thereby leading to formation of drug resistance by particular microorganisms [3].

In recent era, nanoscience and nanotechnology are gaining tremendous popularity. The various applications of nanoparticles in various fields has proved as a novel alternative to overcome resistance towards bacterial & fungal drugs reported globally due to misuse of antibiotics. Use of nanoparticles as antimicrobial agents could overcome mechanisms of bacterial resistance as the microbicidal nature of nanoparticles result from direct contact with the bacterial cell wall, without the need to penetrate into the cell [4]. Chitosan nanoparticle is considered as effective biopolymers for biomedical application. This is due to the fact that chitosan has a unique structure, various properties, and ubiquitous functionalities in character and provides the possibility for extension of this biopolymer in the in green chemistry, drug delivery, an anticancer agent, as well as wound healing etc. Another nanoparticle that is Silver nanoparticles (AgNP) also proved from various researches that they have unique properties which help in molecular diagnostics, in therapies, as well as in devices that are used in several medical procedures. They all exhibit fast and broad-spectrum antibacterial activity against

both Gram-positive and negative bacteria as well [5].

Thereby considering all this aspect, the present research is an attempt towards developing a new silicone materials one with Chitosan nanoparticles and other is with Hybrid nanoparticles (Combination of Chitosan and Silver Nanoparticles) through functionalization of medical grade silicone material (Factor II-2186) in the patients with maxillary defect and will also evaluate and compare its efficacy in various time intervals. It is a randomized control trial which we have already filed and completed with pilot study.

1.1 Objective

The present study aims at to evaluate compare the antimicrobial activity of different nanoparticles through functionalization of silicone in the patients with maxillary defect.

2. METHODS

2.1 Study Design

The present study is a prospective interventional study that will be conducted in two years. Study comprising of 21 number of patients undergoing a surgical intervention of maxilla (developmental or acquired defect), after which obturators as a rehabilitation prosthesis is the treatment of choice.

Total number of patients randomly selected in 3 groups out of which Group A is control group and Group B & Group C are Interventional group.

Inclusion criteria:- Patients with surgical resection of maxilla, for which interim obturator will be a treatment option.

Exclusion criteria:- Patients with systemic disease.

Control Group:

- For Group A ie:- Control group of patients, after one month of surgery, interim obturator will be fabricated in conventional manner and patient is recalled after 2 weeks, 6 weeks and 12 weeks of insertion for alteration of prosthesis and at every visits (ie:0, 2,6,12 weeks) swab will be made again from defect site and from intaglio surface of obturator

with paper points to check microbial colonization growth.

Interventional Group:

- For Group B ie:- Interventional group of patients, new impression of defect site will be made and obturator is fabricated, obturator will be relined with silicone material consist Hybrid nanoparticles. Patient will be recalled on after 2 weeks, 6 weeks and 12 weeks for follow up for alteration of prosthesis and at every visits (ie: 0,2,4,6 weeks) swab will be made again from defect site and from intaglio surface of obturator with paper points to check microbial colonization growth.
- For Group C ie:- Interventional group of patients, new impression of defect site will be made and obturator is fabricated, obturator will be relined with silicone material consist Chitosan nanoparticles. Patient will be recalled on after 2 weeks, 6 weeks and 12 weeks for follow up for alteration of prosthesis and at every visit (ie: 0,2,4,6 weeks) swab will be made again from defect site and from intaglio surface of obturator with paper points to check microbial colonization growth.
- Time tag for swab.
T0-at time of insertion
T1-after 2 weeks
T2-after 6 weeks
T3- after 12 weeks

2.2 Investigations

- For each swab, swab culture will be done using a specific medium to check antimicrobial growth on defect site. From that medium agar plates will be prepared and incubated at 37°C for 24 hours.
- After 24 hours microbial growth will be checked and examined by using colony forming unit (CFU).

3. RESULTS

Results will be calculated on the basis of observations evolved from all the 3 Groups that is Control group and Interventional groups at specific planned intervals. Statistical analysis will be done by using descriptive and inferential statistics using Wilcoxon signed rank test, one way ANOVA test and multiple comparison tukey test and software used in analysis will be SPSS 22.0 version and graphpad prism is 7.0 version

and $p < 0.05$ is considered as level of significance.

4. DISCUSSION

A plethora of microorganisms is being constantly encounters by the oral cavity. Plaque biofilm—a major cause of caries, periodontitis and other dental diseases—is a complex community of bacteria or fungi that causes infection by protecting pathogenic microorganisms from external drug agents and escaping the host defense mechanisms [6] Maxillectomy defects pose a unique surgical and prosthetic challenges and rehabilitation of the patient with such defect requires a multidisciplinary approach.

Nanomaterials are capable in antibacterial therapies because of their improved and unique physicochemical properties. Since, the notion of nanotechnology has been applied in various scientific fields such as physics, engineering as well as in the medical field. Nanotechnology is defined as a science that deals with the development of new materials with new properties and functions through controlling and restructuring of the materials on a nanometer scale of “less than 100 nm” [7] Size of the NP plays a pivotal role. They need to have an optimum size typically in the range of 10–100 nm. Sizes 100 nm are not able to exhibit the therapeutic effect because very small particles are steered clear of the body through kidneys and very large particles are taken up by the reticuloendothelial system for disposal [8].

In the recent years, many researchers have performed research and concludes that chitosan is considered as active biopolymers for biomedical application. This is due to the fact that chitosan has a sole structure, countless properties, and ubiquitous functionalities in character and provides the possibility for extension of this biopolymer in the in green chemistry, drug delivery, an anticancer agent, as well as wound healing etc. The antimicrobial activity of chitosan along with its derivatives has been acknowledged and is deliberated to be one amongst the other vital functions, confirming the possible biological applications [9]. Chitosan revealed antimicrobial properties with bacteria, fungi etc. but all the studies performed in reference to chitosan and silicone are in invitro studies that's the reason in this study we are

considering chitosan as one component to incorporate with silicone for the fabrication of interim obturator in patients of maxillary defect to check its antimicrobial efficacy.

For eras, silver (Ag) compounds and ions have been extensively used for both hygienic and healing purposes, due to their strong bactericidal effects, as well as a broad spectrum antimicrobial activity. Due to increased resistance of bacteria to antibiotics and improvements in polymer technology, it resulted in a large number of Ag-containing dressings being available on the market and that's the reason silver is used in the present study in combination with chitosan nanoparticles termed as hybrid material to check its synergistic effect [10]. C. Sámano-Valencia et al in 2013 studied a Bactericide efficiency of a combination of chitosan gel with silver nanoparticles Bactericidal activity of a combination of chitosan gel with silver nanoparticles and they conclude that, this material presents a good and sustained bactericide activity, this features can be related to the good distribution of the silver nanoparticles inside the chitosan matrix and to the sustained release of silver ions from the matrix. This material could be a good choice for applications in oral diseases [11]. Other studies on maxillary defects and related treatment aspects were reviewed [12-16].

5. LIMITATIONS

Study is restricted to a microbial growth of intraoral defect site. Study will only be performed in silicone maxillofacial material only. This study includes quantitative evaluation only.

6. CONCLUSION

The concept of rehabilitation of patients with maxillary defects provides a means of enhancing mastication, deglutition, speech, and esthetics, thus, finally providing a functional solution to the compromised state of the patient by giving the patient an opportunity to live a life as close to normal as possible.

CONSENT

The subjects involved will be informed regarding the study and signed consent will be obtained from the subjects before starting the procedure.

ETHICAL APPROVAL

Approval of study has been obtained from the institutional ethical committee with reference number DMIMS (DU)/IEC/Aug-2019/8198.

TRANSLATORY COMPONENT

Formulation of functionalized silicone prosthesis which will thus be given to a patient of maxillary defects to prevent further adhesion of microbial growth on surgical site and which ultimately helps in wound healing.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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