IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 6 Ser.2 (June. 2021), PP 22-27
www.iosrjournals.org

Chitosan and Chitosan Loaded Antibiotics as a Pulpotomy Agent in Non-Vital Primary Molars

Lamis A. Abo_Elyazid *; Nagwa Abdel Hady Ghoname **; Nahed Abdelmagid Abo Hamila *** ;Gamal Mohamed El Maghraby****;Radwa Abd Elmotaleb Eissa*****

**Assistant lecture, pediatric dentistry Department, Faculty of Dentistry, Tanta University*
*** Professor of pediatric dentistry, Faculty of Dentistry, Tanta University.*
**** Professor of pediatric dentistry, Faculty of Dentistry, Tanta University.*
*****Professor of Pharmaceutical Technology,Faculty of Pharmacy,Tanta University.*
******Lecturer of Microbiology, Faculty of Medicine, Tanta University.*

Abstract
Objectives: *The present study was carried out to evaluate the clinical and radiographic effect of chitosan and chitosan loaded ciprofloxacin, amoxicillin and metronidazole as a pulpotomy agent in non-vital primary molars.*
Methods*: The study sample was carried out on sixty healthy children aged four to seven years old; they were selected from outpatient clinic of Pediatric Dentistry Department. Each child had at least two non-vital primary mandibular molars indicated for non-vital pulpotomy*
Results: *The overall clinical success rate of chitosan group was 36% and 40% in group I and II respectively. While, the clinical success rate 3Mix was 74%, 75 % in group I and III respectively. Whereas, the clinical success rate of formula was 85%, 95 % in group II and III respectively. There was a statistically significant difference between the tested materials in group I and II; however there was no statistically significant difference between the tested materials in group III during the follow-up periods.*
Regarding radiographic success rate of chitosan, it was 47% and 50% in group I and II respectively, While, the radiographic success rate 3Mix was 73%, 80 % in group I and III respectively. Whereas, the radiographic success rate of formula was 80%, 90 % in group II and III respectively. There was a statistically significant difference between the tested materials in group I and II, however; there was no statistically significant difference between the tested materials in group III during the same follow-up periods.
Conclusion: *Chitosan based antibiotics showed high clinical and radiographic success rate compared to chitosan and 3 Mix as a non-vital pulpotomy agent in primary teeth.*
Keywords: *chitosan, 3MIX, pulpotomy agent; non vital primary molars.*

Date of Submission: 20-05-2021 Date of Acceptance: 05-06-2021

I. Introduction

Lifelong preservation of primary teeth in a healthy state remains the ultimate goal of dentistry. Pulp therapy is considered necessary to maintain the teeth in the arch and reestablish healthy condition to the tissue affected by pulp infection, thus preserving normal development of the permanent successors. **(1)**

Microorganisms play a significant role in the initiation and progression of pulpal and periapical diseases. Therefore, success of endodontic treatment is directly related to the elimination of pathogenic microorganisms from root canals. **(2)**

Lateral and accessory root canals in primary teeth having a complex anatomy lead to difficulty in removing the bacteria by mechanical instrumentation and irrigation, **(3)** so the use of antimicrobial medicaments improves the eliminating residual microorganisms and healing of infected root dentin. **(4)**

Recently, the concept of lesion sterilization and tissue repair therapy involve the use of a mixture of antibacterial drugs for disinfection of dentinal, pulpal, and periapical lesions. Repair of damaged tissues can be expected if lesions are disinfected. **(5)**

Chitosan is a natural and non-toxic polysaccharide with unique biological properties such as antimicrobial, anti-fungal, anti-inflammatory, antiseptic, antitumor, hemostatic, immune adjuvant, regenerative effect and wound healing. In dentistry, it can be used as a dental pulp capping material, mouth rinse, chewing gum, drug device for root canal disinfection, topical treatment of periodontitis and blood hemostasis after tooth extraction. **(6,7)**

Chitosan has significant quality of extending the release of drugs so it can be used as a drug carrier to increase the intracanal medicament stability. [8]

Many studies have reported the antibacterial efficiency of chitosan but inadequate data are available on its effects clinically. Also, there are a few studies using chitosan in pediatric dentistry. So, this study was directed to evaluate effect of chitosan loaded 3Mix in the pulpotomy of non-vital primary teeth.

II. Materials And Methods

This clinical trial was carried out on sixty healthy children, aged four to seven years old; recruited from outpatient clinic of Pediatric Dentistry Department, Faculty of Dentistry, Tanta University after obtaining informed consent from their parents.

Each child had at least two non-vital primary mandibular (first or second) molars indicated for non-vital pulpotomy.

Through clinical as well as radiographic evaluation, each child had bilateral mandibular primary molar with necrotic pulp tissue upon entrance the pulp chamber, presence of gingival swelling or fistula, pain on percussion, evidence of furcation or periapical radiolucency, discontinuity of lamina dura and physiological root resorption not exceeding one third of the root.

The teeth were excluded from this study when the tooth wasn't restorable, patients with medical condition as heart disease or leukemia, patients with history of drug allergy to metronidazole, ciprofloxacin or amoxicillin, extensive root resorption exceeding one third of the root and severe mobility.

Preparation of chitosan

Chitosan powder was mixed with saline in equal ratio 1:1 by volume in addition to one part of barium sulfate as a radioopacifier to form chitosan paste.

Preparation of triantibiotic paste (3 Mix)

The raw materials of ciprofloxacin, amoxicillin and metronidazole were stored in air tight containers away from light and moisture and stored in refrigerator. The drugs were mixed in equal weight ratio (1:1:1). One part of barium sulfate was added to this mixture. The dry mixture was mixed with macrogol / propylene glycol (1:1 v/v, mixture) to produce the radiopaque 3Mix paste. This mix is freshly prepared and the excess was discarded.

Preparation of chitosan based antibiotics formulae

The three antibiotics were grinded with chitosan, for ciprofloxacin and metronidazole, the drugs were separately mixed with the required amount of chitosan before gradual addition of acetic acid solution to form a smooth paste. This paste was subjected to wet grinding until drying; this process was repeated four times. For amoxicillin the drug was subjected to dry co-grinding with chitosan to avoid degradation of the drug with acetic acid. The formulation containing the three mixes was prepared by mixing equal weights of drug particles. This mix is freshly prepared and the excess was discarded.

Clinical procedure

Under local anesthesia and rubber dam isolation, clinical procedure was performed, caries was removed using a sterile high speed rose head bur with continuous water spray. Access opening was gained; roof of the pulp chamber was removed and all overhanging edges were eliminated. The pulp chamber was irrigated with normal saline and dried. In case of teeth presented with abscess, drainage and irrigation with normal saline was done.

One hundred and twenty primary molars out of 60 children were divided randomly into three groups of forty teeth for each according to the materials used as follow:

- **Group I:** Treated with unprocessed chitosan in one side with the other side being treated with 3Mix-MP.
- **Group II:** Treated with unprocessed chitosan in one side with the other side being treated with chitosan loaded antibiotics (formulae).
- **Group III:** Treated with chitosan loaded antibiotics (formulae) in one side with the other side being treated with 3Mix-MP.

The treatment was done in a single visit; the paste of the material used in the study according to each group was placed in the pulp chamber and the cavity was sealed with glass ionomer cement and post-operative x-ray was taken (baseline). All cases were recalled after 7-10 days for placement of the final restoration. The cases which show persistent abscess were excluded from the study.

The children were recalled after 3, 6, 9, 12, 18 months for clinical and radiographic evaluation.

Clinical evaluation was recorded according to success criteria reported by Trairatvorakul & Chunlasikaiwan[9] as absence of pain, no tooth mobility , presence of healthy soft tissue; no swelling, redness or sinus tract.

The radiographic evaluation was recorded according to success criteria [10] as continuity of lamina Dura, static or reduction in the size of existing pathologic intraradicular or periapical radiolucency, no newly formed radiographic lesion, absence of pathological root resorption and evidence of bone regeneration.

III. Results

A total 120 non vital mandibular primary molars from 60 children in the age of 4 to 7 years were treated in three groups; chitosan, 3MIX and formula. All teeth were clinically and radiographically checked at 3, 6, 9, 12, and 18 months.

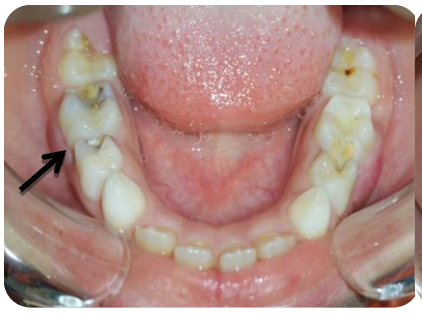
At the end of the study (18month), the overall clinical success rate of chitosan and 3Mix in group I was 36% and 74% respectively, while clinical success rate of chitosan and formula in group II was 40% and 85%, however clinical success rate of formula and 3 Mix in group III was 95% and 75%. There was a statistically significant difference between the tested materials in group I and group II.

Regarding radiographic success rate of chitosan and 3Mix in group I was 47% and 73% respectively, while radiographic success rate of chitosan and formula in group II were 50% and 80% respectively, also the radiographic success rate of formula and 3 Mix in group III was 90% and 80% respectively .

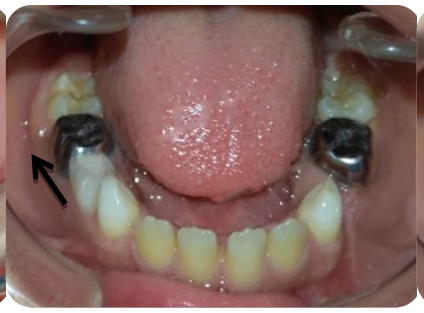
There was a statistically significant difference between the tested materials in group I and group II. Table (1)

Table (1): Overall clinical and radiographic success rates of the tested materials after 18 months follow up.

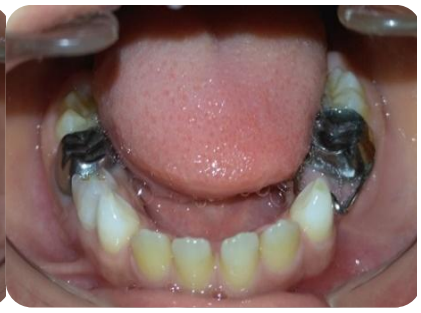
Overall clinical success rate					
Groups		**Success**	**Failure**	χ^2	^{FE}p
		n (%)	**N (%)**		
Group I	Chitosan	7 (36%)	12 (64%)	3.539	□□□□□
	3 Mix	14 (74%)	5 (26%)		
Group II	Chitosan	8 (40%)	12 (60%)	8.047	□□□□□□
	Formula	17 (85%)	3 (15%)		
Group III	Formula	19 (95%)	1 (5%)	2.961	□□□□□
	3 Mix	15 (75%)	5 (25%)		
Overall radiographic success rate					
Groups		**Success**	**Failure**	χ^2	^{FE}p
		n (%)	**n (%)**		
Group I	Chitosan	9 (47%)	10 (53%)	2.736	□□□□□□
	3 Mix	14 (73%)	5 (27%)		
Group II	Chitosan	10 (50%)	10 (50%)	3.963	□□□□□□
	Formula	16 (80%)	4 (20%)		
Group III	Formula	18 (90%)	2 (10%)	0.776	□□□□□
	3 Mix	16 (80%)	4 (20%)		



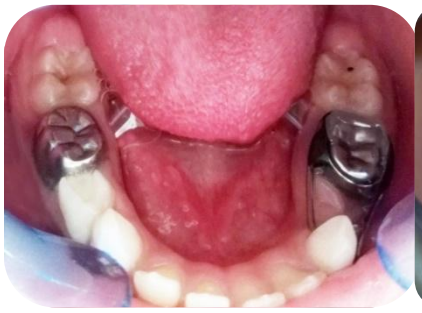
(a) Preoperative photo with bilateral abscesses related to bilateral 2nd molars.



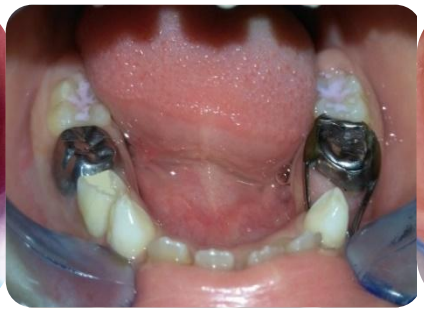
(b) Three months postoperative; healing of abscess and absence of fistula related to bilateral Es.



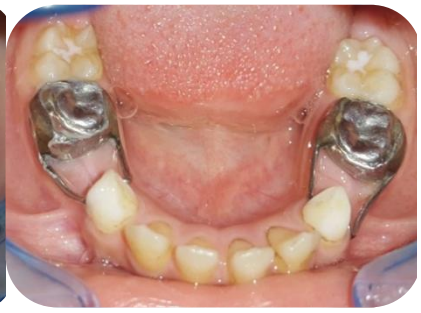
(c) Six months postoperative; there were no swelling and normal gingival tissue related to bilateral Es.



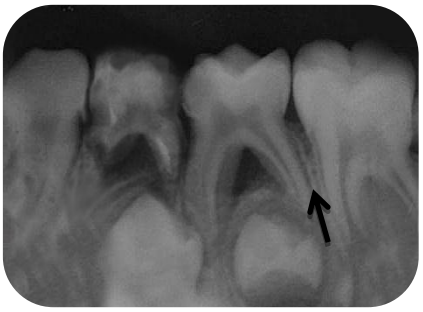
(d) Nine months postoperative; normal gingival tissues related to bilateral Es



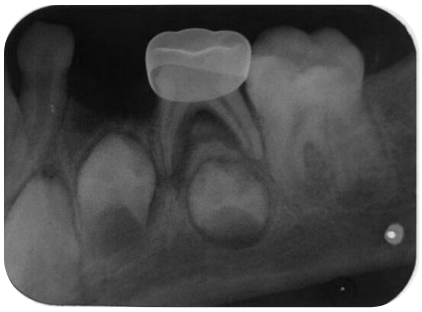
(e) Twelve months postoperative no changes related to bilateral Es.



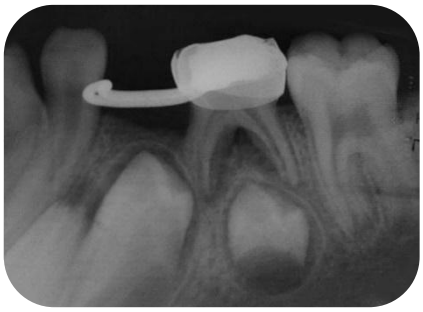
(f) 18 months postoperative no gingival changes related to bilateral Es.



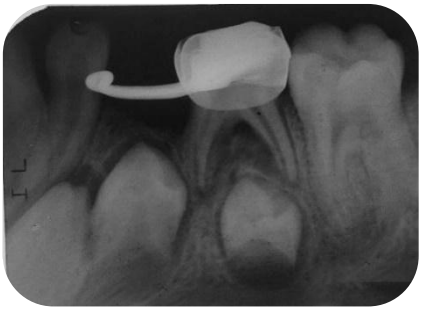
(a) Preoperative ;furcation radiolucency related to lower left E



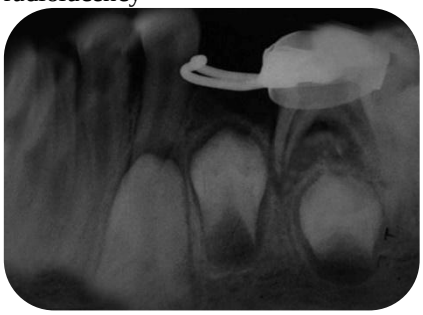
(b) three months postoperative; reduction in the size of furcation radiolucency



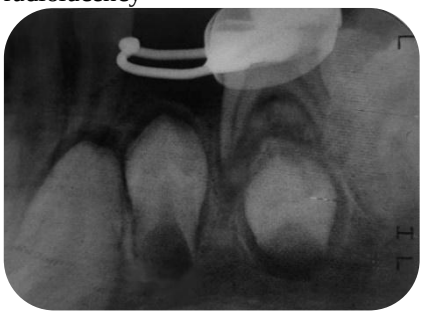
(c) Six months postoperative; ; more reduction in the size of furcation radiolucency



(d) Nine months postoperative; static size of furcation radiolucency



(e) Twelve months postoperative; static size of furcation radiolucency.



(f) 18 months postoperative; decrease in the size of furcation radiolucency

IV. Discussion

The successful management of chronically infected primary teeth is still a challenge owing to complex root canal system, difficulty in mechanical debridement, polymicrobial nature of infection, and root resorption. Hence, the importance of the sterilization of canal has improved the treatment prognosis. The concept of lesion sterilization and tissue repair therapy, which is a non-instrumentation endodontic treatment followed by placement of antibiotics combinations for controlling endodontic pathogens. [11,12]

Functional bioactive materials have received much attention in the scientific research in recent years. So, this study was conducted to assess the efficacy, release and antibacterial effect of chitosan, chitosan loaded antibiotics as a pulpotomy agent in non-vital primary molars.

The age group selected for this study was from four to seven years to reserve the primary molars till the time of exfoliation, as early loss of primary teeth lead to space problem .The selected cases in this study had bilateral non-vital primary lower molars to achieve the treatment on the three groups under the same environmental factors for accurate results.

Non-vital pulpotomy has been advocated when the inflammatory process affecting the coronal pulp and extends to the radicular pulp leading to an irreversible change in the pulp tissue. Another application for this technique is when the pulp is completely non vital with abscess formation [13].

Chitosan was chosen for this study as it is non-toxic, biocompatible and biodegradable material; these properties make chitosan an ideal material to be used as novel drug delivery systems having the quality of extending the release of drugs over a period of time, which improves drug solubility, stability, enhancing efficacy and reduced toxicity [14].

In the current study, 3Mix was used locally as it is more effective when applied directly on infected tissue; furthermore it is effective in decreasing the number of microbial load and promotes normal healing process. [15]

The drug combination comprises a metronidazole, ciprofloxacin and minocycline but discoloration of teeth being a disadvantage, so amoxicillin was used. [16] Macrogol and propylene glycol are specifically used to increase penetration into the dentinal tubules even in the presence of anatomical aberrations and blocked canals. [17]

In this study, the clinical success rate of chitosan was 36% and 40% in group I and II respectively, these results correlate with microbial data which reflect good sensitivity for the antibacterial effect of chitosan but in very high concentration (25mg/ml) to kill the bacteria, but such concentration is difficult to exist in the biological situation.

While, the clinical success rate 3Mix was 74% ,75 % in group I and III respectively, these findings agreed with Trairatvorakul and Detsomboonrat[18], they reported that the clinical success rate was (75%). However this study was disagreed with the study conducted by Prabhakar et al. [19] , Takushige et al. [20] and Nakornchai et al. [21] , who reported higher clinical success rate that were (93%),(100%) and (100%) respectively; this may be related to the difference in sample size and follow up periods.

Whereas, the clinical success rate of formula was 85%, 95 % in group II and III respectively, these results coincide with Shaik et al[22] who reported that combination of chitosan with 3Mix achieved better results than the combination of 3Mix with saline. This may be attributed to the effect of chitosan as a localized drug delivery device which could release antibiotics in an active form slowly and over a long period of time.

Regarding radiographic success rate of chitosan, it was 47% and 50% in group I and II respectively, these results may be attributed to that the weak antibacterial activity of chitosan. In addition, cross linked chitosan is poorly soluble and isn't expected to have the solubility requirements for pharmaceutical activity.

While, the radiographic success rate of 3Mix was 73% ,80 % in group I and III respectively, these findings agreed with the results obtained by Nakornchai et al. [21] and Prabhakar et al. [19]. On the other hand, the present study disagreed with Trairatvorakul and Detsomboonrat[18], their study showed low radiographic success rate (36.7%). This may be attributed to their different radiographic evaluation criteria as they considered cases with the static radiolucency as failure cases.

On the other hand, the radiographic success rate of formula in the present study was 80%, 90 % in group II and III respectively; these results may be attributed to that the release pattern which provide initial rapid release with sustained release over extended period of time.

In the present study, an explanation for the difference between the clinical and radiographic success rates may be related to the fact that the chronic inflammation of the pulp may be present silent without clinical signs. [23].

V. Conclusions

- Chitosan based antibiotics showed high clinical and radiographic success rate compared to chitosan and 3 Mix as a non-vital pulpotomy agent in primary teeth.

- The developed formulae liberated the drugs with a release pattern ensuring availability of drugs immediately after application with a depot effect that maintains the antibacterial effect for extended periods of time.

VI. Recommendations

- Chitosan based antibiotics can be used as a simple alternative technique for treatment of non-vital primary teeth.
- In vitro in vivo correlation studies are recommended.

References

[1]. Ghoddusi J, Forghani M and Parisay I. New approaches in vital pulp therapy in permanent teeth. Iran endod j 2014; 9(1):15-22.
[2]. Narayanan L and Vaishnavi C. Endodontic microbiology. J Conserv Dent 2010; 13(4): 233-239.
[3]. Orstavik D, Kerekes K, and Molven O. Effects of extensive apical reaming and calcium hydroxide dressing on bacterial infection during treatment of apical periodontitis. Int Endod J 1991;24(1):1-7.
[4]. Chong BS and Pitt Ford TR. The role of intracanal medication in root canal treatment. Int Endod J 1992; 25(2): 97-106.
[5]. Sain S, Reshmi J, Anandaraj S, SageenaG, Jyoti S and Sheen A. Lesion Sterilization and Tissue Repair-Current Concepts and Practices. Int J of Clini Pediatr Dent 2018; 11(5): 446-450.
[6]. Zhao D, Sun S, Gao B, Guo S and Zhao K. Biomedical applications of chitosan and its derivative nanoparticles. Polymers (Basel) 2018; 10(4): 462-463.
[7]. Husain S, Al-Samadani KH, Najeeb S, Zafar MS, Khurshid Z and Zohaib S. Chitosan biomaterials for current and potential dental applications. Materials (Basel) 2017; 10(6).
[8]. Malik S, Taneja S ,Chadha R and Kumari M. Effect of chitosan on sustained release of chlorhexidine an in vitro study. J Dent Specialities 2016; 4(1): 21-25.
[9]. Trairatvorakul C and Chunlasikaiwan S. Success of pulpectomy with zinc oxide-eugenol vs calcium hydroxide/iodoform paste in primary molars: a clinical study. Pediatr Dent 2008; 30(4): 303-308.
[10]. Chen K and Hollender L. Digitizing of radiographs with a flatbed scanner. J Dent 1995; 23(4): 205-208.
[11]. Carrotte V. A clinical guide to endodontics. Brit Dent J 2009; 206(2): 79-84.
[12]. Reddy G, Sridevi E, Sankar A, Pranitha K. Pratap S and Vinay C. Endodontic treatment of chronically infected primary teeth using triple antibiotic paste: An in vivo study. J Conserv Dent 2017; 20(6): 405-410.
[13]. Llewelyn D. UK national clinical guidelines in paediatric dentistry. The pulp treatment of the primary dentition. Int J Paediatr Dent 2000; 10(3): 248-252.
[14]. Erwin M, Faller, E,Ramachandra S,Datuk P and Abdullah F. chitosan: a vehicle to carry active drug molecules into the diseased periodontal site. Guident, 2015.
[15]. Agarwal M, Das U and Viswanath D. A Comparative Evaluation of Noninstrumentation Endodontic Techniques with Conventional ZOE Pulpectomy in Deciduous Molars: An in vivo Study. World J Dent 2011; 2: 187-192.
[16]. Chakraborty B, Nayak A and Rao A, Efficacy of Lesion Sterilization and Tissue Repair in Primary Tooth with Internal Resorption: A Case Series. Contemp Clin Dent 2018; 9(2): 361-364.
[17]. Cruz E, Kota K ,Huque J , Iwaku M and Hoshino E. Penetration of propylene glycol into dentine. Int Endodo J 2002; 35(4): 330-336.
[18]. Trairatvorakul C and Detsomboonrat. Success rates of a mixture of ciprofloxacin, metronidazole, and minocycline antibiotics used in the noninstrumentation endodontic treatment of mandibular primary molars with carious pulpal involvement. Int J Paediat Dent 2012; 22(3): 217-227.
[19]. Prabhakar A ,Sridevi E, Raju O and Satish V. Endodontic treatment of primary teeth using combination of antibacterial drugs: An in vivo study. J Indian Soc Pedod Prev Dent 2008; 26(5): 5-7.
[20]. Takushige T, Cruz E, Asgor M and Hoshino E. Endodontic treatment of primary teeth using a combination of antibacterial drugs. Int Endod J 2004; 37(2): 132-138.
[21]. Nakornchai S, Banditsing P and Visetratana N. Clinical evaluation of 3Mix and Vitapex as treatment options for pulpally involved primary molars. Int J Paediatr Dent 2010; 20(3): 214-221.
[22]. Shaik J, Garlapati R,Nagesh B , Sujana V, Jayaprakash T and Naidu S. Comparative evaluation of antimicrobial efficacy of triple antibiotic paste and calcium hydroxide using chitosan as carrier against Candida albicans and Enterococcus faecalis an in vitro study. J Conserv Dent 2014; 17(4): 335-339.
[23]. Fuks A, Eidelman E, Cleaton P and Michaeli Y. Pulp response to ferric sulfate, diluted formocresol and IRM in pulpotomized primary baboon teeth. ASDC J Dent Child 1997; 64(4): 254-259.

Lamis A. Abo_Elyazid, et. al. "Chitosan and Chitosan Loaded Antibiotics as a Pulpotomy Agent in Non-Vital Primary Molars."*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(06), 2021, pp. 22-27.