ACTA SCIENTIFIC DENTAL SCIENCES (ISSN: 2581-4893)

Volume 3 Issue 2 February 2019

Research Article

Effect of Tri-Antibiotic Paste on Tissue Repair Capacity of Rat's Pulp

Rasha H Al-Serwi[1], Hanaa Mahmoud Shalan[2]* and Mohammed E Grawish[3]

[1]*Associate Professor of Oral Biology, Faculty of Dentistry, Mansoura University, Egypt*

[2]*Associate Professor of Pediatric Dentistry, Faculty of Dentistry, Mansoura University, Egypt*

[3]*Professor of Oral Biology, Faculty of Dentistry, Mansoura University, Egypt*

***Corresponding Author:** Hanaa Mahmoud Shalan, Associate Professor of Pediatric Dentistry, Faculty of Dentistry, Mansoura University, Egypt.

Received: October 23, 2018

Abstract

Background: Vital pulp therapy for cariously exposed teeth remains one of the most controversial issues in the dental field. Tri-antibiotic paste (3Mix-MP) is effectively used for sterilization of root canals and healing of periapical pathology.

Aim: Study aimed to investigate rats' pulp response to tri-antibiotic paste.

Methods: Fifty-two albino rats were randomly allocated into three groups. Group I (n = 4) received no treatment. Teeth of group II (n = 24) with exposed pulp were directly capped with 3Mix-MP, while pulps of group III (n = 24) capped with calcium hydroxide. Eight rats from groups II and III were euthanized at 2, 15 and 30 days. Specimens were stained with H&E and examined by light microscope. Data was statistically analyzed using Mann-Whitney and Wilcoxon signed rank tests.

Results: After 2 days, the exposure area of group II was obstructed by fibrous tissue, inflammatory cells. 15 days later, exposure sites were completely obstructed with more fibrous tissue. Amount of fibrous tissue and collagen hyalinization were decreased after 30 days. Group III showed; superficial areas of clot necrosis and small zone of fibrous tissue beneath necrotic tissue, 2 days post capping. Reparative dentin was formed after 15 days and complete dentin bridge was seen after 30 days. Significant differences were observed between 2 days versus 15 and 30 days and 15 versus 30 days for groups II and III.

Conclusions: Tri-antibiotic paste is biologically compatible and maintaining pulp integrity but it hasn't the potentiality to induce dentin bridge formation.

Keywords: 3Mix-MP Tri-antibiotic Paste; Calcium Hydroxide; Dental Pulp; Tissue Repair

Introduction

Tissue damage at sites of injury compromises the pulpal extracellular matrix to mediate reparative events. Thus, providing a suitable matrix to encourage cell migration and differentiation at such sites is of paramount importance [1]. Dental pulp exposure favors the spread of pathogenic bacteria from the contaminated dentin to the exposed dental pulp. Pulp inflammatory cells control the infection and immune cells tend to slow down the progression of the lesion [2]. In addition, the dental pulp contains multipotent undifferentiated progenitor cell that has the capacity for repair and therefore reparative dentin is formed beneath sites of decayed and/or fractured dentin in the pulp chamber [3].

New treatment strategies should be developed based on well-recognized clinical requirements and understanding the related biological events [4]. Vital pulp therapy for cariously exposed teeth remains one of the most controversial issues in the dental field. Because a vital, functioning pulp has the capability of initiating several defense mechanisms against bacterial invasion, it is mandatory to maintain the vitality of an exposed pulp instead of replacing it with a root filling material following pulp exposure [5]. Treatment of an exposed vital pulp can be accomplished through sealing the pulpal wound with a material such as calcium hydroxide or mineral trioxide aggregate to facilitate the formation of reparative dentine and the maintenance of a vital pulp [6].

Antimicrobial scaffolds are required to be toxic to bacterial cells, while promoting local tissue regeneration and minimizing the adverse inflammatory events [7]. Hargreaves., *et al*. in 2014 mention that a scaffold is needed to permit the ingrowth of tissue [8]. Triantibiotic paste (TAP) 3Mix-MP consisting of metronidazole, minocycline and ciprofloxacin with the vehicles macrogol ointment and propylene glycol has been used for decontamination of young permanent teeth aiming the regeneration of dental pulp tissue [9]. Metronidazole is a nitroimidazole compound that exhibits a broad spectrum of activity against anaerobic bacteria. Minocycline is a semisynthetic derivative of tetracycline with a similar spectrum of activity. Ciprofloxacin, a synthetic fluoroquinolone, has a bactericidal mode of action [10].

Macrogol ointment (polyethylene glycol) is a polyether that is used in a host of products and believed to have a low degree of toxicity. Propylene glycol liquid is an organic substance used in various medicines and generally regarded as safe [11]. The goal of the present study was to evaluate the response of the exposed incisor rats' dental pulp to 3Mix-MP TAP, qualitatively and quantitatively. The null hypothesis of the present study was that 3Mix-MP TAP has a benign effect on the exposed incisor rats' dental pulp.

Materials and Methods

Study design

All procedures were performed according to the institutional standards for the care and use of experimental animals at the Medical Experimental Research Center (MERC), Mansoura University, Egypt. A total of 52 male Wistar albino rats (150 - 200g) were used for the study. Before the experiment, rats were fed standard rat chow and water ad libitum and housed in cages with controlled temperature 22°C and 12h light/dark cycle for 1 week. Rats were randomly allocated into three groups. Group I (negative control, n = 3), group II (positive control, n = 24) and group III (tested one, n = 24). Group I rats received no treatment. The lower incisor pulps of group II and group III rats were directly capped with 3Mix-MP and calcium hydroxide, respectively. One-third numbers from each group were euthanized according to experimental periods of 2 days, 15 days and 30 days.

3Mix-MP preparation

Commercially prepared chemotherapeutic agents, namely, metronidazole (Flagyl, Sanofi-Aventis, Thailand), ciprofloxacin (Ciprobay, Bayer, Germany), and minocycline (Minocin, Wyeth, China) were used. The 3Mix-MP TAP was prepared according to the method described by Takushige., *et al*. in 2004 [12]. Briefly, after removal of the capsules or coating materials that enclose the drug products, each of the drugs was pulverized using a mortar and pestle. The powdered antibiotics were stored and sealed in airtight containers separately from moisture and light. The same amount of each drug powder (1: 1: 1) was mixed together. After that, the mixed drugs were combined with macrogol and propylene glycol (Vidhyasom Co., Ltd, Bangkok, Thailand) to form an ointment consistency. 3Mix-MP preparation was prepared and used on the day of preparation.

Operative procedures

The rats were weighed prior to anesthesia so that the dosage of anesthetic could be calculated. Anesthesia was performed using an intraperitoneal injection of diazepam (0.05 ml/100 g, Roche, Welwyn Garden City, England) and ketamine hydrochloride (0.1 ml/100g, Parke-Davis, Morris Plains, NJ, USA). After sedation, the animal was placed on a surgical table in supine position and lower lip was retracted to expose the lower incisors. Before cavity preparation, the teeth were disinfected with 0.2% chlorhexidine gluconate (Corsodyl, Smithkline Beecham, UK). The lower incisors were isolated with buccal and lingual cotton rolls and the pulp-capping procedures were performed according to the method described by Orhan., *et al.* in 2012 [13].

Briefly, Class V cavities were prepared on the right and left mandibular teeth of each rat by micromotor handpiece with a cylindrical diamond (ISO # 004, NTI, Kahla, Germany) running at a maximum 3000 rpm until the pulp was visible through the transparent dentin floor of the cavity. The cavities were prepared under permanent cooling with water spray. A new bur was used on every fifth cavity to avoid excessive heating. The preparations were cut directly above the free gingiva, parallel to cemento-enamel junction. Pulp exposure was subsequently created mechanically and standardized using 0.15 mm diameter tip of endodontic explorer (DG16; Hu-Friedy Co, Chicago, IL, USA). Controlled pulpal bleeding and remnant of blood was removed by a sterile paper point soaked in sterile saline across the exposure site. One operator performed all clinical procedures. The respective teeth were treated according to a predetermined protocol as following; lower incisors of group II rats were capped with freshly prepared 3Mix-MP while lower incisors of group III rats were directly capped with calcium hydroxide (Dycal, DENTSPLY, Milford, DE, USA) as the gold standard. All cavities were then filled with resin-modified glass ionomer cement (GC Fuji Plus, GC Corp., Tokyo, Japan). After the operation the rats were supervised according to the protocol of MERC with a special soft diet and supporting analgesia.

Clinical examination and samples processing

The rats were sedated by halothane and the supporting tissues of the teeth were clinically evaluated for possible tissue alterations, such as redness, swelling, and suppuration. After the respective monitoring periods, rats were chosen from each treatment group and the rats were anesthetized then euthanized with over dosage of i.p. injection of thiopental (5 ml/100g, Triopental, Biochemie GmbH, Vienna, Austria). The mandibular segment containing incisors teeth of the rats were placed in 10% buffered formalin for 24h at 4°C and then decalcified for 4 weeks in ethylenediaminetetraacetic acid. The specimens were embedded in paraffin and 5 µm thickness serial sections were prepared through the exposure site. Light microscopic examination was performed in haematoxylin and eosin stained sections for histological changes.

Histologic assessment

The following criteria [14] were used to assess the specimens:

1. Inflammatory cell response: inflammatory cell infiltration of the pulp tissue was scored as (0), absence of inflammatory cells; (1), a few scattered inflammatory cells; (2), moderate inflammatory cell infiltration around the exposure site; and (3), heavy inflammatory cell infiltration of the coronal pulp or abscess formation.
2. Tissue necrosis: Pulp tissue organization was scored as (0), no necrosis or presence of complete tissue organization in coronal and radicular pulp; (1), partial necrosis to the area under capping material (2), partial necrosis to the half or more of the coronal pulp tissue and (3), complete tissue necrosis of the coronal pulp.
3. Hard tissue formation: The presence of discontinuous or continuous hard tissue around the exposure site in all the sections examined was scored as (0), no dentin bridge (1), partial calcified bridge formation and (2), complete calcified bridge formation.

Statistical analysis

The obtained data were analyzed using Mann-Whitney U test for pairwise group comparison. Wilcoxon signed rank test was used for the group comparison at different time periods.

Results

Histological results

All procedures were performed according to the institutional standards for the care and use of experimental animals at the Medical Experimental Research Center (MERC), Mansoura University, Egypt. A total of 52 male Wistar albino rats (150 - 200g) were used for the study. Before the experiment, rats were fed standard rat chow and water ad libitum and housed in cages with controlled temperature 22°C and 12h light/dark cycle for 1 week. Rats were randomly allocated into three groups. Group I (negative control, n = 3), group II (positive control, n = 24) and group III (tested one, n = 24). Group I rats received no treatment. The lower incisor pulps of group II and group III rats were directly capped with 3Mix-MP and calcium hydroxide, respectively. One-third numbers from each group were euthanized according to experimental periods of 2 days, 15 days and 30 days.

Figure 1: Representative decalcified section of group I showing (A) rat dental pulp (P) with highly cellular connective tissue. Inset, higher magnification showing tubular dentin (D), predentin (Pd), odontoblastic layer (Od). Group II after 2 days (B) the exposed area is obstructed by fibrous tissue (Ft) and the whole pulp infiltrated with inflammatory cells (Ic). Inset, cytoplasmic vacuolization (Vac) of the pulpal cells and partial collagen hyalinization (Hy). Group II after 15 days (C) the pulpal exposure site completely obstructed with more fibrous tissue (Ft), greater area of collagen hyalinization (Hy) with diffuse pulp disorganization (Dis). Inset, higher magnification for pulpal tissue disorganization (Dis) and hyalinization (Hy). Group II after 30 days (D) little amounts of fibrous tissue and collagen hyalinization (Hy) with discrete pulp disorganization (Dis) close to the pulp exposure site. Group III after 2 days (E) a small superficial areas of clot necrosis (Ne) as well as small zone of fibrous tissue (Ft) beneath necrotic tissue. Inset, higher magnification for the zone of fibrous tissue (Ft). Group III after 15 days (F) formation of a reparative dentin bridge (Db) at the site of the exposure. Inset, a cellular dentin bridge (Db). Group III after 30 days (G) complete dentin bridge (Db) formation and normal highly cellularized pulpal connective tissue (p) (H and E x100 and inset x200).

Statistical results

Mann-Whitney U test revealed a significant difference between group II and group III regarding amount of inflammatory cell infiltrate and the areas of tissue necrosis at all examination periods. In addition, a significant difference was found between the two groups regarding amount of hard tissue formation at 15 and 30 days examination periods. No significant difference was found between the two groups at 2 day examination period (P = 1.000) (Table 1). Wilcoxon signed rank test demonstrated significant differences between 2 and 15 days, 2 and 30 days and 15 and 30 days examination periods for group II and III for the parameters tested except the amount of tissue necrosis at the period of 15 days compared to 30 days for group III (P = 0.109) (Table 2).

Periods	2 day					15 day					30 day				
Mann-Whitney	Rank		Mann-Whitney	Z	Sig	Rank		Mann-Whitney	Z	Sig	Rank		Mann-Whitney	Z	Sig
	II	III				II	III				II	III			
Inflammatory cell response	28.77	20.23	185.5	-2.645	0.008	32.31	16.69	100.5	-4.223	0.000	30.50	18.50	144.0	-3.338	0.001
Tissue necrosis	29.67	19.33	164.0	-2.973	0.003	32.50	16.50	96.0	-4.529	0.000	28.50	20.50	192.0	-2.514	0.012
Hard tissue formation	24.50	24.50	288.0	.000	1.000	17.63	31.38	123.0	-3.968	0.000	17.50	31.50	120.0	-4.399	0.000

Table 1: Mann-Whitney U test for pairwise group comparison and its statistical significance.

Variable Groups	Inflammatory cell response ranks						Tissue necrosis ranks						Hard tissue formation ranks					
	Group II			Group III			Group II			Group III			Group II			Group III		
Wilcoxon test	-ve	+ve	Sig	-ve	+ve	Sig	-ve	+ve	Sig	-ve	+ve	Sig	-ve	+ve	Sig	-ve	+ve	Sig
2day*15 day	5.94	0.00	0.005	10.50	1.50	0.000	7.15	6.50	0.046	7.08	6.00	0.003	0.00	11.50	0.000	0.00	12.50	0.000
2 day*30 day	10.00	0.00	0.000	11.50	0.00	0.000	8.00	0.00	0.000	10.00	0.00	0.000	0.00	12.50	0.000	0.00	12.50	0.000
15 day*30 day	7.92	5.00	0.006	6.00	6.00	0.007	8.00	0.00	0.000	6.19	5.50	0.109	5.50	6.05	0.008	0.00	5.00	0.003

Table 2: Wilcoxon signed rank test for group comparison between 2, 15 and 30 days and its statistical significance.

Discussion

Despite the progress made in the field of pulp biology, there is no single therapeutic regimen for direct pulp capping that can achieve, predictably and reliably, the goals of preserving tooth vitality and tooth function [15]. Calcium hydroxide being considered the gold standard for vital pulp therapy, it has been shown that calcium hydroxide seriously impeded the healing process [16]. With the advent of non-instrumentation endodontic treatment and lesion sterilization and tissue repair, local application of antibiotics has been investigated.

3Mix-MP TAP has been used for decontamination of young permanent teeth aiming the regeneration of dental pulp tissue [17]. *In vivo* researches, have shown that this specific combination of antibiotics is the most successful; but no study to date has confirmed that it is the most efficient one available [10,12,18,19]. Revascularization/Revitalization of open-apex primary incisors has become a viable treatment option, particularly in cases of traumatic pulp injuries [20]. In these cases, direct pulp capping might be indicated for maintaining pulp vitality and function [21].

Primary teeth shows close similarity to those is the rat incisors which called open rooted teeth that, refers solely to the large apical opening [22]. Regeneration in teeth with open apices presents multiple challenges for successful treatment. Depending upon the above concepts, the goal of the present study was to evaluate the response of the exposed incisor rats' dental pulp to 3Mix-MP TAP, qualitatively and quantitatively. Limited data available regarding histological reaction to the use of 3Mix-MP, thus the findings of this study can only be compared to other medicament used as a pulp capping.

In the present study, pulp response in group III after 2 days showed small superficial areas of clot necrosis as well as small zone of fibrous tissue beneath necrotic tissue. A pattern which was already described by several studies [23-25]. Most interesting was that during this period a significant difference was found between groups II and III. This might be attributed to the bactericidal activity provided by TAP in group II and the lower pH provided by calcium hydroxide in group III. The necrotic layer can serve as a surface on which pulp cells absorb, polarize, and transform to odontoblast like cells [26].

The production of fibrous tissue was a prominent feature in both groups, such character were also evident in a study of direct capping with platelet-rich plasma and enamel matrix derivative that showed dense reticular fiber deposition where odontoblast-like cells differentiate and organize to produce dentin [27]. A significant difference between groups II and III was found regarding amount of inflammatory cell infiltrate and the areas of tissue necrosis at all examination periods. The observed presence of a moderate amount of inflammatory cell infiltration within the pulp tissue is consistent with Browne*., et al.* [28] and Cox [29] as they stated that favorable pulpal responses accompanied by the presence of some inflammatory cells indicate a bacterial-tight seal preventing microleakage.

Regarding amount of hard tissue formation no significant difference was found between the two groups at 2 day examination period. According to Moazzami., *et al*. [30], the dentine bridge was histologically detectable after two weeks of pulp capping with mineral trioxide aggregate. In a recent study [31], one day of pulp capping dispersed dentin particles was visible as signs of mechanical trauma due to the pulp exposure procedure.

Two weeks after direct capping with 3Mix-MP TAP, the pulpal exposure sites was completely obstructed with more fibrous tissue formation underlined by greater area of collagen hyalinization with diffuse pulp disorganization which decreased after 30 days. The intense fibroblastic proliferation tends to isolate the exposure area [25]. Group treated with calcium hydroxide showed, formation of reparative bridge with a tubular dentin at the exposure site after 15 days. Later on, complete dentin bridge formation and normal highly cellularized pulpal connective tissue were seen after 30 days.

Formation of mineralized barrier was concluded to the formation of dentin bridge [32]. The density of odontoblast-like cells was suggested to be the most important factor influencing dentin bridge formation [33], whose potential depends on several pre- and post-operative factors such as pulp status, the prevention of bacterial infection, and the exposed pulpal size [34].

A significant difference was found between the two groups regarding amount of hard tissue formation at 15 and 30 days examination periods. Also, significant differences at different time periods for group II and III for the parameters tested except for the amount of tissue necrosis for group III at the periods 15 days compared to 30 days.

With respect to the hard tissue formation on the exposed pulp tissue, the average amount of generated hard tissue in the calcium hydroxide treated group was significantly better compared to the experimental group used 3Mix-MP TAP. It is well known that calcium hydroxide have a defect in the continuity of dentine bridge-like structures, allowing the penetration of microorganisms into the pulp tissue via microleakage from the cavity margin [35], and also its antimicrobial properties are lost [36]. Probably if evaluation period were longer, signs of complete dentinal bridge formation would be seen.

On the other hand TAP can maintain pulp tissue integrity as it contains both bactericidal (metronidazole, ciprofloxacin) and bacteriostatic (minocycline) agents [19]. Tetracycline causes inhibition of collagenases and matrix metalloproteinases also increase the level of interleukin-10, which is an anti-inflammatory cytokine. In addition, metronidazole and ciprofloxacin can generate fibroblasts. These fibroblast cells play a significant role in tissue regeneration by involving pulp progenitors via complement activation, which throws light on the probable reparative procedure of targeting pulp fibroblasts in dentin–pulp regeneration [37-40].

Also in this study, It was observed that 3Mix-MP seem to preserve pulp tissue and promote the regeneration of soft tissue. The nearly normal pulpal architecture indicates that the TAP has good biocompatibility and regeneration ability. The criteria that characterize a successful direct pulp capping vary among authors. Clinically successful pulp capping is considered if the tooth is free of symptoms, reacts adequately to sensibility tests and has a normal

radiographic appearance. However, the clinical criterion is inadequate for an evaluation of the long-term prognosis for teeth treated by pulp capping. Therefore, a critical evaluation of the results of pulp capping can only be made histologically [41].

Conclusion

Based on the present study, 3Mix-MP tri-antibiotic paste in pediatric dentistry seems to be optimistic. It is biologically compatible maintaining pulp integrity, but it hasn't the potentiality to induce dentin bridge formation. Further studies with a larger sample size and longer follow-up periods both clinically and histologically are recommended.

Conflict of Interest

All authors deny any conflict of interest.

Funding Statement

Not financially supported.

Bibliography

1. Dobie K., *et al*. "Effects of alginate hydrogels and TGF-beta 1 on human dental pulp repair in vitro". *Connective Tissue Research* 43.2-3 (2002): 387-390.

2. Colombo JS., *et al*. "Scaffolds to control inflammation and facilitate dental pulp regeneration". *Journal of Endodontics* 40.4 (2014): S6-S12.

3. Ishimoto K., *et al*. "Topical application of lithium chloride on the pulp induces dentin regeneration". *PLoS One* 10.2 (2015): e0121938.

4. Tziafas D. "Dentinogenic potential of the dental pulp: facts and hypotheses". *Endodontic Topics* 17.1 (2010): 42-64.

5. Ward J. "Vital pulp therapy in cariously exposed permanent teeth and its limitations". *Australian Endodontic Journal* 28.1 (2002): 29-37.

6. Lin LM and Rosenberg PA. "Repair and regeneration in endodontics". *International Endodontic Journal* 44.10 (2011): 889-906.

7. Johnson CT and García AJ. "Scaffold-based anti-infection strategies in bone repair". *Annals of Biomedical Engineering* 43.3 (2015): 515-528.

8. Hargreaves KM., *et al*. "Paradigm lost: a perspective on the design and interpretation of regenerative endodontic research". *Journal of Endodontics* 40.4 (2014): S65-S69.

9. Trairatvorakul C and Sastararuji T. "Indirect pulp treatment vs antibiotic sterilization of deep caries in mandibular primary molars". *International Journal of Paediatric Dentistry* 24.1 (2014): 23-31.

10. Windley W 3rd., *et al*. "Disinfection of immature teeth with a triple antibiotic paste". *Journal of Endodontics* 31.6 (2005): 439-443.

11. Nalawade TM., *et al*. "Bactericidal activity of propylene glycol, glycerine, polyethylene glycol 400, and polyethylene glycol 1000 against selected microorganisms". *Journal of International Society of Preventive and Community Dentistry* 5.2 (2015): 114-119.

12. Takushige T., *et al*. "Endodontic treatment of primary teeth using a combination of antibacterial drugs". *International Endodontic Journal* 37.2 (2004): 132-138.

13. Orhan EO., *et al*. "Odontoblast-like cell numbers and reparative dentine thickness after direct pulp capping with platelet-rich plasma and enamel matrix derivative: a histomorphometric evaluation". *International Endodontic Journal* 45.4 (2012): 317-325.

14. Koliniotou-Koumpia E and Tziafas D. "Pulp responses following direct pulp capping of healthy dog teeth with dentine adhesive systems". *Journal of Dentistry* 33.8 (2005): 639-647.

15. Koh ET., *et al*. "Mineral trioxide aggregate stimulates A biological response in human osteoblasts". *Journal of Biomedical Materials Research* 37.3 (1997): 432-439.

16. Mathewsen RJ and Primosch RE. "Fundamental of pediatric Dentistry". 3rd edition. Chicago: Quintessence Publishing Co (1995): 259.

17. Vijayaraghavan R., *et al*. "Triple antibiotic paste in root canal therapy". *Journal of Pharmacy and Bioallied Sciences* 4.2 (2012): S230-233.

18. Banchs F and Trope M. "Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol?" *Journal of Endodontics* 30.4 (2004): 196-200.

19. Iwaya SI., *et al*. "Revascularization of an immature permanent tooth with apical periodontitis and sinus tract". *Dental Traumatology* 17.4 (2001): 185-187.

20. Forghani M., *et al*. "Apexogenesis and revascularization treatment procedures for two traumatized immature permanent maxillary incisors: a case report". *Restorative Dentistry and Endodontics* 38.3 (2013): 178-181.

21. Stanley HR. "Pulp capping: conserving the dental pulp--can it be done? Is it worth it?" *Oral Surgery, Oral Medicine, Oral Pathology* 68.5 (1989): 628-639.

22. Wiggs B and Lobprise H. "Dental anatomy and physiology of pet rodents and lagomorphs". In Crossley DA, Penman S (eds): Manual of Small Animal Dentistry, ed 2. Cheltenham, British Small Animal Veterinary Association (1995): 68-73.

23. Schröder U. "Effects of calcium hydroxide-containing pulp-capping agents on pulp cell migration, proliferation, and differentiation". *Journal of Dental Research* 64 (1985): 541-548.

24. Hasheminia SM., *et al*. "A comparative study of three treatment methods of direct pulp capping in canine teeth of cats: a histologic evaluation". *Lasers in Medical Science* 25.1 (2010): 9-15.

25. de Albuquerque DS., *et al*. "Histologic evaluation of pulpotomy performed with ethyl-cyanoacrylate and calcium hydroxide". *Brazilian Oral Research* 20.3 (2006): 226-230.

26. Veis A. "The role of dental pulp--thoughts on the session on pulp repair processes". *Journal of Dental Research* 64.4 (1985): 552-554.

27. Maden M., *et al*. "The inflammatory response of the pulp after direct capping with platelet-rich plasma and enamel matrix derivative: A controlled animal study". *Open Journal of Stomatology* 4 (2014): 14-21.

28. Browne RM., *et al*. "Bacterial microleakage and pulpal inflammation in experimental cavities". *International Endodontic Journal* 16.4 (1983): 147-155.

29. Cox CF. "Biocompatibility of dental materials in the absence of bacterial infection". *Operative Dentistry* 12.4 (1987): 146-152.

30. Moazzami F., *et al*. "A histological comparison of a new pulp capping material and mineral trioxide aggregate in rat molars". *Iranian Endodontic Journal* 9.1 (2014): 50-55.

31. Dammaschke T., *et al*. "Reaction of rat pulp tissue to Carisolv 'new gel'--a histocytological evaluation". *Australian Dental Journal* 51.1 (2006): 57-63.

32. Qudeimat MA., *et al*. "Calcium hydroxide vs mineral trioxide aggregates for partial pulpotomy of permanent molars with deep caries". *European Archives of Paediatric Dentistry* 8.2 (2007): 99-104.

33. Murray PE., *et al*. "Histomorphometric analysis of odontoblast-like cell numbers and dentine bridge secretory activity following pulp exposure". *International Endodontic Journal* 36.2 (2003): 106-116.

34. Tziafas D., *et al*. "Designing new treatment strategies in vital pulp therapy". *Journal of Dentistry* 28.2 (2000): 77-92.

35. Cox CF., *et al*. "Tunnel defects in dentin bridges: their formation following direct pulp capping". *Operative Dentistry* 21.1 (1996): 4-11.

36. Cox CF., *et al*. "Pulp capping of dental pulp mechanically exposed to oral microflora: a 1-2 year observation of wound healing in the monkey". *Journal of Oral Pathology* 14.2 (1985): 156-168.

37. Reynolds K., *et al*. "Pulp revascularization of necrotic bilateral bicuspids using a modified novel technique to eliminate potential coronal discolouration: a case report". *International Endodontic Journal* 42.1 (2009): 84-92.

38. Lakhani AA., *et al*. "Efficacy of Triple Antibiotic Paste, Moxifloxacin, Calcium Hydroxide And 2% Chlorhexidine Gel In Elimination of E. Faecalis: An In vitro Study". *Journal of Clinical and Diagnostic Research* 11.1 (2017): ZC06-ZC09.

39. Goswami S. "Lesion sterilization and tissue repair in pediatric dentistry". *SRM Journal of Research in Dental Sciences* 9.2 (2018): 79-82.

40. Chakraborty B., *et al*. "Efficacy of lesion sterilization and tissue repair in primary tooth with internal resorption: A case series". *Contemporary Clinical Dentistry* 9.2 (2018): 361-364.

41. Woehrlen AE Jr. "Evaluation of techniques and materials used in pulpal therapy based on a review of the literature: part I". *Journal of the American Dental Association* 95.6 (1977): 1154-1158.

Volume 3 Issue 1 January 2019