

Belarusian State Medical University, Minsk

INTRACANAL DISINFECTION AND MEDICAMENTS IN REGENERATIVE ENDODONTICS



Department of Pediatric dentistry

Shabnam Saleh, 5th course, medical faculty for international students

Scientific adviser: associated professor. PhD. M.Klenovskaya



Introduction:

Immature necrotic permanent tooth presents a distinctive challenge. Various treatment modalities have been employed to create hard tissue barrier at the apex, which includes non-vital pulp therapy with calcium hydroxide, apexification with mineral trioxide aggregate, pulp revascularization and regeneration. Regenerative endodontics is a novel modality which involves physiological replacement of the damaged structures of tooth like dentin, root and cells of the pulp-dentin complex.[1]

Root canal irrigation and disinfection is One of the most significant stages of root canal therapy, removing infectious microorganisms and microbial components from root canals to preventing re-infection of canals. Various chemical and mechanical methods have been used to reach this purpose. Ethylenediamine-tetra-acetic acid (EDTA), sodium hypochlorite (NaOCl) and chlorhexidine (CHX) are some of the best-known chemical components for root canal disinfection.[2]

In Recent years, the advent of nanomaterials and their ability in targeted drug delivery have led to significant progress in the disinfection of root canal and accessory canals. . Nanoparticles showed higher antibacterial potency because they have higher polycationic/polyanionic nature and higher charge density so their interaction with the bacterial cell is higher.[3]

Purpose, material and methods:

PURPOSE:

To review new approaches in intracanal disinfection and medicaments in regenerative endodontics And evaluate the results.

MATERIAL AND METHODS:

A primary search were performed within articles of the last ten years using PubMed and Google Scholar search motors and a total of 50 articles were recognized. The search was conducted by using these keywords: "polymers", "nanoparticles", "polymeric nanoparticles", "root canal disinfection", and "regeneration". Then, the studies were classified in the following order: root canal irrigation and disinfection, obturating materials, root-repair materials, regenerative endodontics therapy.

Concerns in Endodontic Disinfection:

- 1) Disinfection resistance is found more in teeth in comparison with soft tissues, this is mostly because of Tubular structure of dentin and presence of biofilm culture communities[4]
- 2) More numerous and faster bacterial growth can be found more in the coronal part of the canal in comparison with middle and apical part. [5]
- 3) Limitations in mechanical debridement in large canals
- 4) Bacterial resistance against antibiotics

Significant Effects of persisting or post operative infection on healing process in regenerative endodontic treatment:

- Perpetuation of inflammation within the area
- Decrease migratory capacity of stem cells
- Altered differentiation fate of stem cells(stem cells differentiated to osteoblast instead of odontoblast)[6]

Difficulties in bacterial disinfection of immature compared with mature teeth:

- Deeper tubular penetration of bacteria in immature teeth
- More complex anatomical structure of immature teeth leads to more difficult eradication
- Thin walls of immature teeth lead to limited mechanical debridement of root canals

- ❖ The degree of disinfection determines the success of the treatment.[7]

Disinfection in regenerative endodontic procedures (REPs):

REP can be performed in 2 ways :

- 1) Irrigant solutions
- 2) Intra-canal medicaments

Requirements of An Ideal Irrigant To Be Used in REPs:

- Chemical bacterial destruction
- Removal of disrupted biofilms
- Detoxify bacterial antigens
- Removing intracanal medicaments

NaOCl:

- NaOCl is an alkaline material with a PH ranging from 10.9 to 12
- Excellent bactericidal efficacy[8]
- Tissue dissolution capacity
- Effective hemostatic agent when used topically [9]

- ❖ 1.5% NaOCl concentration doesn't change in odontoblastic differentiation [10]
- ❖ Use of EDTA as the final Irrigant partially reversed the detrimental effects of NaOCl.
- ❖ 1.5% NaOCl is optimal for its dissolution and disinfecting capabilities followed by 17% EDTA as a final Irrigant to promote stem cell survival, attachment and differentiation.

Drawbacks of High Concentration NaOCl in REPs:

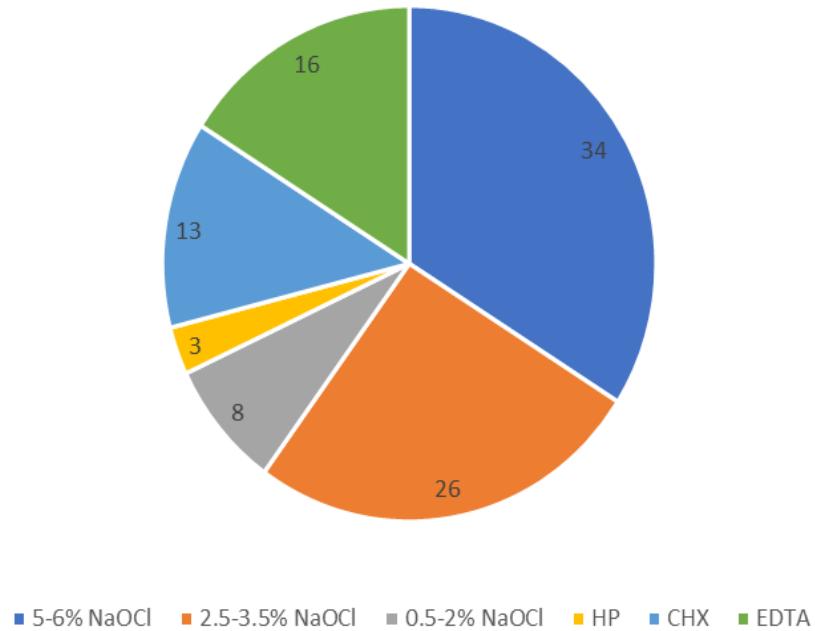
1) Direct effects:

- Decrease stem cell survival, decrease attachment and differentiation of stem cells [11]

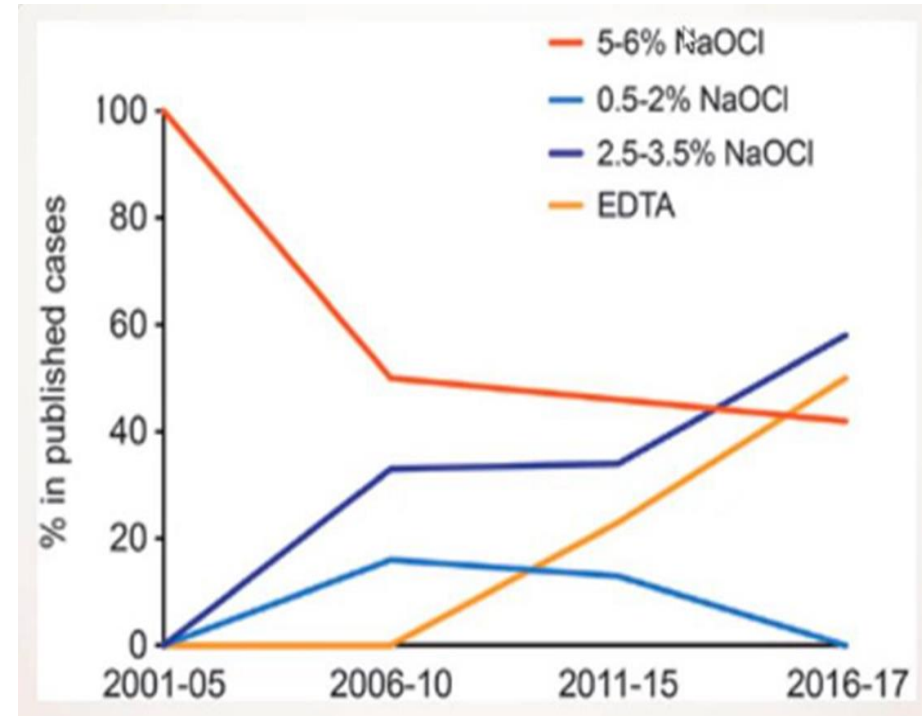
2) Indirect effects:

- Decrease Carbon and nitrogen content in dentin and leads to its demineralization [12]
- Clastic effect on dentin: resorptive defects [13]
- Decrease Odontoblastic differentiation
- Decrease dentin-derived growth factors
- Sustained deleterious effects on dentin

Irrigants Used in REPs from 2001 to 2017:



PIC. 1 - RUPAREL ET AL; CLINICAL APPROACH IN ENDODONTIC REGENERATION, 2017.



PIC. 2 - RUPAREL ET AL; CLINICAL APPROACH IN ENDODONTIC REGENERATION, 2017.

Intracanal Antimicrobial Agents:

General Objectives and Considerations for Use of Intracanal Antimicrobial Agents in RET Cases [14]

- Broad spectrum
- Biocompatible and anti-inflammatory
- Low minimum inhibitory concentration for key pathogens
- Infiltrates biofilm
- Minimal effect on dentin matrix proteins
- Reduced discoloration of enamel and dentin
- Substantivity and residual antibiofilm effect
- Ability to be incorporated into, and remain effective in, common carriers and biodegradable scaffolds
- Specific efficacy to patient's own microflora

Triple Antibiotic Paste (TAP):

Most commonly intracanal medicaments was TAP (triple antibiotic paste) which is Initially developed by Hoshino et al. 1996:

- Disinfect Escherichia coli infected dentin
- Efficient against a wide range of pathogens in necrotic teeth
- May not eliminate all cultivable bacteria
- 75% of pathogen elimination by TAP



PIC. 3 - TRIPLE ANTIBIOTIC PASTE

Composition of TAP :

1) Metronidazole (METRO)

- A nitroimidazole compound
- Toxic to anaerobes
- Effective against protozoa

2) Ciprofloxacin (CIPRO)

- Synthetic fluoroquinolone
- Bactericidal effect
- Effective against G- bacteria / limited effectiveness against G+. Many anaerobic bacteria are resistant to ciprofloxacin

3) Minocycline (MINO)

- Bacteriostatic effect
- Activity against G+ and G- bacteria
- Increase amount of Interleukin-10
- A strong anti-inflammatory effect (like all tetracyclines)
- Improve revascularization

Double Antibiotic Paste (DAP):

First reported by Iwaya et al. in 2001 as an intracanal medicament in a clinical case of REP, it is composed of CIPRO and METRO.

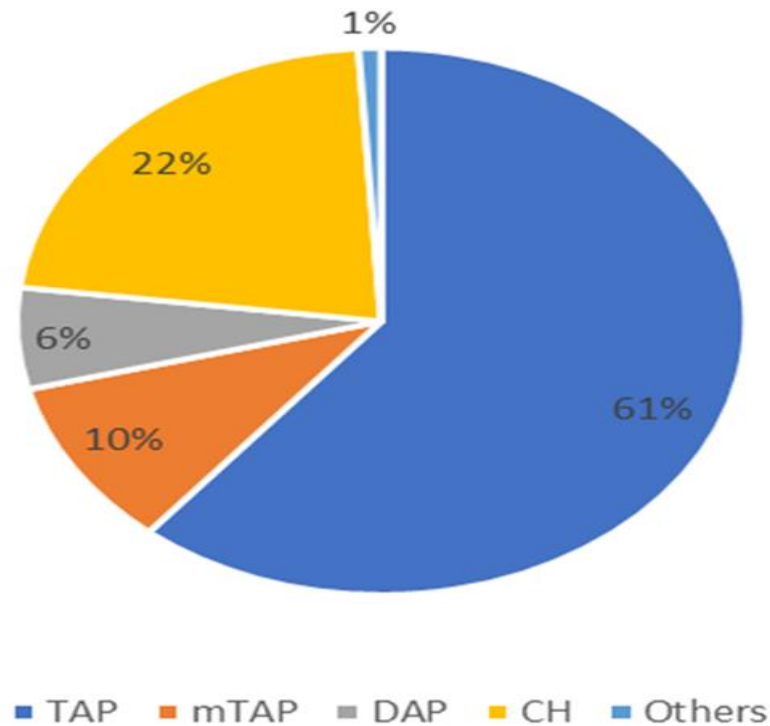
Advantages:

Significant direct antibacterial effects regardless of the bacterial biofilms at 5 mg/mL

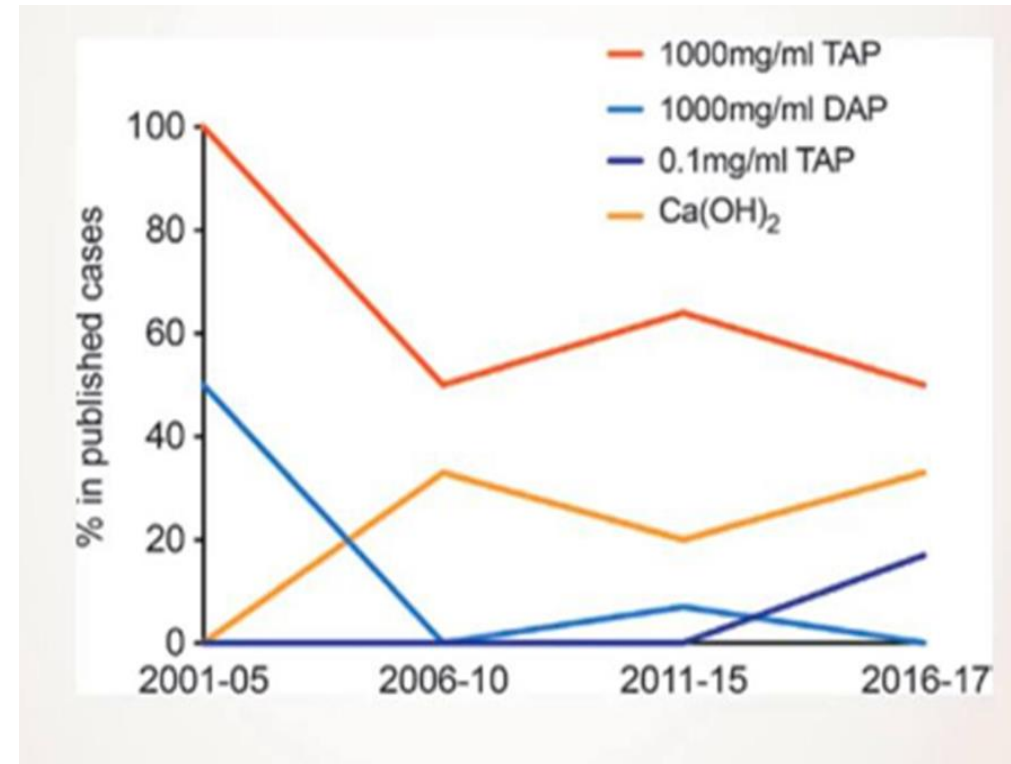
At 1 mg/mL:

- A significant decrease in amount of *E. faecalis* and *P. intermedia* biofilms
- No significant decrease in viability, proliferation and mineralization of dental pulp stem cells
- Optimal for antibacterial properties against endodontic pathogens
- DAP + EDTA combination have significant increase in dental pulp stem cells attachment compared to treatment with the DAP alone
- ❖ Residual antimicrobial effect on dentin in 5 mg/mL is more than 1 mg/mL

Medicaments Used in REPs from 2001 to 2017:



PIC. 4 - RUPAREL ET AL; CLINICAL APPROACH IN ENDODONTIC REGENERATION, 2017



PIC. 5 - RUPAREL ET AL; CLINICAL APPROACH IN ENDODONTIC REGENERATION, 2017

Challenges and Strategies to Improve Disinfection:

Appropriate microbial targeting:

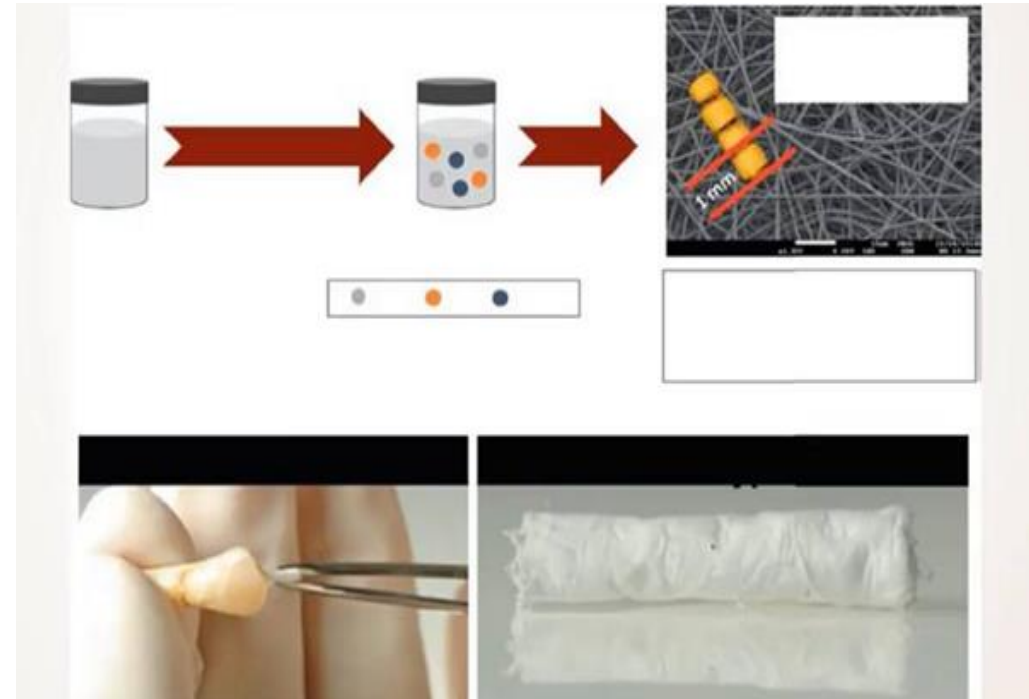
In the case of resistance to other antibiotics during elimination of bacteria, following alternatives can be used:

- 1) Augmentin:** 100% efficacy against all 24 tested endodontic pathogens[15], Could potentially improve clinical outcomes.
- 2) Metronidazole:** least efficacy ,low bacteriostatic efficacy
- 3) Clindamycin:** least efficacy

Use of Antibiotic-Eluting Fibers as Drug Delivery Systems:

Nanofibers can be manufactured from a variety of natural polymers which include: chitosan, fibronectin, gelatin, collagen and silk as well as from artificial polymers such as poly lactic acid (PLA), poly glycolic acid (PGA) and poly lactic-co-glycolic acid (PLGA).

Often, polymer combinations or different additives are used to finely tune mechanical and drug loading/releasing properties of resulting Nanofibers.



PIC. 6 - INCORPORATION OF TAP INGREDIENTS VIA ELECTROSPINNING INTO SMALL-SIZED POLYMERIC AND BIODEGRADABLE FIBERS PROCESSED

Use of Antibiotic-Eluting Fibers as Drug Delivery Systems:

- More cell-friendly: it has Minimal cytotoxicity
- Less total drugs released than TAP
- Increase (9x) Proliferation of stem cells compared with pure TAP
- Lower content of antibiotics within the fibers
- Well- controlled release of antibiotics
- Minimal remaining drug in each fiber: minimal risk of sustained antimicrobial action
- Minimal tooth discoloration of TAP-eluting nanofibers when compared with TAP
- Significant antimicrobial effect compared with pure Tap

Use of Antibiotic-Eluting Fibers as Drug Delivery Systems:

Use of Natural compounds:

1) Propolis:

- Good antimicrobial and anti-inflammatory properties
- Well-known antifungal and antimicrobial activity

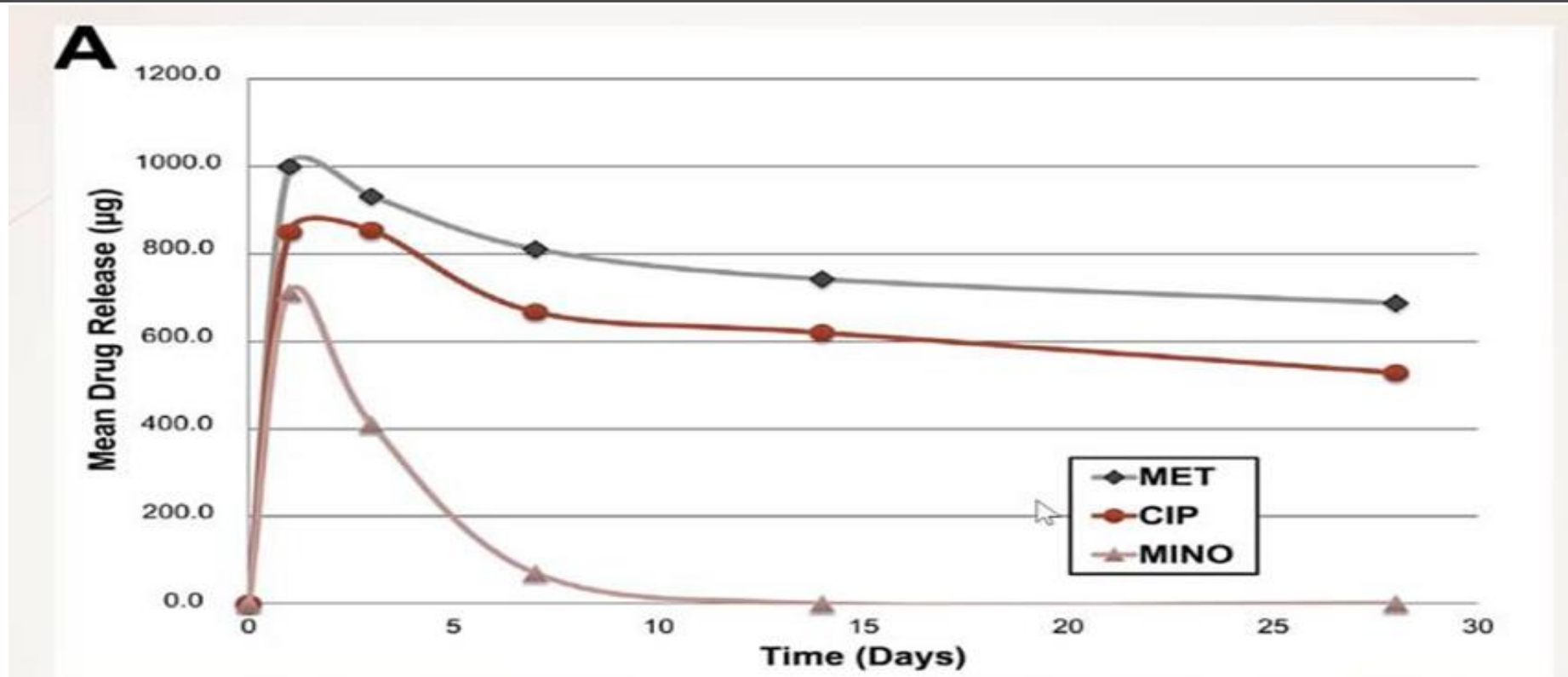
2) Mesoporous Bioactive Glass:

- A drug delivery system which is used especially for guided bone regeneration in periodontal tissue
- Antibacterial action against *E. faecalis* biofilm
- Leaching of silver ions

3) Chitosan:

- Natural compound used as a drug carrier
- Inherent antimicrobial action
- Excellent wound dressing material
- Biocompatibility, degradability, and nontoxicity
- An adjunct in photodynamic therapy

Drug release profile of TAP antibiotics from the TAP-eluting nanofibers:



PIC. 7 - DRUG RELEASE PROFILE OF TAP ANTIBIOTICS FROM THE TAP-ELUTING NANOFIBERS

Results and its discussion:

- 1) The degree of disinfection determines the success of the treatment. 1.5% NaOCl concentration doesn't change in odontoblastic differentiation .Use of EDTA as the final Irrigant partially reversed the detrimental effects of NaOCl.1.5% NaOCl is optimal for its dissolution and disinfecting capabilities followed by 17% EDTA as a final Irrigant to promote stem cell survival, attachment and differentiation.
- 2) In regenerative endodontic treatment use of antibiotic-eluting fibers as drug delivery systems which is composed of nanofibers increase (9x) proliferation of stem cells compared with pure TAP , well- controlled release of antibiotics during the procedure and minimal tooth discoloration of TAP-eluting nanofibers when compared with TAP can improve the quality of treatment.