

FACILITATING OSTEOGENESIS OF MINERAL TRIOXIDE AGGREGATE AND BIODENTINE BY AUTOGENOUS BONE MARROW. (EXPERIMENTAL STUDY ON RABBIT).

HARETH H. KASKOS and AHMED ALI

Dept. of oral and maxillofacial surgery, College of Dentistry, University of Duhok, Kurdistan Region Iraq

(Received: April 29, 2020; Accepted for Publication: June 21, 2020)

ABSTRACT

Maxillofacial surgery employs several surgical procedures in soft and hard tissues. When hard tissues are involved, for instance, periapical surgery, cyst enucleation, tumor resection, preprosthetic surgery, when the large bony defect remaining intact it is necessary to replace by bone grafting. An in vivo and vitro studies has also shown that Mineral trioxide aggregate (MTA) and biodentine promotes both dental and bony regeneration in pulp and periradicular tissues and both have excellent biocompatibility. **Materials and Methods:** 20 rabbits of both sexes were enrolled in this study, three monocortical defects were created on Mandible, one considered as control and the others implanted with MTA and biodentine, on tibia, three monocortical defects were created on the same animal. Post-operative follow up date 7,14,21and 28 Days. C.T. scan was used as parameter for bone density measurement. **Results:** showed that non-significant difference at Day7 and14 in Mandible and significant at Day21 and 28 compared to control, While nonsignificant at Day 7 in Tibia and significant at 14 and21 post-operatively with highly significant at Day28 compared to control. **Conclusion:** MTA and biodentine have effect on process of osteogenesis and will facilitatng when it implanted with Bone marrow .

KEY WORDS: MTA, Biodentine, Bone Marrow.

INTRODUCTION

The term bone grafting refers to the process by which bone is stimulated from a source (donor) to it (recipient). Bone grafts are used as a filler and scaffold to facilitate bone formation and promote wound healing .(S.Titsinides et al.,2019)

Bone graft are involved in successful bone graft include osteoconduction (guiding the reparative growth of the natural bone), osteoinduction (encouraging undifferentiated cells to become active osteoblast), and osteogenesis (living bone cells in the graft material contribute to become remodeling). Osteoinduction involves the stimulation of osteoprogenitor cells to differentiate into osteoblasts that then begin new bone formation. A remarkable biocompatible materials, MTA and newly developed ,Biodentine has been recently launched in the dental market as a 'dentin substitute'.both are bioactive calcium silicate-based cement with exciting clinical applications was developed. at Loma Linda University , CA, USA in 1993. Septodont Biodentine™ Active Biosilicate Technology™ Scientific file 2010.These materials regarded a

material of choice for pulp capping, pulpotomy, apexogenesis and apexification and it has many characteristics of the ideal biomaterial favorable for many endodontic treatment types and concluded that they were associated with regenerative periapical tissue response when used as root-end filling material.(TORABINEJAD et al 1993)

Both MTA and Biodentine there mechansim of action depend on to the release of calcium hydroxide ions by increase the alkalinity of the surrounding medium . (Sivaprakash, 2013; Accorinteet al, 2008)

Biodentine has higher calcium release, alkalizing activity, and solubility but higher open and apparent porosity, water sorption and a markedly shorter setting time than that of MTA. They concluded that porosity increases surface contact and ion release involved in the formation of calcium- phosphate deposits (hydroxylapatite)

(Ozbay, 2014; Gandolfi et al.,2013)

In Experiments were carried out by Gallas etal to demonstrate the ability of MTA the induce bone formation ,(Gallas et al., 2004)

Growth factors (GF) bind to target cell receptors and induce an intracellular signal

transduction that reaches the nucleus and determines the biological response.

(Gandolfi et al., 2013)

The main GF acting on the skeleton are bone morphogenetic proteins (BMPs), transforming growth factor- β (TGF- β), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF). (Phillips, 2005)

even though the subcutaneous injection of BMP-2 had been demonstrated to accelerate fracture repair in a rat model local application at the site of bone defect is likely to be more effective, as the systemic clearance of BMPs is high. (Einhorn et al., 2003)

However, despite significant evidence of the potential benefit of BMPs to bone repair and regeneration, to date evidence is still required to show superior results in comparison with autologous bone grafts. (Ten, 2006)

The acceleration of the bone healing process in humans may require longer exposure time to BMPs. (Gautschi, 2007)

MATERIALS AND METHODS

Twenty rabbits were elected weight (2000-2500 g), they were randomly classified into four groups five for each and they were anaesthetized intramuscularly with Ketamine and Xylazine. The surgical operation done on mandible and tibia then sacrificed at day 7, 14, 21 and 28 post-operatively. Fig.(1). Surgical procedure on the Mandible begins with a skin incision was made along the inferior border of mandible to expose the underlining bone. Three monocortical holes was performed with trephine bur (3mm) width and (2mm) in depth with by slow speed handpiece with copious irrigation and suction. The first defect approximated to angle implanted by Biodentine. The second was MTA and third one is considered as control, a 5 mm. space was lifted between defects, then the flap approximated and sutured. Fig. (2)

While the surgery on tibia begin with a full-thickness flap was reflected to expose the underlining tibia bone. two monocortical holes was performed with trephine bur with (3mm) in width and (4mm) depth until reach the marrow space. the first hole near the tibia articulator with femur left empty and considered as control, the second hole implanted with MTA, and third hole was implanted with biodentine a 5 mm space was lifted between defects then flap was approximated and sutured as shown in Fig. (3).

Post-operation care by gentamicin sulfate ampule (80mg) and gentamycin ointment externally of both mandible and tibia immediately following the surgery till day 7 post operatively. The specimens of mandible and tibia were planned for CT scan for bone density measurements Fig. (4).

RESULTS

1- Mandible :At the end of day 7, there was non-significant difference in bone density the mean in MTA (114.3 ± 1.35) and the mean for Bio-dentine (116.17 ± 1.41) when compared to control one the mean was (112.3 ± 1.36), ($P \leq 0.144$). At the end of day 14, there was non-significant difference in bone density in MTA the mean was (151.03 ± 1.8) and the mean for Biodentine (153.43 ± 1.86) when compared to control the mean (148.2 ± 1.78), ($P \leq 0.130$). At the end of day 21, there was significant difference in bone density, in MTA the mean was (4.24 ± 356.37) and Biodentine the mean (359.27 ± 3.56) when compared to control the mean (344.07 ± 4.08), ($P \leq 0.019$). At the end of 28 Days showed significant difference in measurements when compared control to MTA and biodentine, the bone density in control defect the mean was (963.43 ± 11.41) and in MTA the mean was (987.5 ± 11.66), and in Biodentine the mean was (1012.07 ± 11.95), ($P \leq 0.016$). As shown in (Table1)

2- Tibia : At the end of day 7, there was no significant difference in bone density between MTA the mean (131.37 ± 1.54) and Biodentine the mean (133.5 ± 1.63) when compared to control defect the mean (129.17 ± 1.56), ($P \leq 0.158$). At the end of day 14 there was significant difference in bone density, in MTA it was the mean (155 ± 1.84) and for Biodentine was the mean (158.87 ± 1.88), while it in control the mean was (151.2 ± 1.78), ($P \leq 0.015$). At the end of day 21 there was significant difference in bone density, the mean was (350.93 ± 4.17) in control defect while the mean was (359.77 ± 4.27) in MTA and for Biodentine the mean was (368.87 ± 4.41), ($P \leq 0.015$). At the end of the day 28, there was highly significant difference in bone density, the mean was (1036.77 ± 12.25) for MTA and for Biodentine the mean was (1093.8 ± 12.91) and in control the mean was (982.57 ± 11.63), ($P \leq 0.00$). As shown in Table (2)

DISCUSSION

MTA and Biodentine in Mandible: There were non significant differences between both MTA and Biodentine at day 7. At day 14 there were non significant differences between both MTA and Biodentine , Both MTA and Biodentine the mechanism of action depend mainly on Ca⁺⁺ ions released although MTA released calcium ions faster than Biodentine, as the calcium ion concentration plays an important role in bone regeneration. MTA and Biodentine undergo dissolution on the surface in physiological environments to form a Hydroxy Carbonate Apatite (HCA) layer. The greater the degree of solubility of the bioactive glass material, the more obvious is its effect on tissue growth .(Hench, 2002)

While at day 21 and 28 both experimental materials showed significance of differences in bone density measurements , these results supported by that recorded by the literature of Torabinejad and Parirokh (2010) ,they stated that these materials are not only have a good biocompatibility, as it also enhances hard-tissue formation.(Parirokh and Torabinejad, 2010)

Another study The author used the rabbit for both MTA and Biodentine implantation by created bony defects on mandible and significantly results were observed Bone formation was better and more pronounced

around MTA implants and the significance of difference was noticed in two till four weeks after implantation by samples of histopathological specimens.(Rayyan, 2017)

MTA and Biodentine In Tibia: The non significant results at day 7 of MTA and Biodentine was notice in the present study when both materials were implanted in bony marrow of Tibia, the significant results at day 14 and 21 with highly significant at day 28 as that clearly observed by the mean of bone density of MTA. The BMP-2 homodimeric protein and their associated signalling molecules is a cytokine that plays an important role in proliferation and differentiation process of osteoblasts.(Bleuming et al., 2007)

To investigate the effects of MTA and Biodentine on activities of the osteoblast phenotype, the expression of mineralization-related genes (Runx2) was measured, Runx2 expression increased from low levels in the 24-hour to an abundance 2 weeks of growth and differentiation.(Hiran , 2009)

Runx-2 plays a crucial role in the activation of osteoblast-related genes the expressions of Runx-2 in all differentiated cell groups were significantly higher This finding is especially valuable because it clearly shows the stimulatory effect of calcium silicate on osteoblasts on the expression of the Runx-2 gene.(Hiran , 2009)

List of Tables

Table (1): Measurements of Bone Density at Mandible by C.T scan.

Days	Day 7	Day 14	Day 21	Day 28
sites	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Control	112.3 ± 1.36	148.2 ± 1.78	344.07 ± 4.08	963.43 ± 11.41
MTA	114.3 ± 1.35	151.03 ± 1.8	356.37 ± 4.24	987.5 ± 11.66
Biodentine	116.17 ± 1.41	153.43 ± 1.86	359.27 ± 3.56	1012.07 ± 11.95
P value	0.144	0.130	0.019	0.016
≤ 0.01			*	*

* Significant difference at P≤0.01

Table (2): Measurements of Bone Density at Tibia by C.T scan

Days	Day 7	Day 14	Day 21	Day 28
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Control	129.17 ± 1.56	151.2 ± 1.78	350.93 ± 4.17	982.57 ± 11.63
MTA	131.37 ± 1.54	155 ± 1.84	359.77 ± 4.27	1036.77 ± 12.25
Biodentine	133.5 ± 1.63	158.87 ± 1.88	368.87 ± 4.41	1093.8 ± 12.91
P value	0.158	0.015	0.015	0.00
≤ 0.01		*	*	*
≤ 0.001				**

*Significant difference at P≤0.01

**highly Significant difference at P≤0.001

List of Figures

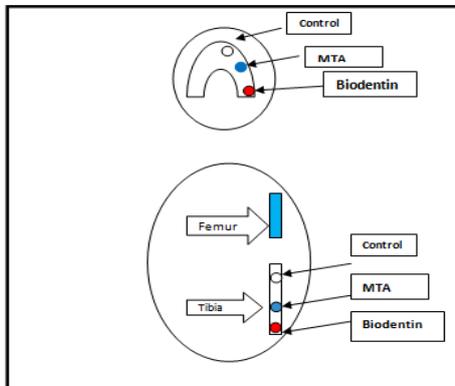


Fig. (1): diagram illustrate holes created on mandible and tibia

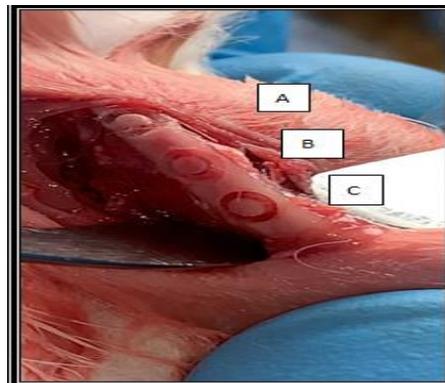


Fig (2): Created holes along the mandible, A:control. B: MTA. C: Biodentin



Fig (3): Created holes along the tibia, A:control. B: MTA. C: Biodentin

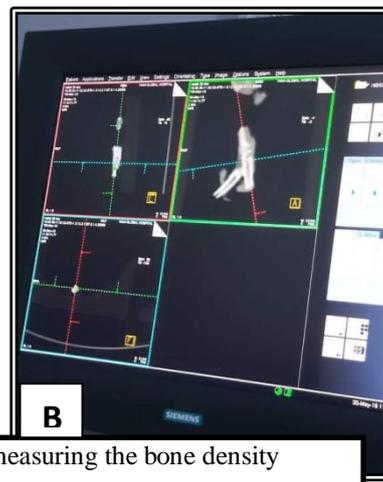


Fig.4 A-CT scan equipment B-: measuring the bone density

REFERENCES

Accorinte ML, Holland R, and Reis A, (2008). Evaluation of mineral trioxide aggregate and calcium hydroxide cement as pulpcapping agents in human teeth. *J Endod*; 34:1–6. ,

Asgary S, Eghbal MJ, and Ehsani S. (2010). Periradicular regeneration after endodontic surgery with calcium-enriched mixture cement in dogs. *J Endod.* 36(5):837-41. doi: 10.1016/j.joen.2010.03.005.

Bleuming SA, He XC, Kodach LL, Hardwick JC, Koopman FA, Ten Kate FJ, van Deventer SJ, Hommes DW, Peppelenbosch MP, Offerhaus GJ, Li L,

van den Brink GR (Sep 2007). "Bone morphogenetic protein signaling suppresses tumorigenesis at gastric epithelial transition zones in mice". *Cancer Research.* 67 (17): 8149–55.

Einhorn TA, Majeska RJ, Mohaideen A et al (2003) :A single percutaneous injection of recombinant human bone morphogenetic protein-2 accelerates fracture repair. *J Bone Joint Surg Am* 85- A:1425–1435.

Gallas Torreira M., Dos Santos A.A., Rodriguez Cobos M.A., Fuentes Boquete I., Crespo Abelleira A. The osteoinductive potential of MTA (Mineral Trioxide Aggregate): A

- histologic study in rabbits *Eur J Anat*, 8 (3): 101-105 (2004)
- Gandolfi M. G. , Siboni F., Polimeni A. , Bossù M., Riccitiello F., Rengo S. and Prati C. (2013). In Vitro Screening of the ApatiteForming Ability, Biointeractivity and Physical Properties of a Tricalcium Silicate Material for Endodontics and Restorative Dentistry *Dent. J.* 1, 41-60; doi:10.3390/dj1040041
- Gautschi OP, Frey SP, Zellweger R (2007) Bone morphogenetic proteins in clinical applications. *ANZ J Surg* 77:626–631.
- Hench LL, Jones JR, Sepulveda P: 2002 *Bioactive Materials for Tissue Engineering Scaffolds* Imperial College Press. p. 3-19.
- HiranPerinpanayagam.EbtehalAl-Rabeah: Osteoblasts interact with MTA surfaces and express Runx2. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* Volume 107, Issue 4, April 2009, Pages 590-596.
- Joseph M. Bojrab and Don Ray Walbron. (1997). Bone Grafting principles and techniques. In *Current technique in small animals surgery* (book). (4th Ed). Pp:901-910.
- Ozbay G, Kitiki B, Peker S, Kargul B. Apical sealing ability of a novel material: analysis by fluig filtration technique. *Acta Stomatol Croat.* 2014;48(2):132–39.
- Parirokh M, Torabinejad M (2010). Mineral trioxide aggregate: a comprehensive literature review—part III: clinical applications, drawbacks and mechanism of action. *Journal of Endodontics* , 36, 400–13.
- Phillips AM (2005) Overview of the fracture healing cascade. *Injury* 365:S5–S7
- Rayyan Mohammed Abdullah: an experimental comparative study of osseous and soft tissues responses to amalgam, mineral trioxide aggregate and biodentine. a thesis submitted to the council of college of dentistry/ university of mosul as a partial fulfilment of the requirements for the degree of master of science in oral surgery.2017
- Sivaprakash Rajasekharan, (2013). The efficacy of Biodentine™ and white Mineral Trioxide Aggregate in deciduous molar pulpotomy.- A Randomized Control Trial, Msc thesis, Universiteit Gent.
- S.Titsinids, G.Agrogiannis, T.Karatzas. Bone grafting material in dentoalveolar reconstruction:A comprehensive review. *Japanese dental science review* ,volume 55 issue I, November 2019,pages 26-32.
- Ten Dijke P (2006) Bone morphogenetic protein signal transduction in bone. *Curr Med Res Opin* 22:S7–S11.
- TORABINEJAD M, WATSON TF AND PITT FORD TR (1993). Sealing ability of a mineral trioxide aggregate when used as a root end filling material. *J Endod*, 19: 591-595.