European Review for Medical and Pharmacological Sciences 2016; 20: 1665-1668

Injectable bioactive glass in the restoration of oral bone defect

C.-B. HAN, S.-C. AN

Department of Oral and Maxillofacial Surgery, Weifang People's Hospital, Weifang, Shandong, China

Abstract. – OBJECTIVE: To explore the application value of injectable bioactive glass in the restoration of the oral bone defect.

PATIENTS AND METHODS: This study included 58 consecutive patients with oral bone defect > 1 mm, these patients were randomly assigned to a control group (n=26, Hydroxyapatite bioceramics) and an observation group (n=32, Injectable bioactive glass). The purpose of this study was to assess the comparison of the healing of oral bone defect.

RESULTS: X-ray examination was performed at 6-month and 12-month following treatment. The bone healing in the observation group was significantly better than the control group (p <0.05), the incidences of local rejection reactions were not significantly different (p >0.05). Cone-beam Computed Tomography (CBCT) was performed at 6-month and 12-month following treatment. The mean bone thickness in the observation group was significantly lower than the control group, p <0.05. Both the levels of bone morphogenetic protein 2 (BMP-2) and transforming growth factor β (TGF-β) in the observation group were significantly higher than the control group, p <0.05.

CONCLUSIONS: The effect of injectable bioactive glass in the restoration of the oral bone defect was better than hydroxyapatite bioceramics. Thus, injectable bioactive glass has great application value.

Key Words:
Injectable bioactive glass, Hydroxyapatite ceramics, Oral bone defect, Bone morphogenetic protein, Transforming growth factor.

Introduction

Either delayed or immediate dental implantation after tooth extraction may leave residual bone defects of varying degrees, which would affect the healing between implant and self bone tissues[1]. Currently used dental filling materials included demineralized freeze-dried bone, bioceramics, titanium and hydroxyapatite, autologous ilium and oral bone were the optimal graft material, but these materials had some limitations[2]. The injectable bioactive glass had good bioactivity and biocompatibility, ion exchange that occurred between the bioactive glass and soft tissue as well as bone may be directly involved in the metabolism and restoration of human bone tissue. As a result, identical inorganic mineral, i.e., carbonated hydroxyapatite could form on the material surface, inducing growth of new bone tissue[3,4]. Most previous studies explored the application value of bioactive glass through animal models[5,6], while this study would further confirm the value of bioactive glass through clinical controlled trial in humans.

Patients and Methods

Patients

This study included 58 consecutive patients who underwent tooth extraction and denture implantation from September 2013 to September 2014. All patients had oral bone defect >1 mm. With the approval from the Ethics Committee and informed consent from patients or families, these patients were assigned to a control group and an observation group by a random number table. The control group included 26 patients, 12 male and 14 female, aged 32.5±6.6 years (23-45 years), bone defect 2.2±0.4 mm (1.2-3.3 mm); the observation group included 32 patients, 14 male and 18 female, aged 33.4±7.2 years (21-46 years), bone defect 2.5±0.3 mm (1.3-3.2 mm). The differences in sex, age and the size of the bone defect between observation group and control group were not significant (p >0.05).

Materials

Hydroxyapatite bioceramic was used in the control group (Beijing Yihua Kemao Co., Ltd.) and injectable bioactive glass (Model 45S5) was used in the observation group (NovaBone®, LLC, Alachua, US). Surgical instruments included tooth planter (Nouvag), ITI, Nobel and Anthogyr kit.

Corresponding Author: Shichang An, MD; e-mail: asr744@163.com

Surgical Techniques

After local infiltration anesthesia, we performed a sulcus incision and full-thickness periosteal flap elevation, left interdental papilla tissue, debrided the surface of the tooth root, flattened the surface with an ultrasound device, and removed all granulation tissue. According to the protocol for implantation of biomaterials, we added 0.5 g bioactive glass in a disinfected plate then we added 3 drops of patient's blood, mixed by gentle agitation. We implanted the biomaterials gradually into the bone defect, pressed with a spatula and wet gauze until the defect was fully filled. We next restored the periosteal flap, sutured and fixed closely with 4-0 Gore-Tex suture, and covered the surgical area with periodontal preparation. The filling of bioceramics was performed in the same way. After surgery, the patient was advised to take oral anti-inflammatory drugs for 5 days and gargle with compound chlorhexidine mouthwash (tid) to maintained oral health.

Observational Measurements

An X-ray examination was performed at 6-month and 12-month follow-up to evaluate bone healing, which could be classified as; complete healing, delayed healing and non-healing. Complete healing referred to no significant difference in bone mineral density (BMD) between implant site and normal bone tissue, and significant boundary between the cortical bone and cancellous bone; Delayed healing referred to no significant boundary between implant site and normal bone tissue, no significant boundary between cortical bone and cancellous bone; Non-healing referred to clear boundary between implant site and normal bone tissue. Local rejection reactions included redness, exudation, infection, fever and allergy. CBCT was used to measure mean bone thickness, which was the mean thickness of the neck, body and root tip of the implant. The levels of BMP-2 and TGF-β were measured by ELISA. The BMP-2 kit was provided by Jinan Ohno Biological Engineering Co., Ltd.; TGF-β kit was provided by Shanghai Jimian Industrial Co., Ltd.

Statistical Analysis

Statistical analysis was performed by SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). Measurement data was represented by $\bar{x} \pm s$, the *t*-test was used for inter-group comparison; Categorical data was represented by percentage, the chi-square test was used for inter-group comparison. $p < 0.05$ indicated a significant difference.

Results

Bone Healing and Local Rejection Reaction

As shown in Table I, X-ray examination was performed at the 6-month follow up, 17 patients (53.1%) in the observation group and 7 patients (26.9%) in the control group achieved complete healing. The rate of complete healing in the observation group was significantly higher than the control group ($\chi^2=4.060$, $p=0.044$). At the 12-month follow-up, bone healing in the observation group was significantly better than the control group, $p<0.05$; however, the difference in the incidence of local rejection reactions was not significant, $p>0.05$.

Mean bone thickness by CBCT

As shown in Table II, CBCT was performed at the 6-month and the 12-month follow-up, mean bone thickness in the observation group was significantly lower than the control group, $p<0.05$.

The levels of BMP-2 and TGF-β

As shown in Table III, both the levels of BMP-2 and TGF-β in the observation group were significantly higher than the control group, $p<0.05$.

Discussion

Injectable bioactive glass predominantly composed of SiO_2, CaO, P_2O_3 and Na_2O, is similar to the human bone as a compound[7]. Therefore, strong chemical bonds were formed between

Table I. Bone healing and local rejection reactions at 12-month follow up [n (%)].

Group	Number	Complete healing	Delayed healing	Non-healing	Incidence of local rejection reactions
Observation group	26	12 (46.2)	7 (26.9)	7 (26.9)	3 (11.5)
Control group	32	25 (78.1)	4 (12.5)	3 (9.4)	2 (6.3)
χ^2		6.348			0.059
p		0.012			0.808

Table II. Mean bone thickness by CBCT (mm).

Group	Postoperative	6 months	12 months
Observation group	6.5±0.4	3.4±0.3	2.3±0.2
Control group	6.4±0.3	2.9±0.2	1.6±0.2
t	0.624	4.724	5.123
p	0.239	0.036	0.027

the injectable bioactive glass and human bone tissues, the bond strength may produce a stable interface between the implant and tissue, and the conductivity was better than hydroxyapatite[7]. *In vitro* experiment showed that mature osteocytes could be found in HCA-collagen layer and fully mineralized after the bioactive glass was implanted[8]. This experiment found the rate of complete healing was 53.1% and 78.1% in the observation group at 6th month and 12th month, respectively.

It was reported that subcutaneous implantation of bioactive glass may not produce allergy or inflammatory reactions, and vascular growth could be seen in surrounding region, which means that bioactive glass is biocompatible[9,10]. This study demonstrated that the prevalence of local rejection reactions was only 6.3% in observation group at 12th month, and the occurrences of local rejection reactions between bioactive glass and human bone tissue were not significantly different. Also, the bioactive glass had good biological, osteoconductive and osteoinductive activities, and could induce both intracellular and extracellular responses between the bioactive glass and the human bone tissue[11]. Yuan, et al[12] made 45S5 bioactive glass into a porous cylinder and implanted it into muscle pouches in dogs. After 3 months, the histological examination found the formation of bone tissue in the implant, demonstrating an osteoinductive activity of the bioactive glass. Kirk prepared biomaterial with gelatin and the combination of bioactive glass powder and allogeneic bone powder; this biomaterial had a good osteoconductive and osteoinductive activities[13]. The soluble ion released from the surface of bioactive glass particles could stimulate cellular autocrine activity, including the secretion of osteoinductive molecules, such as BMP, TGF, insulin-like growth factor, platelet-derived factor and fibroblast growth factor[14,15]. These molecules could maintain in high levels and sustained release not only locally but also in systemic circulation, increase cellular activity, accelerate osteogenesis and chondrogenesis, and increase successful rate of implantation[16,17]. This study suggested that both the levels of BMP-2 and TGF-β in observation group were significantly higher than the control group at 12th month.

The bone defect could lead to approximately 50% loss of alveolar bone volume, the change of bone volume could directly result in gingival recession and morphological change of soft tissue, and affect the normal formation of cancellous bone and cortical bone[18,19]. CBCT provided good imaging of bone tissue and low radiation dose; thus, could be used for multiple oral examinations and accurate measurement of bone volume[20,21]. This work demonstrated that the mean bone thickness in the observation group was significantly lower than the control group at 6-month and 12-month follow-up, indicating that the implant material in the observation group had better absorption and less bone volume decrease.

In comparison to human bone tissue, the bioactive glass had certain limitations, such as the presence of silicon, which could not be degraded *in vivo*[22]. The mechanism of silicon metabolism hasn't been clarified. Irrespective of the duration of the implant, the bioactive glass could not be transformed into the materials similar to human bone tissue. The degradation rate of bioactive glass may lead to decreased mechanical strength in the short term this was not beneficial for the restoration of the bone defect.

Table III. The levels of BMP-2 and TGF-β.

Group	BMP-2 (pg/mL)	TGF-β (μg/L)
Observation group	32.8±9.6	72.6±26.8
Control group	65.3±14.5	102.3±35.7
t	5.623	6.237
p	0.023	0.014

Conclusions

The effect of injectable bioactive glass in the restoration of the oral bone defect was better than hydroxyapatite bioceramics. Thus, injectable bioactive glass has great application value.

Conflict of Interests

The Authors declare that they have no conflict of interests

References

1) Martins CS, Ferraz EP, Castro-Raucci LM, Teixeira LN, Maximiano WM, Rosa AL, De Oliveira PT. Changes in actin and tubulin expression in osteogenic cells cultured on bioactive glass-based surfaces. Microsc Res Tech 2015; 78: 1046-1053.
2) Cortez PP, Brito AF, Kapoor S, Correia AF, Atayde LM, Dias-Pereira P, Afonso A, Goel A, Ferreira JM. The in vivo performance of an alkali-free bioactive glass for bone grafting, FastOs® BG, assessed with an ovine model. J Biomed Mater Res B Appl Biomater 2015 Sep 22. doi: 10.1002/jbm.b.33529. [Epub ahead of print].
3) Fiedler T, Videira AC, Bártolo P, Strauch M, Murch GE, Ferreira JM. On the mechanical properties of PLC-bioactive glass scaffolds fabricated via Bio-Extrusion. Mater Sci Eng C Mater Biol Appl 2015; 57: 288-293.
4) Popa AC, Stan GE, Enculescu M, Tanase C, Tulyaganov DU, Ferreira JM. Superior biofunctionality of dental implant fixtures uniformly coated with durablebioglass films by magnetron sputtering. J Mech Behav Biomed Mater 2015; 51: 313-327.
5) Yao Q, Li W, Yu S, Ma L, Jin D, Boccaccini AR, Liu Y. Multifunctional chitosan/polyvinyl pyrrolidone/45S5 Bioglass® scaffolds for MC3T3-E1 cell stimulation and drug release. Mater Sci Eng C Mater Biol Appl 2015; 56: 473-480.
6) Jones JR. Reprint of: Review of bioactive glass: From Hench to hybrids. Acta Biomater 2015; Suppl: S53-82.
7) Azenha MR, De Lacerda SA, Marão HF, Filho OP, Filho OM. Evaluation of Crystallized Biosilicate in the Reconstruction of Calvarial Defects. J Maxillofac Oral Surg 2015; 14: 659-665.
8) Simpson RL, Nazhat SN, Blaker JJ, Bismarck A, Hill R, Boccaccini AR, Hansen UN, Amis AA. A comparative study of the effects of different bioactive fillers in PLGA matrix composites and their suitability as bone substitute materials: A thermo-mechanical and in vitro investigation. J Mech Behav Biomed Mater 2015; 50: 277-289.
9) Cai Y, Guo L, Shen H, An X, Jiang H, Ji F, Niu Y. Degradability, bioactivity, and osteogenesis of biocomposite scaffolds of lithium-containing mesoporous bioglass and mPEG-PLGA-b-PLL copolymer. Int J Nanomedicine 2015; 10: 4125-4136.
10) Ardeshirylajimi A, Farhadian S, Adegani FJ, Mirzaei S, Zomorrod MS, Langroudi L, Doostmohammadi A, Seyedjafari E, Soleimani M. Enhanced osteoconductivity of polyethersulphone nanofibres loaded with bioactive glass nanoparticles in in vitro and in vivo models. Cell Prolif 2015; 48: 455-464.
11) Porwal H, Estili M, Grünewald A, Grasso S, Detsch R, Hu C, Sakka Y, Boccaccini AR, Reece MJ. 45S5 Bioglass (®)-MWCNT composite: processing and bioactivity. J Mater Sci Mater Med 2015; 26: 199.
12) Yuan H, Bruijn JD, Zhang X, van Blitterswijk CA, de Groot K. Bone induction by porous glass ceramic made from Bioglass (45S5). J Biomed Mater Res 2001; 58: 270-276.
13) Kirk JF, Ritter G, Waters C, Narisawa S, Millán JL, Talton JD. Osteoconductivity and osteoinductivity of NanoFUSE® DBM. Cell Tissue Bank 2013; 14: 33-44.
14) Stevanović M, Filipović N, Djurdjević J, Lukić M, Milenković M, Boccaccini A. 45S5 Bioglass®-based scaffolds coated with selenium nanoparticles or with poly(lactide-co-glycolide)/selenium particles: Processing, evaluation and antibacterial activity. Colloids Surf B Biointerfaces 2015; 132: 208-215.
15) Zeimaran E, Pourshahrestani S, Djordjevic I, Pingguan-Murphy B, Kadri NA, Towler MR. Bioactive glass reinforced elastomer composites for skeletal regeneration: A review. Mater Sci Eng C Mater Biol Appl 2015; 53: 175-188.
16) Ajita J, Saravanan S, Selvamurugan N. Effect of size of bioactive glass nanoparticles on mesenchymal stem cell proliferation for dental and orthopedic applications. Mater Sci Eng C Mater Biol Appl 2015; 53: 142-149.
17) Durgalakshmi D, Balakumar S. Phase separation induced shell thickness variations in electrospun hollowBioglass 45S5 fiber mats for drug delivery applications. Phys Chem Chem Phys 2015; 17: 15316-15323.
18) Barngkgei I, Joury E, Jawad A. An innovative approach in osteoporosis opportunistic screening by the dental practitioner: the use of cervical vertebrae and cone beam computed tomography with its viewer program. Oral Surg Oral Med Oral Pathol Oral Radiol 2015; 120: 651-659.
19) Brehler M, Görres J, Vetter SY, Franke J, Grützner PA, Meinzer HP, Wolf I. Intra-operative assessment of fractured articular surfaces in cone beam CTimage data. Int J Comput Assist Radiol Surg 2016; 11: 603-612.
20) Pereira-Maciel P, Tavares-de-Sousa E, Oliveira-Sales MA. The mandibular incisive canal and its anatomical relationships: A cone beam computed tomography study. Med Oral Patol Oral Cir Bucal 2015; 20: 723-728.
21) Muinelo-Lorenzo J, Suárez-Quintanilla JA, Fernández-Alonso A, Varela-Mallou J, Suárez-Cunqueiro MM. Anatomical characteristics and visibility of mental foramen and accessory mental foramen: Panoramic radiography vs. cone beam CT. Med Oral Patol Oral Cir Bucal 2015; 20: 707-714.
22) Henstock JR, Canham LT, Anderson SI. Silicon: the evolution of its use in biomaterials. Acta Biomater 2015; 11: 17-26.