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MAGNESIUM BASED SURGICAL IMPLANTS: A NEW MODALITY FOR OSSEOINTEGRATION- A REVIEW OF CURRENT RESEARCH

*[1]Kumar, V., [1]Thapliyal G.K. and [2]Dausage, P.

[1]Department of Oral & Maxillofacial Surgery, Rama Dental College Hospital and Research Centre, A-1/8, Lakhanpur, Kanpur, Uttar Pradesh 208024, India
[2]Jabalpur Hospital & Research Centre, Russel Crossing, Mepier town, Jabalpur, M.P 482002, India

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ABSTRACT

Over the past few years there has been a considerable increase in interest in the potential of magnesium alloys to be used as surgical implants. This is due to the fact that magnesium implants can be used both, as a scaffolding to allow new bone formation and also as fixative devices, to hold the reduced fractured segments till bone healing takes place. Magnesium is biocompatible and has a modulus of elasticity closer to bone, thus desired over other materials presently being used. Another major advantage of using magnesium as a surgical implant is in its ability to biodegrade in situ and prevents the need for second surgery for removal. Here we present a review of current research into magnesium based surgical implants.

INTRODUCTION

Gold and silver alloys were the first materials, used to repair trephination in 3000 BC, due to their property of malleability, they provided good bone coverage (Sanan, 1997) and in 2300 BC, iron, wood and ivory were combined to produce artificial tooth, owing to their strength (Seguin, 2014). The field of biomaterials is constantly evolving, in order to develop better and more biocompatible materials, for dentofacial orthopaedics. According to the definition proposed by American National Institute of Health (NIH): " a biomaterial is a substance that has been engineered to take a form which, alone or as part of a complex system, is used to direct, by control of interactions with components of living systems, the course of any therapeutic or diagnostic procedure, in human or veterinary medicine" (Williams, 2009). Based on this definition, first generation of biomaterials were designed to fulfill the mechanical, chemical and physical requirements, with minimal toxicity (Hench, 1980). But the metal alloys used, in these materials were not inert and showed tissue toxic responses, this led to the use of titanium and its alloys in orthopaedic applications.

****Corresponding author: Kumar, V.,***
Department of Oral & Maxillofacial Surgery, Rama Dental College Hospital and Research Centre, A-1/8, Lakhanpur, Kanpur, Uttar Pradesh 208024, India.

Titanium showed good results, as it is stronger than bone and causes stress-shielding effect (Noyama, 2012), but on long term follow ups the implant was observed to wear down gradually, resulting in formation of debris at the operating site and causing osteolysis, sepsis and finally loosening of the implant itself (Haleem-Smith, 2012). Also foreign body reaction leading to inflammation and implant encapsulation was seen (Anderson, 2008). To overcome this problem, second generation of biomaterials were introduced and divided into two classes: (1) "resorbable" meaning that it should maintain mechanical integrity till primary bone healing occurs and thereafter absorbed by the body, and (2) "bioactive" which induces specific tissue response or strengthen the contact between implant and bone. In this generation, polymers (poly lactic acid, poly glycolic acid and polydiaxone) (Ciccone, 2001), bioactive glass, calcium phosphates (hydroxyapatite) (Jones, 2013), peptides (Adden, 2006) and phospholipids (Luthringer, 2014) are used. Currently the newest generation of biomaterials "smart materials" are being developed, these materials (metal-based scaffolds) are both bioactive and biodegradable and release bioactive agents e.g drugs and growth factors (Kim, 2014 and Hum, 2012).) Magnesium based implants are bioresorbable and have osteoinductive properties, (Lensing, 2014; Mushahary, 2013 and Witte, 2005) thus are classified as bioactive materials. The objective of this review is to bring to the knowledge of surgeons the advantages of magnesium alloy implants over other materials currently being used, recent research work undergoing in this field and to evaluate suitability of this material both at the level of biocompatibility and bioengineering methods. This review is based on 3 electronic databases (MEDLINE, EMBASE, Cochrane). In addition, selected journals were searched by hand for relevant articles on Magnesium based implants and their application in surgery.

Properties of Magnesium as a Biomaterial

Bone is a living tissue and constantly remodels and adapts based on the stresses exerted on it, this phenomenon is called as "*stress shielding effect*". When an implant bears more amount of load applied, than the bone, it results in loss of density, of the bone (Agrawal, 1998; Staiger, 2006 and Nagels, 2003). Modulus of elasticity of cortical bone is about 3-20 GPa, whereas modulus of elasticity of stainless steel is around 200 GPa, for chrome-cobalt alloys it is 230 GPa and for titanium alloys it is 115 GPa. Due to their higher modulus of elasticity, these metal alloys tend to carry greater portion of the load and results in stress shielding of the bone. Magnesium alloys, have a modulus of elasticity of 45 GPa, which is much more near to that of bone and therefore reduces the stress shielding of the bone and maintains its proper density. Biocompatability, is one of the necessary property, any material should possess, when considered to be placed in the body, this means, it should be non toxic, non carcinogenic and tolerated well by the body. Magnesium is biocompatible (Saris, 2000), and excreted through the kidneys. Magnesium alloys are considerably light weight, in comparison to their counterpart. They are 1/3 as dense as titanium based alloys and only 1/5 as dense as stainless steel and chrome-cobalt alloys. The advantage of magnesium alloys over bioresorbable polymers is strength, they are twice as strong as bioresorbable polymers and thus provide more rigidity, during fracture healing (Witte, 2005).

History on use of Magnesium in Surgeries- the first reported use of magnesium in surgery dates back to 1878, when magnesium wires were used for ligation of blood vessels by Edward C. Huse (Huse, 1978). This was followed by various research on its effectiveness as (i) connectors to treat vessel, nerve and intestinal anastomoses (Moravej, 2011 and Liu, 2014), (ii) plates, sheets and screws in arthroplasty or fractures, (Mantripragada, 2013) (iii) in treatment of haemangioma cavernosum (Kraus, 2012). During this period, few problems were raised for example, postoperative subcutaneous gas cavities, difficulty in obtaining pure magnesium and material machining. This led to a gradual decline in its use. Recent advances in material science and engineering, have enabled us to overcome these problems and also allowed to have precise control over its mechanical properties and corrosion rates (Staiger, 2006). Also improvement in patient care and complications seen with long term placement of implants have increased the interest in degradable materials as surgical implants. This led to a renaissance of magnesium alloys as a material of choice for primary bone healing.

Current applications of magnesium - based materials in oral and maxillofacial surgery: In vivo studies have shown, Magnesium alloy MgYREZr (magnesium-yttrium-rare earth-zirconium alloy) to have good biocompatibility, osteoconductive properties and no allergic reactions (Waizy, 2014; Witte et al., 2008). Thus it has been used as a substitute for titanium screws in both orthopedic and maxillofacial surgeries. A study conducted on 26 patients, to fix mild hallux valgus using MAGNEZIX compression screws (Syntellix AG, Hannover, Germany) (Figure 1) has shown improved osseointegration with better bone density. Furthermore, no negative effects such as complications, pain or allergic reactions were observed. The production of gas inherent to magnesium degradation generated neither bone erosion nor necrosis. The independent authors concluded that there was an equivalent clinical outcome between both types of screw, and recommended a larger and longer follow-up study (Windhagen, 2013).

Figure 1. MAGNEZIX compression screw Courtesy of Syntellix AG, Hannover, Germany

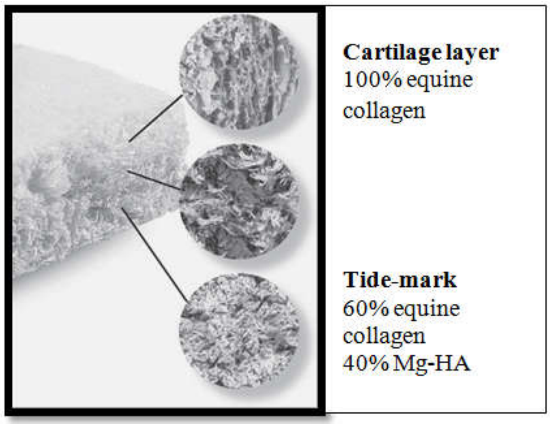

Figure 2. MaioRegen three-dimensional matrix. This multilayer scaffold mimics the entire osteocartilaginous tissue: cartilage, tide-mark, and sub-chondral bone. Courtesy of Fin-Ceramica Faenza S.p.A., Faenza, Italy

In 2007, Manfre et al (Manfré, 2007) used a new injectable bioceramic made of magnesium and hydroxyapatite (Mg-HA), in patients with lower bone density due to osteopenia and osteoporosis. They injected the Mg-HA cement in five non-fractured vertebrae in three patients, planned for preventive percutaneous vertebroplasty to reduce risk of vertebral compression fractures. Follow-up was done by CT and MRI at intervals of 15, 30 and 60 days. Sclerosis of bone was observed at injection site. Following the observations of the result, the authors have proposed the above mentioned treatment in percutaneous vertebroplasty, but they have also advised for further studies, to be performed on larger groups. MaioRegen (Fin-Ceramica Faenza S.p.A., Faenza, Italy) is a multi-layered scaffold composed of Type I equine collagen and Mg-HA, mimicking osteocartilage tissue (figure 2)). It is used as a scaffold to treat severe chondral/osteochondral lesions. In vivo studies, it has been proved as a good material to promote tissue regeneration[31] and presently, is under clinical trial, done as a multicentre, prospective, randomized, controlled, two-armed and single-blinded study in eleven European centres on 150 patients (Delcogliano, 2014).

Challenges to be aware of: While magnesium implants have many desirable properties, it has few issues to work upon. First and foremost is, in order to achieve good reduction of fractured segments, the plates have to be bent a little bit, as per the contour of the bone, for this the metal alloys should possess certain amount of ductility (Hayes, 2010). Previously the magnesium based plates and screws, lacked this property and were brittle in nature and broke easily, even on slight pressure applied to contour it. Recently a patent has been applied, with details of processing of magnesium alloys with high ductility (Haferkamp, 2001). Secondly, any implant should have sufficient strength for sufficient period of time to allow healing of bone, for this corrosion rate of the alloy should be controlled.[35] Magnesium alloys on corrosion increases the pH level in the localized area, this basic environment can cause improper bone healing. Witte et al (Witte, 2007), observed formation of subcutaneous gas bubbles of hydrogen, at the site of surgery post operatively. They suggested that these bubbles can cause gas gangrene and has to be eliminated.

Conclusion

Commercially available magnesium implants have been successfully used in many vivo and vitro studies, with no ill effects. It is important to understand and improve the quality of the material by upgrading the production process. This is possible by researching on underlying effects of magnesium on biological cell and tissue healing mechanism and establish correlation between biological, biochemical and mechanical properties for the material. In summary we conclude that there is a significant potential of magnesium based alloys, to be used in maxillofacial surgery and offer much more advantages than titanium alloys and biodegradable polymers. It is advised, that more prospective randomized controlled clinical trials should be done to achieve a better and definitive outlook.

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