Biodegradable magnesium implants for pediatric trauma surgery

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INTRODUCTION:

Biodegradable implants might present a suitable tool for pediatric trauma surgery. Their self-degrading properties would render surgical interventions for implant removal after tissue healing unnecessary. This is particularly important in children because surgical interventions and the associated hospital stays represent a major stress for them and are extremely cost intensive. Use of biodegradable implants would prevent this stress and reduce the therapy costs.

Magnesium seems to be an ideal material for biodegradable implants. Its mechanical strength is appropriate for load-bearing implant application and its elastic properties resemble those of bone. Furthermore, magnesium has shown a good biocompatibility with no systemic inflammatory reaction or affection of the cellular blood composition. The aim of our study was to investigate the behavior of the biodegradable magnesium alloys ZX50 and WZ21 in vivo and in vitro.

METHODS:

The magnesium alloy ZX50 is composed of Mg (balanced) with 5% Zn, 0.25% Ca and 0.15% Mn, whereas WZ21 consists of Mg (balanced) with 1% Zn, 0.25% Ca, 0.15% Mn and 2% Y. For in vivo studies the growing rat skeleton was chosen as appropriate model. Cylindrical pins were implanted in the femoral bones of male Sprague-Dawley rats. Volume and surface changes of these pins as well as the amount of hydrogen gas that formed due to biodegradation of the pins were assessed by µCT analysis throughout the study period of 24 weeks. For quantification of these parameters the Medical Image Processing software program “Mimics” was used. This program allows a 3-D reconstruction of the pin. Bone reaction to the implants was studied histologically via Levaï-Laczkó stain.

An osteoblast cell line (hFOB 1.19, ATCC) was chosen to perform in vitro experiments. In vitro experiments were performed only for ZX50 implants, as ZX50 degraded faster than WZ21 and is therefore considered the more aggressive material. Cell viability and metabolic activity of the osteoblasts in response to the alloy’s eluate were measured by neutral red (NR) and MTT conversion respectively. For the eluate preparation the alloy was immersed in simulated body fluid (SBF) for 40h at 37°C with agitation. Then various volumes of the eluate preparation the alloy was immersed in simulated body fluid (SBF) and incubated for 48 hours. As controls, the same volumes of pure SBF were added.

Data analysis was performed with SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Data was evaluated by means of descriptive statistics. The data of the in vivo experiments was displayed as medians and standard deviations. Non-parametric Friedman’s test was used to determine significant results in the in vitro studies.

All animal experiments were conducted under animal ethical respect and were authorized by the local Ministry of Science and Research. The study protocol for the in vitro studies had been approved by the local ethics committee.

RESULTS SECTION:

Both ZX50 and WZ21 pins were well tolerated by the animals. Mild reddening and wound swelling related to surgery resolved after 3-5 days post operationen and no wound infections were observed. All animals tolerated full weight bearing post operation. ZX50 pins started to corrode immediately after implantation and exhibited surface pits within the first week. The pin surface initially slightly increased as a result of the degradation. This accelerated further corrosion and made the pin surface area and volume decrease. The overall volume decrease was about 1.2% per day. 50% median degradation was reached after approximately 6.5 weeks. The pin degradation was accompanied by considerable hydrogen release within short time. The gas accumulated in the intramedullary cavity and also extrasternal around the pin. The gas pressure disturbed bone resorption to some extent leading to distinct callus formation, especially at the medial pin outlet. Histology showed that the gas bubbles impeded a good connectivity with the implant surface. However, bone remodeling was not accompanied by inflammation as indicated by the histological sections. The fast Mg ion release of the pins during degradation led to an enhanced neo-formation of bone tissue around the implant. After 16 weeks the pin was fully degraded and no hydrogen bubbles were detected by µCT scan. At this time point the cortical bone defects were already almost entirely healed. After 24 weeks also the medullary cavity was regenerated to a nearly normal extent.

The volume of WZ21 pins decreased only moderately during the initial weeks after implantation. Merely 2.3% of the initial pin volume degraded within the first 8 weeks. Thereafter the degradation proceeded in a linear manner with an average volume loss of around 0.5% per day. 50% pin degradation was reached after approximately 21.5 weeks. The observed hydrogen gas volume during WZ21 corrosion was moderate. The WZ21 alloy resulted in enhanced bone formation around the pins in the medullary cavity and especially in the medial corticalis. The newly formed bone showed close contact to the implant.

The in vitro experiments showed that the viability and metabolic activity of the osteoblasts in response to the SBF-based eluate of ZX50 started to decrease with increasing eluate concentration. Viability and metabolic activity of the cells decreased with increasing volume of the eluate. This decrease was significant compared to the control SBF once the volume reached 100µl. A decrease in viability and metabolic activity was observed also for the control SBF but at a higher volume of 100 µl. This indicates that a dilution of the growth medium higher than 17% causes adverse effects on both viability and metabolic activity.

DISCUSSION:

This study provided important insight into both the in vivo and in vitro degradation behavior of a magnesium-based implant material and the corresponding bone response. Magnesium showed good biocompatibility, osteoconductivity and osteoinductivity in vivo. The in vitro experiments confirmed the good cytocompatibility on the basis of the alloy’s eluate. Bone recovered restitutio ad integrum after complete degradation of the magnesium implant, even in the case of massive gas formation (as for ZX50 degradation). WZ21 is better suitable for use in pediatric trauma surgery as it combines good mechanical properties and an appropriate degradation rate. Also regarding the gas formation WZ21 is the more ideal material. However, there are some concerns in using rare-earth containing alloys (e.g. the element Y) in degradable implant solutions for children. It is recommended that their influence is studied in detail, particularly since bone and bone marrow are known to exhibit very slow release rates of such substances and the tolerance limits in children are small.

SIGNIFICANCE:

The results of our study propose magnesium as promising material for degradable implant application in pediatric trauma surgery.