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Polyethylene glycol improves elution properties of polymethyl methacrylate bone cements

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ABSTRACT

Background: Bone cements are used as adjuncts to fracture fixation methods and can also function as a local drug delivery system. The ability to elute drugs makes bone cement a promising and powerful chemotherapy treatment modality for osseous tumors. However, because of poor elution rates, the clinical application of this drug delivery mode remains challenging. Soluble fillers, such as sugars, salts, or biocompatible polymers, offer a solution to improve elution rates. This study quantified the effect of polyethylene glycol (PEG) on the elution properties of three commercially available bone cements.

Methods: Two grams of Vertebroplastic, Palacos, and Confidence bone cement powder containing three concentrations (0%, 20%, or 50%) of PEG filler were hand mixed with 10 mg of methotrexate. This powder mixture was then polymerized with 1.0 mL of the cement specific liquid monomer. The cylindrical elution samples were placed in saline solution and methotrexate elution was recorded for 720 h.

Results: The cumulative and daily elution rate increased as the concentration of PEG increased for each bone cement. However, the percent of increase depended on the bone cement used. Cumulative methotrexate elution increased by 40%–54% in case of the highest PEG filler concentration when compared with controls.

Conclusions: PEG soluble filler offers a promising method for improving methotrexate drug elution in bone cement. Future studies need to optimize the PEG and bone cement ratio that produces the greatest drug elution profile without sacrificing the biomechanical properties of bone cement.

1. Introduction

Polymethyl methacrylate (PMMA)-based cements are an effective, established method for local antibiotic drug delivery in bone and surrounding tissues [1–5]. The combination of durability, biocompatibility, and cost makes bone cement a commonly used drug delivery system. Bone cement can potentially serve as an excellent candidate for local chemotherapeutic drug delivery. Similar to antibiotic bone cements, by providing a high dose of drug directly to the affected site, this decreases the systemic absorption and limits deleterious side effects [6]. Previous reports have demonstrated an

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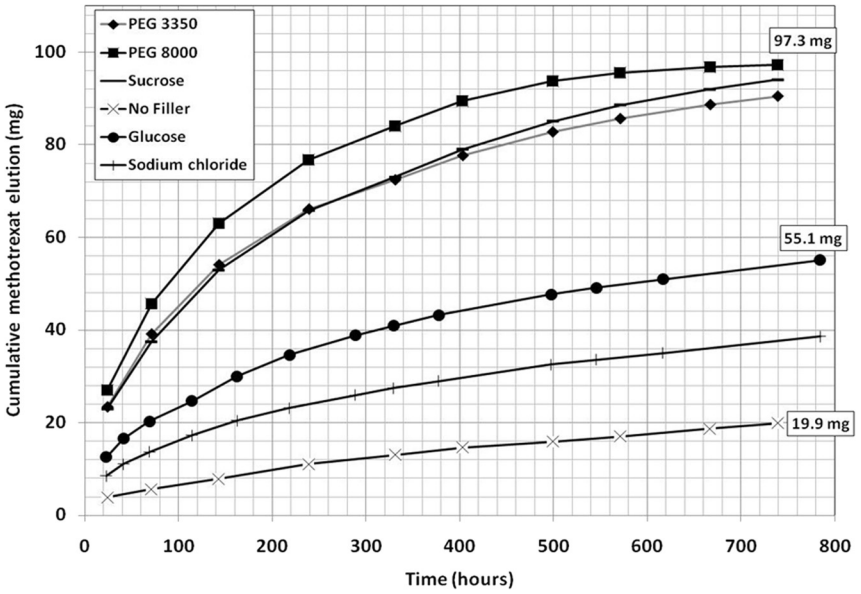

Fig. 1 – The cumulative methotrexate elution profile of Vertebroplastic bone cement containing different soluble fillers obtained during the screening experiment. In this experiment, Vertebroplastic bone cement specimens contained a 100-mg initial methotrexate concentration and 50% desired soluble filler. The soluble fillers tested included glucose, sodium chloride, sucrose, PEG (MW 3500), and PEG (MW 8000).

interest in treating osseous tumors locally through the use of chemotherapy drug containing bone cements or polymers [7–14]. Before bone cement is universally accepted as a chemotherapeutic drug delivery system, many challenges remain. Current literature demonstrates a paucity of knowledge regarding the elution properties of bone cement containing low doses of chemotherapeutic agents.

The rate of drug elution from a nondegradable material, such as PMMA, is dependent on several factors. The initial concentration of drug in the cement, surface area, and pore interconnectivity all affect the rate of drug elution [1,15]. Drugs from bone cement are released in a biphasic manner. An initial burst of drug elution is followed by a decreased, steady state of drug release. Previous studies have shown that up to 80%–90% of an initial drug added to the PMMA remains immobilized within the bone cement [10,16]. Adding soluble fillers, or porogens, to PMMA is a technique to improve drug elution rates and increase the cumulative amount of drug eluted [17–27]. The filler dissolves and increases the pore channel formation within the cement construct. This increased interconnectivity of pores results in an increased drug elution. However, the addition of secondary substances may jeopardize the mechanical properties of bone cement, creating a possible disadvantage when using soluble fillers [23,28].

As previously stated, if 80%–90% of drugs added to bone cement remain immobilized, this approach may be clinically ineffective when attempting to locally treat osseous tumors [10,16]. Although the use of soluble fillers may increase drug elution, several criteria exist when selecting these porogens for clinical use. Fillers should be easily soluble, nontoxic, chemically inert, and easily eliminated. Some examples of biocompatible fillers that may fit these criteria include simple sugars, salts, and hydrophilic polymers. This study evaluated the elution properties of three commercially available bone cements that were modified with polyethylene glycol (PEG) soluble filler and a commonly used chemotherapy drug, methotrexate.

2. Materials and methods

Vertebroplastic (DePuy AcroMed Inc, Raynham, MA), Confidence (DePuy AcroMed Inc), and Palacos (Heraeus Medical GmbH, Wehrheim, Germany) were the three bone cements used in this study. PEG (molecular weight 8000) was selected as the experimental porogen or soluble filler as it had the greatest elution profile in a separate screening experiment using Vertebroplastic bone cement. Figure 1 demonstrates the elution profile results of this screening experiment. In this

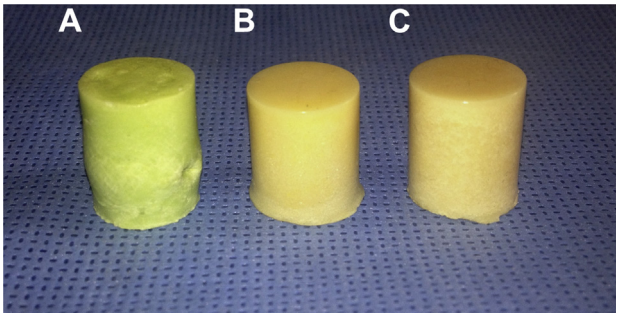

Fig. 2 – A sample of each bone cement with 20% PEG concentration. (A) Palacos (B) Vertebroplastic, and (C) Confidence. (Color version of the figure is available online.)