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Pre-packing of cost effective antibiotic cement beads for the treatment of traumatic osteomyelitis in the developing world – an in-vitro study based in Cambodia

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ABSTRACT

The developing world often lacks the resources to effectively treat the most serious injuries including osteomyelitis following open fractures or surgical fracture treatment. Antibiotic cement beads are a widely accepted method of delivering antibiotics locally to the infected area following trauma. This study is based in Cambodia, a low income country struggling to recover from a recent genocide. The study aims to test the effectiveness of locally made antibiotic beads and analyse their effectiveness after being gas sterilised, packaged and kept in storage

Different antibiotic beads were manufactured locally using bone cement and tested against MRSA bacteria grown from a case of osteomyelitis. Each antibiotic was tested before and after a process of gas sterilisation as well as later being tested after storage in packaging up to 42 days.

The gentamicin, vancomycin, amikacin and ceftriaxone beads all inhibited growth of the MRSA on the TSB and agar plates, both before and after gas sterilisation. All four antibiotics continued to show similar zones of inhibition after 42 days of storage. The results show significant promise to produce beads with locally obtainable ingredients in an austere environment and improve cost effectiveness by storing them in a sterilised condition

Introduction

The global burden of injury in the developing world is increasing with 5.1 million deaths cited in 2010, an increase from 20 years previously [1]. Trauma systems in the developing world are less advanced than those in higher income countries, resulting in poorer outcomes of all injuries [2,3]. Many of these severe injuries include open long bone fractures, resulting in severe complications [4,5]. Very little has been described worldwide on quantifying the clinical burden of osteomyelitis itself. In Uganda, a sample of orthopaedic patients reviewed in the clinics revealed 10% had a diagnosis of osteomyelitis and only 20% of these patients with osteomyelitis were over the age of 20, thus describing a significant burden of disease on a young population group. Surgical treatment of osteomyelitis represented 3.5% of all orthopaedic operations in this setting [6]. Cambodia is a country in Southeast Asia with a tragic modern history of genocide. Although progressing, the country still sees the effects of this era including civilian casualties of landmines and other disabilities, infectious diseases, and poverty. The Children's Surgical Centre (CSC) is a non-government organization located in Cambodia's largest and capital city, Phnom Penh The centre sees a large number of patients with neglecting trauma with severe complications including advanced osteomyelitis (Figs. 1 and 2). These conditions prove incredibly difficult to treat, often requiring serial surgical debridement and systemic antibiotic use. However, systemic long term use of intravenous antibiotics in this setting is expensive and often impractical. Antibiotic cement beads have now been recommended in guidelines for the acute management of open lower limb fractures in the UK [7]. As well as a prophylactic prevention of traumatic osteomyelitis, antibiotic cement beads are also an important adjunct in treating established osteomyelitis that have resulted from open fractures [8,9].

The spectrum and severity of the trauma and osteomyelitis present within Cambodia is likely to represent similar pathology throughout the developing world [2]. There are very few commercially available or licensed antibiotic beads and are often far too expensive for use in the developing world (Table 1). Subsequently, the surgeon must individually manufacture the

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Fig. 1. An example of osteomyelitis presenting late to the Children's Surgical Centre.

Fig. 2. An example of osteomyelitis presenting late to the Children's Surgical Centre.

beads manually intra-operatively for clinical use using their own recipe. The properties of these hand-made antibiotic beads are therefore more difficult to predict [10]. The availability of antibiotic cement beads are therefore limited in Cambodia but in much demand. By creating low cost, effective antibiotic cement beads that can be premade and possibly sterilized in the developing world, an effective tool can be utilised for the treatment of open fractures and osteomyelitis that is sustainable to a low resource environment. The aims of this study are to test the efficacy of multiple types of antibiotic beads as well as their efficacy once they are prefabricated, sterilised and stored in a way that reduces their cost whilst maintaining their effectiveness.

Table 1
Cost of cement and antibiotics in Cambodia.

Product	Quantity	Cost ($)
Synicem PMMA bone cement	40 g	$35
Tobramycin	N/A	N/A
Gentamycin liquid	Box of 10 × 80 mg ampules	$0.5
Amikacin liquid	500 mg ampule	$2.5
Ceftriaxone powder	1 g	1$
Vancomycin powder	1 g	$12.5

Methodology

Bead manufacture

The antibiotic beads were made using an aseptic technique, with each batch of beads created in the operating theatre environment, using sterile instruments and drapes. After each batch of beads were made, new instrumentation was used for the following batch to prevent cross contamination of antibiotics. The silicone moulds were thoroughly physically washed and sterilised between uses.

1. Control beads (not impregnated with antibiotics) were created. A 40 g packet of Synicem (expiry September 2015) bone cement containing 40 g of powdered polymethylmethacrylate (PMMA) and 20 ml of a liquid monomer, methylmethacrylate (MMA) was used. The 40 g of bone cement and the 20 ml of the liquid monomer were divided into four batches.