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Introduction

Cobalt-chrome (Co-Cr) alloys are widely used in biomedicine owing to their resistance to corrosion, mechanical properties, and biocompatibility. Co-Cr alloys are preferred in orthopaedics to nitinol and titanium alloys due to improved strength, wear resistance, toxicity, and cost. Recently, in order to reduce the amount of wear debris produced by joint replacements, the use of new surface bearings, such as metal-on-metal (MoM), made of Co-Cr alloys, has rapidly increased

mineral [5]. During physiological conditions, bone resorption and bone formation are closely related. Although osteolysis has also been associated with the early failure of MoM joint replacement [6-8], it is a rare phenomenon which occurs at a lower rate than that reported for patients with polyethylene implants. However, it is important to understand what are the effects of high metal ion concentrations on osteoclasts, the bone-resorbing cells and osteoblasts, the bone-forming cells. Despite previous studies investigating the effects of metal ions on rodent osteoclasts [9,10], little is known about the capacity of human circulating osteoclast precursors to transform into bone-resorbing osteoclasts in the presence of Co and Cr ions. Similarly, few studies have investigated the capacity of metal ions to induce osteoblastic cell death or alteration of osteoblastic metabolism [11,12]. However, these studies have been conducted in rodent cells or with concentrations higher than those commonly found in joint fluids of patients with MoM implants. As such, it is poorly understood whether in the presence of metal ions, osteoblasts can produce and mineralize a new collagen matrix.

for the expression of tartrate resistant acid phosphatase (TRAP), one of the osteoclastic markers, as previously described [16]. Coverslips were then counterstained with 4',6'-diaminido-2-phenylindole for 20 minutes and TRAP positive cells, with more than three nuclei, were identified as osteoclasts. The number of newly generated osteoclasts

osteoclast activity was reduced dose-dependently in the presence of Co^{2+} and Cr^{3+} . This finding was surprising for Co^{2+} as the number of osteoclasts was increased; we expected that the activity would be also increased. Weinstein et al. reported similar findings in patients treated for prolonged period with alendronate [28]. These patients exhibited a significant increase in the number of osteoclasts compared with patients under placebo administration. However, the extent of osteoclastic bone resorption was decreased in alendronate-treated patients. However, the mechanism by which Co^{2+} reduced the activity of the newly-formed osteoclasts is unclear and will need further investigation. Nevertheless, it appears from our study that the effect of metal ions (both Co and Cr) on human osteoclasts is to decrease osteoclast activity and as such bone resorption. Recently, Andrews et al. reported similar findings on human osteoclasts, however, unlike our study, these authors did not characterise osteoclast parameters as size, number of nuclei and TRAP content [29]. Previous studies conducted on rodent osteoclasts have reported similar findings [9,10]. This is also in the agreement with the fact that periprosthetic osteolysis is rare with MoM implants.

Metal ions at a concentration of 100 μM were also capable of affecting the osteoblastic response. Although Co^{2+} increased ALP activity and the mineralisation rate, Cr^{3+} decreased these two parameters. These results suggest that cobalt has an anabolic effect on osteoblast and matrix/mineralisation formation whereas chromium (III) has a catabolic effect on matrix/mineralisation formation. Previous published studies reported that ALP activity was decreased in the rat FFC cell line after treatment with Cr^{3+} [12]. Anissian et al., reported that Cr^{3+} ions induced

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