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Toxicology of wear particles of cobalt-chromium alloy metal-on-metal hip implants Part I: Physicochemical properties in patient and simulator studies

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Abstract

The objective of Part I of this analysis was to identify the relevant physicochemical characteristics of wear particles from cobalt-chromium alloy (CoCr) metal-on-metal (MoM) hip implant patients and simulator systems. For well-functioning MoM hip implants, the volumetric wear rate is low (<1 mm^3 per million cycles or per year) and the majority of the wear debris is composed of oxidized Cr nanoparticles (<100 nm) with minimal or no Co content. For implants with surgical malpositioning, the volumetric wear rate is as high as 100 mm^3 per million cycles or per year and the size distribution of wear debris can be skewed to larger sizes (up to 1000 nm) and contain higher concentrations of Co. In order to obtain data for risk assessment of wear debris in MoM hip implant patients, future studies need to focus on particle characteristics relevant to those generated in patients or in properly conducted simulator studies.

Key words: Metal-on-metal; Hip implant; Cobalt-chromium; Wear debris

Introduction

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Recent concerns have been raised about the toxicological implications of particles generated from the wear of orthopedic implants. Wear debris collected from patients with metal-on-metal (MoM) hip implants made of cobalt-chromium-molybdenum (CoCrMo) alloy, as well as generated from hip simulators, shows that the majority of wear particles (by number) exist in the nanometer size range (below 100 nm). Because of their small size, nanoparticles have a large surface area per unit of mass and the potential for greater particle surface-cell interactions than particles of micron size. It has been hypothesized that due to the enhanced particle–cell interactions, nanoparticles are readily taken up by macrophages and transported to intracellular phagolysosomes (e.g., acidic subcellular compartments), which results in enhanced dissolution of wear particles, release of metal ions, and dose-dependent inflammation.

First generation MoM hip implants were introduced in the 1950s. However, metal-on-polyethylene (MoP) implant devices

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gained popularity in the 1960s due to the low frictional properties (e.g., low coefficient of friction) and resistance to wear of ultra high molecular weight polyethylene (UHMWPE), as well as concerns about higher rates of aseptic loosening for the first generation MoM implants compared to the Charnley MoP implants. Despite an incomplete understanding of the causes of failure of the first generation MoM implants, these bearings were largely abandoned by the mid-1970s. Over time, MoP hip implants were discovered to have limitations with respect to the long-term implant survival as a result of degradation of the polyethylene cup after several years of wear. The primary problem that emerged with MoP hip implants was that large, micron-sized wear particles accumulated in synovial fluid and periprosthetic tissues, which were believed to promote chronic inflammatory processes and subsequent osteolysis, implant loosening, and, in some cases, pseudotumor formation.[1-5]

Concurrent to issues recognized for MoP hip implants in the late 1980s and early 1990s, improvements in metallurgy (e.g., higher carbide levels) and refined specifications for the tolerance of clearance between implant bearing surfaces to augment lubrication and improve tribology (friction, lubrication and wear) showed that lower wear rates could be achieved for newly designed second generation MoM devices.[6,7] More specifically, the second generation MoM hip implants showed significantly less volumetric wear (up to 1/100th) and far smaller individual wear particles (mostly in the nanosize range) compared to MoP implants, which provided some confidence that MoM were less likely to invoke a macrophage-mediated immune response similar to what had been seen with MoP implants.[8-12] For many physicians, the new MoM implant provided an attractive alternative to the problems that were being observed with the MoP device.[13] However, a number of recent scientific reviews and experimental studies have suggested that nanoparticles in MoM wear debris may have the capacity to cause local or systemic health effects in patients with MoM hip implants.[9,12,14-16] Despite the suggested role of nanoparticles in MoM wear debris, interpretation of the existing experimental studies on the health effects of CoCr debris is highly complex, particularly when one attempts to extrapolate such data to evaluate the possible human health risks to patients.

In order to evaluate the relevance and implications of the published toxicology studies on CoCr wear particles from MoM implants, one needs to understand the physical and chemical characteristics of these particles in patient and various simulator settings.[17-20] Specifically, most published papers have not evaluated the physicochemical characteristics of test particles (e.g., particle size distribution or metal content) utilized in toxicology studies in the context of their relevance to wear debris in implant patients. Therefore, the objective of Part I of our analysis was to identify and critically evaluate the relevant physicochemical characteristics of CoCr wear particles from hip implant patients and simulator systems. We attempted to characterize the factors which influence the physicochemical characteristics of wear debris in patients with well and malpositioned implants, as well as in simulator systems under array of simulated physiologic conditions. This information was used in Part II of our analysis to evaluate the 1) physicochemistry, metal solubility, and dosimetry of nano and micron sized CoCr test particles used in vivo and in vitro toxicology studies, and 2) the health effects observed in toxicology studies of CoCr particles in the context of their relevance to the doses, sizes and chemical composition of particles observed in MoM implant patients. Lastly, we identified data gaps which deserve additional study so that risks of CoCr nanoparticles can be fully understood.

Physical and chemical characteristics of MoM implants and wear debris

There are a number of factors which can influence the physical and chemical characteristics of MoM wear debris including the implant type, cycle number, implant position, swing phase loading (the level of force applied across the prosthesis during gait), fluid chemistry, wear process, and isolation technique (Figure 1).[10,21-26] Each of these variables needs to be taken into account when attempting to understand whether the test particles utilized in toxicology studies are clinically relevant to particles observed in patients and when drawing conclusions about the potential biological responses to MoM wear debris. For example, Table 1 compares on a relative basis the reported chemical composition of CoCr wear debris generated by simulators either in serum or water and compares this to the composition of the wear debris found in patient tissues. The results of these studies show that chemical compositions from debris generated in MoM patients can be significantly different from particles generated from simulator systems in certain settings.

MoM implant surface characteristics

To know what kind of particles need to be tested, the physical and chemical properties of the MoM implant surface need to be understood as this is the location at which wear debris is primarily generated.[27-29] CoCr alloy is considered to be highly biocompatible and resistant toward corrosion due to the spontaneous formation of a passive oxide layer in synovial fluids, which enhances the chemical and mechanical stability of the implants.[30] Although the bulk alloy material contains approximately 62-68% Co and 25-30% Cr, the stable passive layer of the implant material under normal physiological conditions has a reported thickness up to 85 nm and is primarily composed of Cr in the form of oxides, phosphates and hydroxides (Figure 2).[31] This is significant because little, if any, Co is present in the articulating surface of the CoCr prostheses. The passive surface oxide film of CoCr alloy materials incubated in simulated biological solution at 37 °C contains approximately 90% Cr in the form of Cr(III) oxide and Cr(III) hydroxide, but only around 5% Co (Figure 2, *B*).[30]

The surface compositions correlate well with the higher reactivity of Cr bulk metal compared to Co, in which the standard electrode potentials for the oxidation of Cr to Cr(III) and Co to Co(II) are 0.74 and 0.28 eV, respectively.[7,32] Co exists in the form of CoO, $Co(OH)_2$, and $Co_3(PO_4)_2$ on the surface of CoCr alloy in serum or synovial fluid solution.[32-36] Milosev and Strehblow[37] reported that in the potential range of 0-0.7 V, the