Development and Validation of a Robust Method to Measure Chromium and Cobalt in Whole Blood of Patients with Metal Implants using Dual Reaction Mode ICP-MS

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Background

The hip joint is one of the most important joints in the human body designed to allow for fluid motion and to bear a significant amount of weight. The ball-and-socket joint is formed between the femur (ball) and the acetabulum (socket) in the pelvis. A smooth cushion of articular cartilage covers the ends of the bone to prevent friction. However, age and use can cause the cartilage to wear down to bare bone causing persistent pain and limited range of motion. In cases where conservative treatment, such as physical therapy does not improve these symptoms, patients may be advised to undergo hip replacement surgery. Hip implants are intended to restore mobility and relieve pain. There are various types of total hip replacement devices comprised of different materials. Specifically, in metal-on-metal (MoM) devices, both components, the ball and the socket, are created from various metal alloys. The most commonly used alloy is a combination of chromium (Cr) and cobalt (Co). As a means to avoid the complication of debris wear from plastic/polyethylene implants, metal devices have become attractive alternatives due to increased durability and improved stability. While all hip implant device types can have complications, wear of certain MoM devices has recently raised concerns about their use.

Friction between component parts of MoM implants results in wear and corrosion that can release metal debris (ions and particles) into the space surrounding the implant, as well as enter the bloodstream. Reports in orthopedic literature link the failure of some MoM devices to bone and/or tissue damage surrounding the implant and joint. Other case reports in the medical literature highlight systemic reactions that may affect patients with MoM implants including: hypersensitivity reactions, cardiomyopathy, neurological changes, and renal function impairment. Consequently, the Food and Drug Administration (FDA) has recommended that in

combination with their overall clinical evaluation, orthopedic surgeons should consider measuring and following serial measurements of metal ion concentrations in symptomatic patients with MoM hip implants. Additionally, due to the potential for contamination, the FDA recently recommended testing metals in EDTA anti-coagulated whole blood.

Methods

The method to measure Cr and Co was developed on an ICP-MS (Perkin Elmer NexION 350) configured with collision/reaction cell technology. Aqueous acidic salt matrix calibrating standards, reagent blanks, quality control specimens, and patient samples were diluted with aqueous diluent containing EDTA, while the t-line introduced an acidic solution with a gallium internal standard. The sample introduction system was an O-ring-free quartz cyclonic spray chamber fitted with a PC^3 Peltier chiller (Elemental Scientific) operating at 2 °C and PFA-ST nebulizer (Elemental Scientific). The nebulized solutions suspended in the carrier argon gas stream were directed to and injected into a high temperature (6800 °K) argon gas discharge (plasma). Chromium ions were separated from concomitants using the dynamic reaction cell (DRC) mode with ammonia gas to react away polyatomic interferences. Cobalt ions were separated from interfering substances by the quadrupole mass spectrometer using the kinetic energy discrimination (KED) mode. This mode utilizes helium as a non-reactive gas that when introduced into the cell, collides with polyatomic interferences such as calcium oxide (CaO) and magnesium chloride (MgCl). The large CaO and MgCl molecules undergo more collisions in the cell. The molecules lose increasingly more energy until they are excluded from the quadrupole mass filter by the kinetic energy barrier, thereby attenuating the interference. Analytical performance was established according to the Clinical Laboratory and Standards Institute (CLSI) EP10-A3 guideline. Specifically, the limit of blank (LOB) and limit of detection (LOD) was determined with replicates of blank material (n = 60) and replicates of analyte (n = 60) in patient matrix at low concentrations, respectively. Additionally, the reference interval was validated in whole blood samples (n = 121) collected in trace element free EDTA tubes from healthy adults.

Results

We were able to successfully quantify the total Cr and Co in whole blood with high analytical sensitivity and specificity. The methodology described herein required minimal sample preparation using a simple dilution with a matrix modifier. The ICP-MS method was capable of simultaneously quantifying Cr concentrations spanning 1 ng/mL to 1,000 ng/mL with accuracy ranging from 87-97% and Co concentrations from 1 ng/mL to 200 ng/mL with accuracy ranging from 93-98%. Assessment of Cr and Co intra-assay imprecision (n = 20) demonstrated CV ranges of 0.8-6.1% and 0.7-3.3%, respectively, across four different concentrations within the linear range tested. The range for inter-assay imprecision (n = 20) for Cr was 3.5-5.9%, while Co was 2.0-3.5%. The study demonstrated that interfering polyatomic ions could be attenuated sufficiently to achieve acceptable performance measurements. This method is particularly suitable for the evaluation of MoM orthopedic implant wear in symptomatic patients.

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