Presence of Cobalt and Chromium Ions in the Seminal Fluid of Young Patients With Metal-on-Metal Total Hip Arthroplasty

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Abstract: We aimed to investigate the effect of metal ions on the semen of males of child fathering age with metal-on-metal (MM) total hip arthroplasty (THA). Semen was collected form 11 patients with MM THA and 5 control of comparable age. Cobalt and chromiun concentrations were measured in both the seminal plasma and in the blood of patients. Results showed that cobalt level was higher in the seminal plasma of MM THA patients (2.89 μg/L) compared to control patients (1.12 μg/L) (P = .011). The ejaculate volume, the sperm density, the total sperm count, the pH, and the percentage of cells with normal morphology were in the range of the World Health Organization criteria for fertile population. **Keywords:** metal on metal, total hip arthroplasty, metal ions, sperm parameters, fertility.

Several studies have shown the presence of elevated cobalt (Co) and chromium (Cr) ion levels in blood, urine, and organs of patients after total hip arthroplasty (THA) using Co-Cr alloy-based implants [1]. The outstanding question that remains is the clinical impact of these elevated ion levels. Although concerns about chromosome aberrations [2], changes in peripheral blood lymphocytes [3,4], and the risk of cancer [5] were continuously raised in the literature, there is no conclusive evidence that the elevated levels of cobalt (Co) and chromium (Cr) have any detrimental effects on the patients [1].

Previous study has shown that cobalt and chromium ions are able to cross the placenta of pregnant women with a metal-on-metal hip resurfacing and reach the developing fetus [6]. This finding has lead many centers, including ours, to avoid metal-on-metal (MM) THAs in women of childbearing age. On the other hand, it is well known that exposure to heavy metals (lead, copper, mercury, nickel, cadmium) may lead to significant alterations in human sperm morphology and motility [7-11]. However, less is known on the effect of Co and Cr on semen parameters.

Studies in mice showed a decrease of sperm motility and/or an increase of abnormal sperm cells after inhalation, acute exposure, or dietary administration of Co [12-14]. Alteration in sperm morphology and increase semen abnormalities were reported in industrial workers occupationally exposed to Cr [15,16]. Studies on non-human primates strongly suggested that the effect of Cr on semen parameters is associated with oxidative stress [17]. Co and Cr ions have the potential to induce the production of reactive oxygen species [18], making them prime suspects for inducing oxidative stress. Spermatozoa are sensitive to oxidative stress because they lack cytoplasmic defenses [19,20]. More specifically, the sperm plasma membrane contains lipids in the form of polyunsaturated fatty acids that are vulnerable to attack by reactive oxygen species, leading to the formation of lipid peroxides [21]. In fact, the level of circulating peroxides has been described as a valuable marker of oxidative stress [22]. Because MM hip implants are widely used for young, active patients, it is very important to resolve the clinical implication, if any, of elevated metal ion levels in men in age of fathering a child and having a MM THA.

The present *pilot* study aims at investigating the possible crossover of metal ions at the semen of men

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in age of fathering a child and having a MM THA and determining the effect of metal ions on semen quality and parameters.

Materials and Methods

Blood Sampling and Metal Ion Analysis

Blood samples (5 mL) from 11 patients with MM THA (mean time from implantation, 4.1 years) and 5 control patients of comparable age with no metal implant of any kind in their body (40.6 ± 8.2 years [range, 29-46] in control compared to 44.3 ± 5.7 years [27-48] in MM THA patients) were collected into Sarstedt Monovette tubes for trace metal analysis with 21G needles also specific for trace metal analysis (Sarstedt, Montreal, QC) and analyzed for Co and Cr ion levels by inductively coupled plasma–mass spectrometry, as previously described [23]. The study was approved by our institutional review board, and patients signed the approved consent forms for the use of their blood and clinical data. The reference SeroNorm Trace Elements Whole Blood, Level 2 (Sero AS, Billingstad, Norway) was analyzed as a quality-control sample. Typically, the detection limits were very low at around 0.01 to 0.03 μg/L (ppb) with variability in the SeroNorm values of less than 5%. All laboratory analyses were performed by personnel blinded to protocol.

Lipid Peroxides

Blood samples (1 mL) were collected in Sarstedt (Montreal, QC, Canada) Li-Heparin LH/1.3 tubes and centrifuged at 500*g* for 10 min for plasma preparation. Lipid peroxidation was measured as the total peroxide concentration in this plasma using the Biomedica OxyStat assay (Medicorp, Montreal, QC). Plasma was chosen for this part of the project instead of whole blood because the assay for lipid peroxide is not recommended for blood and can lead to erroneous data (manufacturer recommendation).

Measurement of Semen Parameters

Semen were collected by masturbation after 3 days of abstinence. Samples were collected in a sterile container and examined at the CDL laboratories (Montreal, QC) within 1 hour after ejaculation for morphology, motility, and number of sperm cells following standard criteria [24].

Metal Ions and Peroxides in Seminal Plasma

Thirty (30) min after collection, liquefied semen samples were centrifuged at 1000*g* for 10 minutes for the preparation of seminal plasma. Co and Cr ion and peroxide levels were measured as previously described [23]. Typically, the detection limits were very low at around 0.01 to 0.03 μg/L (ppb) with variability in the SeroNorm values of less than 5%.

Statistical Analysis

As previously described [23], metal ion data distribution was asymmetric and a nonparametric equivalent of a Student *t* test (Mann-Whitney) was used to compare *the median* metal ions in the two groups (control vs. patient). For peroxides and semen parameters that were symmetrically distributed, Student *t* test was used to compare the different study groups. Correlations of metal ion values with the different semen parameters were performed using the Spearman's rank correlation coefficient. $P < .05$ was considered as significant.

Results

Figs. 1 and 2 compare the levels of Co and Cr in the blood and the seminal plasma of control and MM THA patients. Results showed that Co level was higher in the blood of MM THA patients, with median levels reaching 1.44 (range, 1.39-1.46) and 1.99 μg/L (ppb) (range, 1.5-9.0 and 1 outlier at 15.3) in the blood of control and THA patients, respectively ($P = .002$; Fig. 1A). Median Co level was also higher in the seminal plasma of MM THA patients (2.89 μg/L; range, 1.15-6.1 and 1 outlier at 23.09) compared to control patients (1.12 μg/L; range, 0.71-1.94) ($P = .011$; Fig. 1B). Cr median level was also higher in the blood of patients with MM THA (0.57 μg/L;

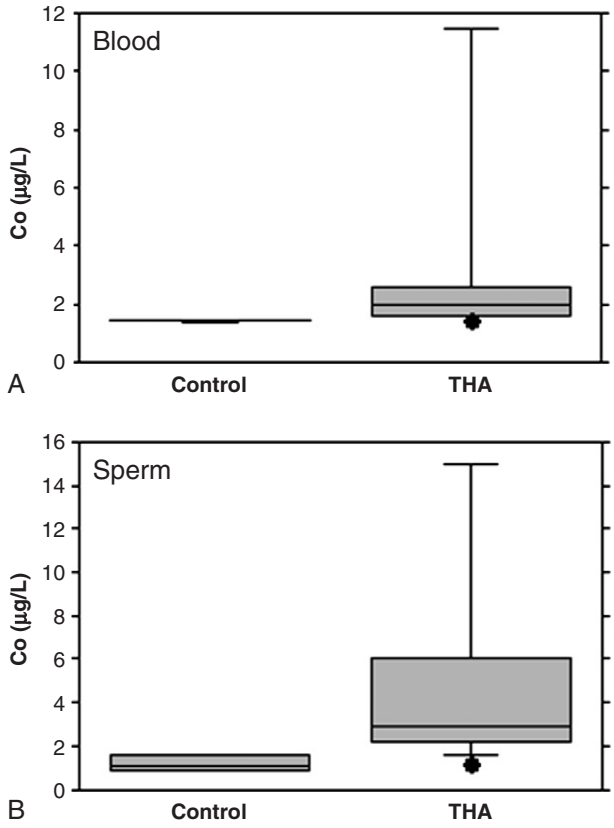

Fig. 1. Co ion levels in the blood (A) and seminal plasma (sperm) (B) of control and MM THA patients.