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Levels of metal ions after small- and large-diameter metal-on-metal hip arthroplasty

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Metal-on-metal (MOM) bearings for hip arthroplasty are increasing in popularity. Concern remains, however, regarding the potential toxicological effects of the metal ions which these bearings release.

The serum levels of cobalt and chromium in 22 patients who had undergone MOM resurfacing arthroplasty were compared with a matched group of 22 patients who had undergone 28 mm MOM total hip arthroplasty (THA).

At a median of 16 months (7 to 56) after resurfacing arthroplasty, we found the median serum levels of cobalt and chromium to be 38 nmol/l (14 to 44) and 53 nmol/l (23 to 165) respectively. These were significantly greater than the levels after 28 mm MOM THA which were 22 nmol/l (15 to 87, p = 0.021) and 19 nmol/l (2 to 58, p < 0.001) respectively.

Since the upper limit for normal patients without implants is typically 5 nmol/l, both groups had significantly raised levels of metal ions. MOM bearings of large diameter, however, result in a greater systemic exposure of cobalt and chromium ions than bearings of small diameter. This may be of relevance for potential long-term side-effects. It is not known to what extent this difference is due to corrosion of the surfaces of the component or of the wear particles produced.

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Metal-on-metal (MOM) bearings were first used in total hip arthroplasty (THA) over 40 years ago.[1-3] Because of a limited understanding of the engineering of these bearings and early failures in some cases, they lost popularity to the low-friction stainless-steel/ultra-high-molecular-weight polyethylene bearing developed by Charnley.[4] Over the past 15 years, with an improved understanding of the aetiology of aseptic loosening and of the science of wear, there has been increased interest in the use of MOM bearings.[5,6] Of the many engineering factors which have contributed to the success of the MOM bearing, the metallurgy, diametric bearing clearance, sphericity and surface finish are thought to be most important.[7-9]

All metal implants, especially those which include MOM bearings corrode at a rate determined, in part, by their surface area.[10] Further, side-effects relate directly to the particles of metal which are produced and their subsequent fate within the body. Our hypothesis was that the production of wear debris, and thus metal ion release, would be less after resurfacing arthroplasty than after THA using a 28 mm MOM bearing. This was based on the theoretical fluid film lubrication and reduced potential for the production of wear debris which is thought to occur in MOM bearings of large diameter, despite the increased surface area available for corrosion with these implants.[11]

Patients and Methods

Evaluation of patients. All joint arthroplasties are prospectively registered on a computerised database. We contacted patients who had undergone either unilateral MOM or resurfacing arthroplasty at least six months earlier and asked them to attend dedicated clinics. They completed a questionnaire and provided a sample of blood for analysis of cobalt and chromium. Since we were interested in estimating the systemic release of metal ions from the implanted prostheses, we specifically addressed factors which could have affected the results. These included occupational exposure, the ingestion of prescription or non-prescription medications and the presence of other metal implants within the body; we also recorded the patient's weight in kilograms, the date after surgery in months and the level of activity.

In order to evaluate the level of activity, we devised a system which grouped the patients into one of four catego-

ries, A, B, C or D. To be considered in category A, patients were allowed to have engaged in limited activity outside their home and unrestricted mobility at home. No sporting or activity-based recreational pastimes were followed. For category B, patients were expected to be more mobile outside the home and to walk up to two miles per day on average. Occasional light recreational activity was allowed, such as gardening or bowls. For category C, patients were expected to be mobile for longer periods. Walking from two to five miles daily on average or to undertake regular light to moderate recreational activity such as tennis, golf or walking. For category D, patients were expected to walk more than five miles daily on average. Regular moderate to heavy recreational activity such as competitive sports, running or ski-ing, was also expected.

Exclusions. The following exclusion criteria were applied: 1) less than six months after surgery; 2) limited activity because of symptoms from the MOM THA; 3) clinical or radiological suspicion of loosening; 4) the presence of other metal foreign bodies including arthroplasties unless known to be made of titanium, titanium alloy (Ti6Al4V), or ceramic (zirconia or alumina); 5) occupational exposure to cobalt or chromium; 6) ingestion of multivitamins or medications containing cobalt or chromium such as vitamin B12; and 7) bilateral MOM bearings.

Matching. Once the patients had been reviewed, a matching process was performed between the two groups according to the following objective criteria: 1) date after surgery to within six months; 2) identical activity level group; and 3) body mass to within 10 kg.

Blood sampling. Plastic consumables were certified to be free from cobalt and chromium by batch testing and were supplied by the Trace Metals Unit at the University of Southampton which performed the analyses.

We obtained blood using a disposable intravenous cannula. Once we had entered an appropriate antecubital vein, we immediately withdrew the central stainless-steel needle and left the outer plastic tube *in situ*. An initial 10 ml of blood was withdrawn and discarded to avoid contamination with chromium from blood which may have been in touch with the steel tip of the needle. We subsequently withdrew a further 10 ml of blood and transferred it into separate 2 ml tubes containing lithium-heparin anticoagulant. We centrifuged the blood at 3000 rpm for ten minutes and froze the plasma at -80ºC.

Analysis of cobalt and chromium. We determined the levels of cobalt and chromium using inductively-coupled plasma mass spectrometry (ICP-MS) on a Perkin-Elmer SCIEX Elan 6100 DRC plus (Wellesley, Massachusetts). We ran the plasmas against a bovine serum calibration curve, spiked with 0, 1, 5, 10, 20 and 50 µg/l of cobalt and chromium. Sample volumes of 100 µl were diluted with deionised water and an internal standard (100 µl of rhodium solution at 100 µg/l for cobalt, and gallium solution for chromium) to eliminate imprecision caused by any fluctuations in the plasma temperature and instrumental response. For the chromium analysis we used dynamic reaction cell (DRC) technology to minimise polyatomic interferences for measurement of ^{52}Cr with ammonia as the reactive gas. Internal quality control was provided by the certified reference material, Seronorm (Nycomed, Asker, Norway) and a bovine serum spiked with cobalt and chromium (100 µl of 1 µg/ml of Co and Cr into 20 ml of serum to give internal quality control A, and 200 µl of 1 µg/ml of Co/Cr into 20 ml of serum to give IQC B). All reagents used were of Aristar quality (BDH, Poole, UK) and distilled, deionised water (Milli 'Q' system; Millipore, Billerica, Massachusetts) was used throughout.

Implants. The prostheses used in this study were either large-diameter resurfacings or standard-diameter (28 mm) MOM THAs.

We used two types of resurfacing, both of which are machined from cast cobalt-chromium-molybdenum (CoCrMo) alloy in accordance with British Standard (BS) 7252 part 4. The Birmingham hip resurfacing (BHR; Midland Medical Technologies, Birmingham, UK) is machined from 'as cast' material resulting in a carbide fraction of 5%. The system has an uncemented, hydroxyapatite-coated, press-fit acetabulum and a cemented femoral component. The Cormet 2000 resurfacing arthroplasty (Corin Surgical, Cirencester, UK) is a totally uncemented device with a hydroxyapatite backing on both components. The cast alloy of the Cormet 2000 is subject to hot-isostatic pressing (HIPping) and solution annealing before the machining process which results in a carbide fraction of 2.3%. The typical mean surface roughness (Ra) of both of these devices is of the order of 0.01 µm with a diametric bearing clearance of 200 to 300 µm. The deviation from sphericity is typically less than 10 µm determined either by co-ordinate measuring (Cormet 2000) or by roundness testing (BHR).

The 28 mm MOM bearing which we used is the articulating surface of a hybrid THA (Ultima MOM; Johnson & Johnson, Leeds, UK). The stem is cemented and manufactured from wrought CoCrMo according to the American Society for Testing and Materials (ASTM) specification F1537. The acetabulum is a modular press-fit component with a titanium alloy (Ti6Al4V) shell. The acetabular liner with bearing surface is manufactured in accordance with ASTM F1537 and contains a relatively high carbon content. It is held within the shell by a taper-locking mechanism. The modular femoral head is also manufactured in accordance with ASTM F1537 but with a relatively low carbon content. The femoral head and acetabulum are manufactured to similar specifications of sphericity and surface roughness as the resurfacing designs.

Statistical analysis. We used the Mann-Whitney U test for data which were not normally distributed (serum cobalt, serum chromium, date after surgery). We used the paired Student *t*-test for normally distributed contiguous data (age, weight).

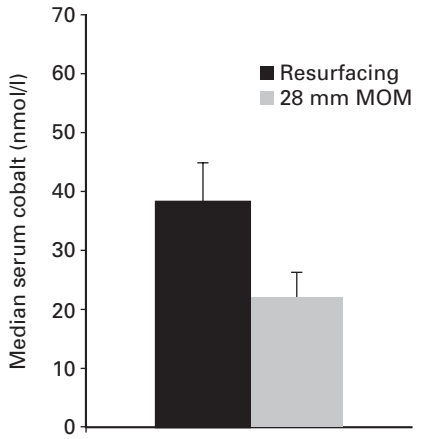

Fig. 1a

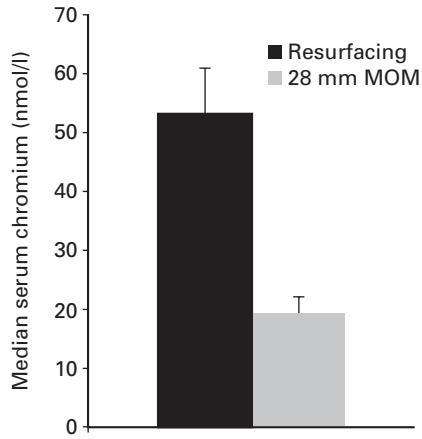

Fig. 1b

Median (± SEM) serum levels of cobalt (a) and chromium (b) after resurfacing and 28 mm MOM arthroplasty.

Table I. Comparative data which relate to the resurfacing and 28 mm diameter prostheses used.

	Resurfacing MOM (n = 22)	**28 mm Ultima MOM THA (n = 22)**	**p value**
Median serum cobalt in nmol/l (range)	38 (14 to 144)	22 (15 to 87)	0.0021
BHR (n = 16)	35.5 (14 to 144)		> 0.05
Cormet 2000 (n = 6)	51 (20 to 117)		
Median serum chromium in nmol/l (range)	53 (25 to 165)	19 (2 to 58)	0.0001
BHR (n = 16)	50 (29 to 165)		
Cormet 2000 (n = 6)	80 (25 to 129		> 0.05
Mean age in years (range)	53 (39 to 68)	60.9 (39 to 77)	0.016
Mean weight in kg (range)	79.8 (50.4 to 105.2	78.8 (54.9 to 101.6)	>0.05
Activity level			
A	2	2	Not applicable
B	7	7	
C	10	10	
D	3	3	
Median bearing surface diameter (range) in mm	48 (38 to 54)	28	Not applicable
Median date after surgery (range) in months	16 (7 to 56)	20 (10 to 43)	> 0.05

Results

Matching (Table I)**.** Using the matching criteria described, we were able to match 44 patients (22 from each group) with MOM bearings. The two groups were, therefore, not significantly different with respect to mean weight ($p > 0.05$) or median date after surgery ($p > 0.05$). The patients in the resurfacing group were, however, significantly younger by a mean of 7.9 years ($p = 0.016$), reflecting our indications for resurfacing in a younger age group.

Forty-two of the patients matched in all three categories (date after surgery, activity level and mass). Two were matched by weight and by level of activity but could not be exactly matched by date after surgery (43 months (THA) and 56 months (resurfacing)). Since both patients had had surgery at least 3.5 years earlier and were within a 13-month time frame of each other (without an alternative appropriate match), we felt that it was appropriate to include them for analysis. All matching was performed and patients were included or excluded before the serum metal levels were known.

Serum cobalt and chromium levels (Fig. 1)**.** Since the serum levels had not been determined before surgery, we used a conservative threshold level of 5 nmol/l for both cobalt and chromium as the upper limit on which to calculate our multiplications of normal. This figure was chosen from a review of the literature on the values in normal individuals.[12-15]

We found the median cobalt level to be 7.6 times normal (median 38 nmol/l, 14 to 144) after resurfacing arthroplasty compared with 4.4 times normal (median 22 nmol/l, 15 to 87) after 28 mm MOM THA ($p = 0.0021$). We found the median chromium level to be 10.6 times normal (53 nmol/l, 25 to 165) after resurfacing arthroplasty compared with 3.8 times of normal (19 nmol/l, 2 to 58) after THA ($p < 0.0001$).

With the numbers available, we did not detect any significant difference in the serum levels of cobalt and chromium when comparing the BHR (n = 16, median 35.5 nmol/l and 50 nmol/l, respectively) with the Cormet 2000 (n = 6, median 51 nmol/l and 80 nmol/l, respectively).

Discussion

We have shown that resurfacing arthroplasty gives a significantly greater increase in serum cobalt and chromium concentrations than a 28 mm MOM THA when matched for level of activity, weight and date after surgery.

At a median time of 16 months after surgery (7 to 56), the median cobalt and chromium levels after resurfacing arthroplasty were 38 nmol/l and 54 nmol/l, respectively, compared with the levels of 22 nmol/l and 19 nmol/l, respectively, after 28 mm MOM THA. Furthermore, the maximum serum levels of cobalt and chromium recorded after resurfacing arthroplasty (165 nmol/l and 144 nmol/l, respectively) were double those after THA (87 nmol/l and 58 nmol/l, respectively). With an upper limit of normal for both cobalt and chromium being typically 5 nmol/l, these represent significant increases above physiological values.[12-15] These findings are important since there is concern that chronic rises in serum cobalt and chromium may have long-term toxicological effects such as immune modulation, chromosomal damage and carcinogenesis.[16-18]

The serum levels of metal ions reported in our study for 28 mm Ultima MOM THA bearing are similar to those published for the 28 mm Metasul bearing (Centerpulse, Winterthur, Switzerland). In 1997 Brodner al al,[12] reported serum cobalt concentrations of 18.6 nnmol/l at one year after surgery for 27 Metasul THAs, and in 2002 Savarino et al[14] described serum cobalt and chromium concentrations of 16.4 nmol/l and 31.9 nmol/l, respectively, at a median of two years after surgery for 26 Metasul THAs.

By contrast, to date there has been no published study which has adequately addressed the serum metal concentrations after resurfacing arthroplasty. In 1996, Jacobs et al[19] reported the serum levels of cobalt and chromium after five resurfacing arthroplasties. One was a Wagner prosthesis with a titanium shell (Centerpulse, Winterthur, Switzerland) and four were McMinn prostheses (Corin Surgical, Cirencester, UK). However, one patient had bilateral prostheses, one had a contralateral CoCrMo THA and another had cobalt- and chromium-containing orthopaedic implants elsewhere in the body. Bearing in mind these confounding factors, the serum cobalt and chromium concentrations taken at a mean of one year after surgery (2 to 19 months) were 63.7 nmol/l (16.9 to 162.2) cobalt and 74.1 nmol/l (50.7 to 109.8) for chromium.

More definitive data regarding levels of metal ions after resurfacing arthroplasty are available only in abstracts from the proceedings of scientific meetings. At the 2001 meeting of the American Association of Orthopaedic Surgeons (AAOS), Skipor et al[20] reported serum cobalt and chromium concentrations of 22.9 nmol/l and 43.3 nmol/l, respectively, for ten resurfacings using the Conserve-Plus prosthesis (Wright Medical, Arlington, Texas). At the 2002 meeting of the Institution of Mechanical Engineers in London, Witzleb et al[21] reported serum concentrations of 33 nmol/l and 44 nmol/l, respectively, at six months after 67 resurfacing arthroplasties using the BHR.

While it is certain that the metal ions must be released because of the combined effect of corrosion at the surface of the implant and the wear debris which is produced, the exact reasons for the differences observed between the two groups in our study are not clear. The potential list of causes is long and includes differences in the lubrication regimes as a result of metallurgy, diametric clearance, sphericity and surface finish. The large-diameter resurfacings are thought by some to benefit from fluid film lubrication and thus reduced production of wear debris.[7,11] These engineering ideals, however, do not take into account the major aspects of biological variability, the potential for third-body wear and the concept of bearing microseparation.[22,23] In this regard, it has been noted that 28 mm MOM bearings are resistant to microseparation during the normal gait cycle.[24] It is not known if the same is true of resurfacing arthroplasties since their diametric clearance is typically much greater and the potential for a 'suction fit' may be less.

While all the bearings in our study were manufactured from CoCrMo, it should be noted that this designation encompasses a heterogenous group of alloys which differ in metallurgy, wear resistance and corrosion. The BHR and Cormet 2000 are machined from cast alloy containing a carbide fraction of 5%, but the Cormet 2000 is further heat-treated before machining which reduces the carbide fraction to 2.3%. The benefits or otherwise of carbides in CoCrMo-bearing surfaces is a controversial issue. In general, the greater the carbide content, the greater is the hardness and thus potential for resistance to wear, although the relationship is not straightforward. A problem with enhanced carbide levels is a reduction in corrosion resistance.[25] This may potentially account for the low levels of metal ions observed in patients with the Ultima MOM THA manufactured from wrought CoCrMo with a low carbon content in the femoral head.

In summary, although all the MOM-bearing implants in our study produced elevated serum levels of cobalt and chromium, we have shown that the serum concentration with a 28 mm MOM THA bearing is significantly lower than that seen with a MOM resurfacing. This finding may be of relevance when the potential for long-term side-effects of chronically elevated metal ions is considered.

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