High blood metal ion levels in 19 of 22 patients with metal-on-metal hinge knee replacements

A cause for concern

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Submitted 2016-09-20. Accepted 2016-12-28.

Background and purpose — There has been increasing alarm regarding metal-on-metal (MoM) joint replacements leading to elevated levels of metal ions and adverse reactions to metal debris (ARMDs). There is little information available concerning the prevalence of and risk factors for these adverse reactions, except with MoM hip joint replacements. We determined the levels of metal ions in blood and the rate of revision due to ARMDs in patients treated with MoM hinge total knee arthroplasty (TKA).

Patients and methods — 22 patients with TKAs and MoM hinge connecting mechanisms were studied for whole-blood chromium and cobalt levels at 6 months, 1 year, and/or ≥ 2 years after surgery. Possible ARMDs were investigated by MRI. 12 patients with TKAs and metal-on-polyethylene (MoP) connecting mechanisms served as controls.

Results — The cobalt levels were over 5 ppb in 19 of the 22 patients in the MoM group and in 1 of the 12 patients in the MoP group. The chromium levels were over 5 ppb in 11 of the 22 patients in the MoM group and in none of the 12 patients in the MoP group. Pseudotumors were operated in 4 of the 22 patients in the MoM group and in none of the patients in the MoP group.

Interpretation — Our results clearly show that the MoM hinge TKA carries a high risk of increased levels of systemic metal ions and also local ARMD, leading to complicated knee revisions. We therefore discourage the use of MoM hinge TKA.

To increase the mechanical durability of the hinge mechanism, a metal-on-metal (MoM) hinge was developed in the early 2000s. It made use of the widely used MoM concept in hip replacement. Modern machinery and tribology enabled the construction of precise metal articulations, which (at least in simulator tests) demonstrated superior mechanical properties and less wear, making it possible to also redesign the restricted rotating hinge knee. However, there has been an alarmingly high incidence of adverse reactions to metal debris (ARMDs) in patients with MoM hip replacements (Cohen 2012), which has led to questions about the fate of the MoM hinge knee replacements. We conducted a case-control study in patients with either bone tumors or complicated knee revisions using hinge TKA MoM. We compared blood metal ion concentrations in patients with MoM hinge TKAs and with metal-on-polyethylene (MoP) hinge TKAs, and also the rates of revision due to ARMDs in patients treated with MoM hinge knee TKR and MoP hinge mechanisms (which acted as a control group).

Patients and methods

Study population

Between September 2010 and December 2014, we performed 22 operations in 22 consecutive patients using the Modular Universal Tumor and Revision System hinge TKA (MUTARS; Implantcast, Buxtehude, Germany) with an MoM connecting mechanism. The mean length of follow-up was 3 (1–6) years. The prosthesis was needed to reconstruct a bone deficit in the distal femur in 17 patients and a bone deficit in...
the proximal tibia in 5 patients. The indication for surgery was malignant bone tumor in 9 patients and revision arthroplasty in 13 patients. Patients who had had other MoM joints earlier were excluded.

Control group

12 patients who had received the MUTARS hinge knee, which used the PEEK-OPTIMA locking mechanism with an MoP connecting mechanism, served as controls and were consecutively operated on during time intervals from July 2007 to August 2010 and from January 2015 to September 2015, with a mean follow-up of 2 (0–7) years. TKAs was needed to reconstruct the bone deficit in the distal femur in all 12 patients. The indication for surgery was malignant bone tumor in 5 patients and revision arthroplasty in 7 patients. We used both CoCr alloy MoM joints and titanium nitride- (TiN-) coated CoCr alloy MoM joints. Patients with other MoM joints were excluded. Demographics for the study population and the control group are summarized in Table 1.

Serum metal ion analysis, blood collection, and histological analysis

After the recall of the ASR hip resurfacing prosthesis, we established a systematic screening program for all patients with any type of MoM joint. From January 2012, all patients attending this program were examined clinically, including measurement of whole-blood levels of cobalt (Co) and chromium (Cr) ions. MRI was done on bone tumor patients routinely as a follow-up study, mainly to investigate local recurrences—and also for revision patients when they had continuous or progressive symptoms. Revision surgery for ARMD was only considered if the patient had elevated levels of metal ions, a continuously symptomatic knee or progressive symptoms, and a pseudotumor visible by MRI.

Blood metal ion levels were regarded as elevated if either Co or Cr exceeded 5 parts per billion (ppb). Whole-blood samples were collected using a 21-mm gauge needle connected to a Vacutainer system (Becton, Dickinson and Company, Franklin Lakes, NJ) and trace element tubes containing sodium ethylenediaminetetraacetic acid (EDTA). At the Finnish Institute for Occupational Health, standard procedures have been established for the measurement of whole-blood levels of cobalt (Co) and chromium (Cr) ions. MRI was done on bone tumor patients routinely as a follow-up study, mainly to investigate local recurrences—and also for revision patients when they had continuous or progressive symptoms. Revision surgery for ARMD was only considered if the patient had elevated levels of metal ions, a continuously symptomatic knee or progressive symptoms, and a pseudotumor visible by MRI.

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Results

The median and mean whole-blood concentrations of Co and Cr were higher in patients with a MoM hinge prosthesis than in those with a MoP hinge prosthesis (Co: 18 ppb vs. 1.7 ppb; Cr: 6.6 ppb vs. 1.4 ppb; p < 0.001) (Table 1, Figure 1). The Co levels were more than 5 ppb in 19 of the 22 patients in the MoM group and in 1 of the 12 patients in the MoP group. The Cr levels were more than 5 ppb in 11 of the patients in the MoM group and none of the patients in the MoP group. The Cr and Co levels increased significantly with time (Table 1). Co levels increased significantly with time, and they were 11 ppb (95% CI 5.8–17), 17 ppb (CI 6.2–29), and 21 ppb (CI 9.4–31) at 6 months, 1 year, and ≥2 years, respectively (p < 0.001) (Figure 2). The increase in Cr ions was 4.2 ppb (CI 2.3–6.1), 7.5 ppb (CI 4.7–10), and 8.3 ppb (CI 6.2–11) at 6 months, 1 year, and ≥2 years, respectively (p < 0.001)(Figure 2). There was no difference in blood metal ion levels in patients with a TiN-coated MoM hinge and in those with a standard MoM hinge.
Based on MRI, in the MoM group, 8 fluid collections with thick or irregular walls resembling Hart grade 2a pseudotumors were detected. A more solid pseudotumor resembling Hart grade 3 was observed in 2 patients. Mean length was 12 (4–20) cm. All these patients had metal ion levels over 5 ppb.

Table 1. Clinical and laboratory findings

|                                | MoP (n = 12) | MoM (n = 22) | p-value |
|--------------------------------|--------------|--------------|---------|
| Male/female                    | 2/10         | 9/13         | 0.1     |
| Mean age, years (range)        | 71 (33–91)   | 53 (16–88)   | 0.02    |
| Mean follow-up, years (range)  | 2 (0–7)      | 3 (1–6)      | 0.01    |
| Alive at follow-up             | 8            | 19           | 0.2     |
| Indication for surgery         |              |              |         |
| Tumor (n = 14)                 | 5            | 9            |         |
| Revision arthroplasty (n = 20) | 7            | 13           |         |
| Aseptic loosening (n = 8)      | 3            | 5            |         |
| Periprosthetic fracture (n = 8)| 3            | 5            |         |
| Infection (n = 4)              | 1            | 4            |         |
| Anatomic site                  |              |              |         |
| Proximal tibia                 | 0            | 5            |         |
| Distal femur                   | 12           | 17           |         |
| Cobalt, number of observations (MoP/ MoM), mean ppb (range) | | | |
| Total (n = 23/40)              | 1.7 (0.3–7.3) | 17.8 (1.5–76.6) | < 0.001 |
| 6 months (n = 10/11)           | 1.1 (0.4–3.6) | 10.8 (2.6–24.1) | 0.001   |
| 1 year (n = 8/12)              | 1.9 (0.3–7.3) | 20.1 (3.1–76.6) | < 0.001 |
| ≥ 2 years (n = 5/17)           | 0.3 (0.3–0.3) | 17.1 (1.5–46.0) | 0.002   |
| Number exceeding 5 ppb         | 1            | 19           | < 0.001 |
| Chromium, number of observations (MoP/ MoM), mean ppb (range) | | | |
| Total (n = 23/40)              | 1.4 (0.7–4.6) | 6.6 (0.7–25.5) | < 0.001 |
| 6 months (n = 10/11)           | 0.8 (0.3–2.0) | 4.4 (1.2–13.0) | < 0.001 |
| 1 year (n = 8/12)              | 1.4 (0.3–4.6) | 7.4 (2.1–25.5) | < 0.001 |
| ≥ 2 years (n = 5/17)           | 1.9 (0.9–2.5) | 6.3 (0.7–11.0) | 0.08    |
| Number exceeding 5 ppb         | 0            | 11           | < 0.001 |
| MRI done                       | 4            | 10           | 0.2     |
| Surgically treated pseudotumors| 0            | 4            | 0.2     |
| Cardiac failure                | 0            | 2            | 0.4     |

In the MoP group, 2 of the 12 MRIs showed fluid collections and 2 of the 12 images were negative for a fluid signal. All these patients had metal ion levels under 5 ppb. Despite the fact that we systematically used a metal artifact-reducing sequences (MARS) technique, prosthesis metal caused severe artifacts in all MRIs.

4 patients in the MoM group underwent revision surgery because of pseudotumors. 2 of these patients had received a MoM hinge prosthesis because of bone malignancy and 2 had received one in complicated knee revision arthroplasty (Table 2, Figures 3 and 4). None of the patients in the MoM group were reoperated. In the MoM group, there was symptomatic cardiac failure in 2 patients with high-grade osteosarcoma. They were also treated with neo- and adjuvant chemotherapy.

Discussion

In this case-control study, we assessed the incidence of having metal ion levels over 5 ppb and ARMD in patients who had undergone a hinge EPR at the distal femur or proximal tibia, with a MoM or MoP joint. We found a strikingly high occurrence of metal ion levels over 5 ppb. Whole-blood metal ion levels exceeding 5 ppb were found in 19 of 22 patients who had received a MoM hinge knee, with the highest values being 77 ppb for Co and 26 ppb for Cr. In 12 patients treated with an otherwise identical hinge knee replacement, except for the MoP hinge mechanism, only a single patient had a Co level of more than 5 ppb.
Metal particles and release of Co and Cr ions from wear and corrosion of orthopedic implants with MoM articulations can cause adverse effects systemically and locally (known as ARMDs) (Langton et al. 2010, 2011, Lainiala et al. 2014, Briggs et al. 2015, Chen et al. 2016). In MoM total hip joints, the incidences of elevated blood metal ions reported have depended on the prosthesis used, but they have varied between 10% and 30% (Langton 2011, Reito et al. 2015). The threshold of 5 ppb for abnormal metal ion levels in systemic circulation has been associated with pseudotumor formation (Bischoph et al. 2013) and unexplained failure of MoM hips (Hart et al. 2011), and is a major reason for revisions in hip arthroplasties (Langton 2010). Thus, the high proportion of patients with blood metal ion levels over 5 ppb in our study is most alarming. The indications for performing revision surgery due to ARMD are controversial (Matharu et al. 2017). Currently accepted guidelines recommend revision arthroplasty in patients with hip replacement when the patient has abnormalities in imaging and progressively rising Co/Cr levels of more than 7 ppb (Drummond et al. 2015). Revision of a TKA because of an evident or suspected ARMD must be carefully considered; the risk of infection leading to amputation is high (Jeys et al. 2003, Hardes et al. 2006, Shehadeh et al. 2010, Dhanoa et al. 2015).

Large resections due to bone tumors or complicated revisions lead to dead space surrounding the TKA. This space tends to fill with fluids, and may resemble fluid collections in pseudotumors. In addition, even though the metal artifact reduction sequence technique in MRI produces good-quality images near metal implants, a TKA still causes substantial metal artifacts and reduced visibility close to the hardware, disturbing the analysis of structures and tumorous masses. We had a high proportion of patients with fluid collections around the TKA; however, it is difficult to distinguish between seroma effusion and liquid pseudotumors. In addition, even though a high number of patients with fluid collections had metal ion levels exceeding 5 ppb, the MRI findings might overestimate pseudotumors.

There have been few data published concerning blood metal ion levels following total joint replacements other than total

Table 2. Revisions due to adverse reaction to metal debris

| Gender | Site          | Age | Reason   | Hart’s classification | Years to revision | Co level ppb | Cr level ppb | ALVAL score |
|--------|---------------|-----|----------|-----------------------|-------------------|--------------|--------------|-------------|
| Male   | Distal femur  | 25  | Tumor    | 2a                    | 1                 | 27           | 11           |             |
| Male   | Distal femur  | 67  | Revision | 2a                    | 3                 | 18           | 5.3          | 8           |
| Female | Distal femur  | 64  | Tumor    | 3                     | 3                 | 46           | 11           | 7           |
| Male   | Distal femur  | 72  | Revision | 3                     | 3                 | 14           | 7.2          |             |

ALVAL score: Aseptic lymphocyte-dominated vasculitis-associated lesion score.
Both blood metal ion measurement and MRI have been useful in the diagnosis of ARMD. However, measurement of metal ions only for systematic screening of ARMD is not supported by the current literature (Pahuta et al. 2016). The patients who are operated with hinge TKA are often young bone sarcoma patients treated simultaneously with chemotherapy, or elderly patients with a long history of multiple revisions. Thus, we do not know the value of measuring blood metal ions in these patients for the purpose of screening and diagnosing ARMD. In our patients, the interpretation of MRI findings was challenging. However, we suggest that there should be closer follow-up of such patients—with clinical examination and metal ion measurement. In cases with a clinical abnormality and elevated metal ion levels (> 5 ppb), additional imaging is advisable.

In summary, our results clearly show that this MoM hinge TKA carries a high risk of having elevated levels of systemic metal ions and local ARMD, leading to complicated knee revisions. Thus, we strongly discourage the use of MoM hinge TKA, as there are safer options available.

ML, AE, and JN designed the study. ML, JN, TKP, PN, TL, and KP participated in data collection. ML and AR performed the statistical analyses. ML wrote the first draft, and revised the manuscript. JP performed the histological analysis. All the authors contributed to preparation of the manuscript.

No competing interests declared.

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