Chronological changes of serum chromium levels after modern metal-on-metal total hip arthroplasty

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ABSTRACT We determined changes in serum chromium concentration every 6 months up to 3 years after implantation in 44 patients (mean age 63 (49–79) years, 35 women) who underwent modern metal-on-metal total hip arthroplasty (Metasul). The serum chromium levels increased between the first and second year after implantation (1 year: 1.05 (SD 0.76) µg/L, 2 years: 1.46 (SD 0.91) µg/L). A small increase was observed during the third year (1.61 (SD 1.31) µg/L). The clinical relevance of this finding is uncertain and should be determined in long-term studies on a large scale.

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Early examples of metal-on-metal prostheses such as the McKee-Farrar, Ring, and Müller designs frequently caused early acetabular loosening (Dandy and Theodorou 1975) and metallosis due to mismatch between the components and high frictional torque (Amstuts and Grigoris 1996). They were therefore abandoned. However, good results with a small number of well-functioning old metal-on-metal prostheses with low abrasion of the metal articulation (Müller 1995) provided the basis for a renaissance of this kind of articulation. Weber (1996) reintroduced a metal-on-metal articulation with improved clearance and hardness. The use of metal-on-metal articulations may be a way of avoiding the use of polyethylene, but concerns remain about the actual extent of metal wear and the long-term effects of local and systemic exposure to metal ions and particles. We attempted to determine whether there were chronological changes in serum chromium ion levels in 44 patients who underwent modern metal-on-metal total hip arthroplasty.

Patients and methods

Between November 1997 and April 2001, 110 patients underwent primary total hip arthroplasty with the Metasul metal-on-metal prosthesis (Centerpulse Orthopedics, Switzerland). 38 of these patients could not be reached at the 3-year follow-up and were excluded. Of the remaining 72 patients, 22 were excluded: 15 of whom had undergone bilateral operations, 5 of whom had aseptic loosening of the acetabular component, and 2 who had died of unrelated causes. In addition, 6 patients were followed at another institution, which left 44 patients (mean age 63 (49–79) years, 35 women) to be studied. Serum samples from these patients were analyzed for chromium every 6 months after implantation. All prostheses were implanted without cement. There were no patients with other metallic implants or dental prostheses containing chromium alloys. None of the patients were exposed to metals during their daily activities. All had a well functioning prosthesis, and none had radiographic evidence of loosening or osteolysis at follow-up. All 44 patients could walk more than 6 blocks without any assistance, and could ascend and descend stairs.

Secondary arthrosis was due to dysplasia in 39 hips, to rheumatoid arthritis in 1 hip, and to femoral head necrosis in 4. The mean body weight and body mass index (BMI) of the 9 men were 66 kg

(SD 8.7) and 25 (SD 2.6), respectively, and the corresponding figures for the 35 women were 53 kg (SD 9.7) and 23 (SD 3.9). 20 patients had unilateral hip disease (Charnley group A) and 23 patients had bilateral hip disease (group B). 1 had multiple joint involvement (group C; Charnley 1979).

The Wagner standard cup (19 hips) and the APR cup (25 hips) were used. The APR cup was inserted into hips which could receive diameters of 49 mm or more, and the Wagner cup into smaller hips because the former design was not available in sizes smaller than 49. Both designs had a 2.4-mm thick articulating surface of CoCr alloy (Protasul-21 WF, Centerpulse) moulded into a shell of UHMWPE with a metal back made of titanium alloy (Ti6Al4V). The APR cup had porous coating and the Wagner standard cup a blasted surface. 28-mm femoral heads made of CoCr alloy (Protasul-21 WF) were used. All patients received femoral components made of titanium alloy with a circumferential proximal porous coating (Natural Hip Stem).

Blood samples were collected from each subject every 6 months after implantation. All vessels and utensils used were verified to be free of chromium contamination. The concentration of chromium in the serum was measured by atomic absorption spectrophotometry and all samples were tested twice at Mitsubishi Kagaku biochemistry laboratories (Tokyo, Japan). The serum chromium level that could be measured (detection limit) was 0.2 µg/L or above.

Statistics

We used StatView (Ver. 5.0, SAS Institute Inc., North Carolina). Fisher's PLSD test was used to determine changes in serum chromium levels and used to evaluate any influence of gender and age at implantation on serum chromium. All samples with chromium values below the detection limit were given a value of 0.1 µg/L in the statistical calculations. The significance level was set at $p < 0.05$.

Results

At 6, 12, 18, 24, 30, and 36 months after implantation, the mean serum levels were 0.73, SD 0.76 (range 0.1–2.7), 1.05, SD 0.76 (range 0.1–3.7), 1.37, SD 0.90 (range 0.1–3.1), 1.46, SD 0.91 (range 0.1–3.8), 1.48, SD 1.06 (range 0.1–5.4), and 1.61, SD 1.31 µg/L (range 0.3–6.6), respectively. Serum chromium levels less than 0.2 µg/L were found up to 2.5 years after the operation. Some patients had low levels throughout the period of observation (Table).

The mean serum chromium levels increased between 6 and 18 months ($p = 0.003$), 6 and 24 months ($p < 0.001$), 6 and 30 months ($p < 0.001$), 6 and 36 months ($p < 0.001$), 12 and 24 months ($p = 0.05$), 12 and 30 months ($p = 0.04$), and 12 and 36 months ($p = 0.006$) after implantation (Fisher's PLSD test). Between 2 and 3 years, there was minimal increase ($p = 0.5$, Fisher's PLSD test). At 3 years, there was no significant difference in the mean serum chromium between men (1.12 (SD 0.95) µg/L) and women (1.74 (SD 1.37) µg/L) ($p = 0.2$, Fisher's PLSD test) or between patients with age below 64 years (27 patients, 1.42 (SD 1.14) µg/L) and those with age over 65 years (17 patients, 1.92 (SD 1.52) µg/L) ($p = 0.2$, Fisher's PLSD test).

Discussion

The short to medium term results of modern metal-on-metal total hip arthroplasty have been similar to those obtained by total hip arthroplasty with metal-on-polyethylene articulation after an average of five years (Dorr et al. 2000). Sieber et al. (1999) reported linear wear rate of 5 µm per year in metal-on-metal articulations and a volumetric wear rate of 0.3 mm3 per year in modern metal-on-metal articulating prosthesis (Metasul) in vivo, which are at least 20 and 60 times lower than the respective rates for metal-on-polyethylene articulating prostheses. Doorn et al. (1996) reported that metal wear particles from Metasul implants were of smaller diameter (< 0.1 µm) than polyethylene wear particles (about 0.5 µm) from conventional implants, and that metal-on-metal implants showed a lower volumetric wear rate. On the other hand, they also pointed out that the calculated number of metal wear particles was higher than for the same volume of polyethylene wear. The biological response is influenced more by the size of wear particles than

List of patients. Chronological changes in serum chromium levels in all 44 patients

No.	Gender	Age	Initial diagnosis	Body height (cm)	Body Feight (kg)	BMI	Postoperative serum chromium levels (μg/L)					
							6 Mo	12 Mo	18 Mo	24 Mo	30 Mo	36 Mo
1	M	72	OA	166	74	26.9	0.7	0.1	0.1	0.1	0.3	0.3
2	F	59	OA	150	43	19.1	0.7	0.1	0.7	1.3	1.9	2.4
3	F	59	RA	164	48	17.8	0.4	0.3	0.1	0.5	0.8	1.1
4	M	62	ON	159	54	21.4	0.1	0.1	0.7	1.2	1.2	1.2
5	F	70	OA	153	37	15.8	0.1	0.4	0.5	3	5.4	6.6
6	M	55	OA	160	63	24.6	0.1	0.1	0.9	1.7	2.5	3.3
7	F	77	OA	157	57	23.1	0.1	0.9	1.7	2.2	1.9	1.7
8	M	63	OA	164	69	25.7	0.1	0.1	0.6	1	0.1	1
9	M	62	ON	161	67	25.8	0.5	0.4	0.1	0.5	0.4	0.4
10	F	56	OA	147	49	22.7	0.1	1	1.2	1.3	1.4	1.6
11	M	75	ON	160	50	19.5	0.1	1	0.7	0.5	0.6	0.8
12	F	64	OA	154	57	24	0.1	2	2	2.1	1.4	1.3
13	F	79	OA	152	68	29.4	0.5	0.9	2	3	3.2	3.4
14	F	74	OA	149	38	17.1	2.2	1.1	2.1	1.9	1.5	1.4
15	F	63	OA	146	64	30	1.3	1.1	1.8	1.3	0.8	0.8
16	F	57	OA	150	51	22.7	1.4	1.3	2.9	3.5	3.5	6.1
17	F	77	ON	150	49	21.8	0.1	1.6	2	2.4	2	2.1
18	F	51	OA	148	45	20.5	0.8	2.8	3	0.1	0.1	1.1
19	F	65	OA	151	61	26.8	0.1	1.4	0.5	0.5	1	0.8
20	F	62	OA	148	47	21.5	0.4	2.1	2	2	1.7	1.9
21	F	77	OA	146	47	22	0.1	1.2	2.5	3.8	3.6	3.4
22	F	73	OA	144	57	27.5	0.4	1.2	2	2.1	2.2	2.3
23	F	76	OA	140	39	19.9	0.1	1	1.9	1.6	1.3	2.3
24	F	58	OA	148	56	25.6	0.5	1	1.6	1.2	0.8	1.4
25	F	72	OA	152	41	17.7	0.1	1.3	2.4	2.8	3.2	2.5
26	F	73	OA	160	73	28.5	1.3	0.7	0.5	1.2	0.9	1
27	F	50	OA	155	64	26.6	0.1	0.3	0.4	0.5	1.8	1.3
28	F	52	OA	146	39	18.3	0.1	0.1	0.4	0.5	0.7	0.8
29	F	54	OA	153	62	26.5	0.3	0.6	0.8	1	1.2	1.5
30	F	55	OA	146	39	18.3	0.8	1.6	1.7	1.9	2	1.7
31	F	64	OA	153	54	23.1	2.3	1.5	1.7	0.4	1.4	1.6
32	M	52	OA	163	70	26.3	1	1.2	1.2	0.9	0.5	0.6
33	F	72	OA	158	63	25.2	1.4	0.6	1.5	1.2	1.3	0.6
34	F	72	OA	155	68	28.3	0.5	0.1	0.8	1.1	0.5	0.8
35	M	59	OA	163	68	25.6	0.9	1.7	2.4	2.2	1.8	1.9
36	F	49	OA	155	46	19.1	2.2	0.9	0.1	1.3	1.6	0.9
37	F	50	OA	150	60	26.7	1	1.3	0.8	0.6	0.6	0.5
38	F	54	OA	155	60	25	0.4	0.8	0.1	0.8	0.7	0.4
39	F	65	OA	146	56	26.3	2.7	1.1	3.1	1.4	1.6	1.5
40	F	54	OA	147	59	27.3	0.3	0.9	0.9	0.6	0.1	0.4
41	F	68	OA	146	44	20.6	2.7	2.3	2	1.9	1.3	1.1
42	F	54	OA	146	55	25.8	1	1.7	2.7	2.6	1.6	1.2
43	F	60	OA	154	55	23.2	1.8	3.7	2.6	2	1.7	1.4
44	M	59	OA	167	76	27.3	0.4	0.4	0.4	0.5	0.8	0.6

by the total amount of debris. Green et al. (1998) showed that only polyethylene particles of a certain size (0.3–10 μm) induce secretion of interleukin-6 by macrophages, with subsequent granuloma formation and osteolysis.

The long-term effect of local and systemic exposure to metal particles and metal ions is a serious concern. Many total hip arthroplasties release metal particles due to wear and tear or as a result of modular head-neck corrosion (Jacobs et al. 1995, 1998), mechanical stress and fatigue. Wear debris from prostheses has been observed in the periarticular (Dorr et al. 1990, Lee et al. 1992) and in the distant tissues (Lee et al. 1992, Case et al. 1994). Small metal particles may more easily become transported away from the joint tissues. Case et al. (1994) demonstrated high tissue concentrations of metals, including chromium, in the lymph nodes and bone marrow in postmortem studies of patients with worn metal-on-polyethylene articulating hip prostheses. Urban et al. (2000) found that metallic wear particles in the liver or spleen were more prevalent in patients who had failed hip arthroplasty than in patients with a primary hip or knee replacement.

Increased concentrations of metal ions have been found in patients with conventional metal-on-polyethylene total hip arthroplasties and especially in patients with a loose prosthesis. Kreibich et al. (1996) found that aseptic component loosening resulted in significant elevation of serum cobalt levels after uncemented porous-coated arthroplasty. Jacobs et al. (1991) reported that serum titanium levels were elevated by approximately 2-fold in patients who had a loose component made of titanium-based alloy, as compared to control subjects. In general, the levels of cobalt and chromium in the serum and urine are higher with metal-on-metal than with metal-on-polyethylene prostheses (Jacobs et al. 1996). In previous studies of modern metal-on-metal articulating total hip arthroplasty, elevation of cobalt and/or chromium concentration in the serum and urine has been reported (Jacobs et al. 1996, Brodner et al. 1997, Schaffer et al. 1999, Maezawa et al. 2002, Lhotka et al. 2003).

Rieker et al. (1998) reported in vivo wear rate for modern metal-on-metal articulation of approximately 25 μm during a running-in period of about one year. Thereafter, the wear rate decreased to about 5 μm per year. Such an alteration of wear behavior might also influence the changes in serum chromium levels.

In the present study, there was a significant difference in mean serum chromium level between the samples collected up to 1 year after implantation and at 2 years after implantation. Between 2 and 3 years, there was minimal increase. Lhotka et al. (2003) reported that the whole-blood chromium concentration of patients with a Metasul metal-on-metal prosthesis rose during the first 3 years after the operation, but decreased markedly in the fourth year. However, these authors did not perform a prospective longitudinal study, but simply divided their patients into 5 groups based on the time from implantation and compared the mean serum chromium levels of each group. Since we investigated changes in serum chromium levels in the one set of patients over a 3-year period, more reliable data were obtained concerning any time-related changes.

Individual factors such as the condition of the implanted components, tissue accumulation of chromium particles and/or ions, and mechanical dysfunction of the prosthesis not detected by radiographic or physical examinations could possibly explain the individual variability of and time-related changes in serum chromium concentration. In our study, the factors that influenced the chronological changes in serum chromium concentration could not be explained, but this requires further investigation.

All 5 sockets that showed aseptic loosening after 1–2 years were of the standard Wagner design. Although the articulating surfaces of the Metasul inlays and the ball-heads showed scratches, metallosis was not recognized in the surrounding soft tissues. The liner wear values measured could be considered normal for a Metasul pairing. Since the main cause of aseptic loosening was considered to be failure of biological fixation due to the surface structure of the Wagner standard cup, we have not used this socket in the past 2 years.

Chromium is an essential trace metal and its depletion from the body consistently results in specific changes, while repletion reverses these abnormalities. Hexavalent chromium, a possible implant degradation product, has been listed as a class-I human carcinogen. Despite the long-standing recognition of the toxicity of this element both in vitro and in animal models, the relationship between cancer risk and the release of metal debris into body fluids has yet to be elucidated (Nyren et al. 1995). Long-term studies on a large scale are needed to determine the clinical outcomes and actual effects of metal particles after metal-on-metal total hip arthroplasty.

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