Differences in ion release after ceramic-on-ceramic and metal-on-metal total hip replacement

MEDIUM-TERM FOLLOW-UP

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Modern metal-on-metal bearings produce less wear debris and osteolysis, but have the potential adverse effect of release of ions. Improved ceramic-on-ceramic bearings have the lowest wear of all, but the corrosion process has not been analysed.

Our aim was to measure the serum ion release (ng/ml) in 23 patients having stable hip prostheses with a ceramic-on-ceramic coupling (group A) and to compare it with the release in 42 patients with a metal-on-metal bearing (group B) in the medium term. Reference values were obtained from a population of 47 healthy subjects (group C). The concentrations of chromium, cobalt, aluminium and titanium were measured.

There was a significant increase of cobalt, chromium and aluminium levels ($p < 0.05$) in group B compared with groups A and C. Group A did not differ significantly from the control group. Despite the apparent advantage of a metal-on-metal coupling, especially in younger patients with a long life expectancy, a major concern arises regarding the extent and duration of ion exposure. For this reason, the low corrosion level in a ceramic-on-ceramic coupling could be advantageous.

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The release of particulate matter derived from total hip replacement (THR) is important in determining the long-term survival of the prosthesis. Polyethylene debris derived from a metal-polyethylene coupling appears to cause the most pronounced tissue reaction. Phagocytosis of wear debris induces an inflammatory reaction associated with the release of cytokines and other inflammatory mediators. Focal bone resorption is initiated largely by osteoclasts. Once osteolysis has occurred, it tends to progress and may ultimately lead to failure of the implant.[1] Consequently, it is appropriate to consider the use of bearing surfaces with a greater resistance to the production of osteolytic wear debris, such as metal-on-metal and ceramic-on-ceramic.[2]

In vitro testing and examination of retrieved implants and synovial fluid suggest that modern metal-on-metal bearings produce minimal early wear and a lower incidence of peri-prosthetic osteolysis than metal-on-polyethylene implants.[3-5]

In spite of the rapidly growing use of metal-on-metal bearings, little is known about the extent of the release of metal ions or its implications. Cases of osteolysis and wear still occur and elevated ion levels have been found post-operatively.[6-9] Adverse local and remote tissue responses have been shown to occur[10-12] and may be implicated in prosthetic loosening.[13-15] Moreover, metal ions may have long-term carcinogenic effects.[16-19]

Previously, we have shown that serum ion concentrations were significantly increased in patients who had well-fixed implants with metal-on-metal coupling at a follow-up of 14 to 38 months.[20] After implantation for five years, some patients still had elevated ion levels, although these were lower than at the initial implantation.[21] Immunological changes in the short term have been found in subjects with metal-on-metal bearings. The possibility that metal ions, such as chromium and cobalt may have a toxic effect on myelopoiesis and the immune system has been considered. By contrast, subjects with ceramic-on-ceramic prostheses with normal ion values did not show immunological changes.[22] Therefore, we thought that modern ceramic-on-ceramic couplings, with a low wear rate, little osteolysis and a good clinical outcome[23] would be worthy of investigation.

We measured and compared the release of chromium, cobalt, titanium and aluminium in the medium term in two groups of patients who had well-fixed implants with either a ceramic-on-ceramic coupling, or a metal-on-metal bearing.

We aimed to establish if ceramic-on-ceramic bearings continued to produce low ion levels at

Table I. Details of the ceramic-on-ceramic (group A) and metal-on-metal (group B) patients and the control subjects (group C)

	Group A (n = 23)	Group B (n = 42)	Group C (n = 47)
Gender			
Male	11	23	37
Female	12	19	10
Age (yrs)			
Mean ± SEM (median)	63 ± 2 (67)	57 ± 2 (57)	43 ± 2 (40)
Range	40 to 79	31 to 79	20 to 80
Diagnosis			
Primary osteoarthritis	17	35	-
Secondary osteoarthritis			
Developmental dysplasia of the hip	2	2	
Trauma	3	4	
Infection	-	1	
Osteonecrosis	1	-	
Follow-up (mths)			
Mean ± SEM (median)	49 ± 4 (48)	53 ± 1 (56)	-
Range	28 to 78	30 to 66	

Table II. Spectrophotometric parameters and furnace programme for determination of titanium

Sample volume 15 μl	λ 364.4 nm			
Slit: 0.2	Background correction: Zeeman[26]			
Furnace programme				
Phase	**Temp (°C)**	**Time (s)**	**Ramp (°C/s)**	**Commands***
1	90	40.0	10	
2	150	30.0	5	
3	480	20.0	50	
4	700	10.0	100	
5	1600	5.0	100	
6	2800	3.0	0	Read TC
7	2900	5.0	0	TC

* TC: temperature control

longer follow-up and if the high cobalt and chromium levels detected in patients with metal-on-metal articulations were confirmed when larger numbers of patients were examined.[20-22]

Patients and Methods

The study protocol was approved by the institutional ethical committee on human research and was performed in compliance with the Helsinki Declaration.[24]

Between 2002 and 2005, 65 patients (34 men and 31 women; mean age 59 years (31 to 79)), with a stable THR were studied. The patients had received a unilateral primary THR for primary osteoarthritis or a secondary THR for developmental dysplasia of the hip (DDH), trauma, infection or osteonecrosis of the hip and did not have any other metal implant. There were 23 patients (group A) consisting of 11 men and 12 women who had a ceramic-on-ceramic coupling (ANCA-FIT; Wright-Cremascoli Ortho SpA, Milano, Italy). The acetabular component was made of titanium-aluminium-vanadium alloy with an alumina-ceramic insert and a matching ceramic femoral head with a 28 mm to 32 mm diameter (Biolox Forte, Ceramtec, AG Medical Products Division, Plochingen, Germany). An uncemented stem made of titanium-aluminium-based alloy was implanted in 19 patients and four had a cobalt-chromium-molybdenum stem. The patients were enrolled in the same institution and were operated on by the same team, using the same surgical technique.

Group B consisted of 42 patients (23 men and 19 women) who had a metal-on-metal bearing (Metasul; Sulzer Orthopedics Ltd, Winterthur, Switzerland). The acetabular component consisted of a titanium-aluminium-niobium alloy shell and a polyethylene insert reinforced with a cobalt-chromium-molybdenum inlay (Protasul-21 WF, Sulzer Orthopedics Ltd, Winterthur, Switzerland). The femoral head was also made of a cobalt-chromium-molybdenum alloy and had a 28 mm diameter. All patients had an uncemented femoral stem made of titanium-aluminium-based alloy. The metal-on-metal population, previously evaluated in the short- and medium-term,[21] was enlarged in number by enrolling a second series of patients, operated on in a different institution, but with the same type of prosthesis and surgical technique.

The patients were interviewed about medication, coffee and alcohol use, smoking history, and chronic occupational exposure to hazardous substances, in order to detect possible interactions with their trace-element status. Those with environmental chemical exposure were excluded. All had a well-functioning prosthesis at the time of testing, as determined by a good or excellent Harris hip score.[25] None had radiological evidence of loosening, osteolysis or infection.

A total of 47 healthy subjects (37 men and ten women) without any implant or systemic disease, served as a control group (group C). The details of the patients are given in Table I.

Analysis of metal ions. Environmental and sampling contamination was avoided by the use of a dedicated room for furnace testing with efficient fume extraction and temperature monitoring. All the disposable material was used after soaking and rinsing in 2% HNO_3 in bi-distilled and deionised water. Whole peripheral blood was collected from the fasted patients into metal-free vacutainers (Becton Dickinson and Co, Meylan, France). The serum was separated by centrifugation at 400 x g for 10 minutes at 4°C, and frozen at -70°C until analysis.

Serum samples were analysed for chromium, cobalt, titanium, and aluminium content using a graphite furnace atomic absorption spectrometer, equipped with double background correction Deuterium/Zeeman, autosampler and pyrolytic carbon-coated graphite tubes (unicam Model Solaar 939 QZ, Cambridge, United Kingdom).[26] Furnace thermal programmes and spectrometric parameters for the determination of cobalt, chromium and aluminium were the same as previously reported,[20,21] while the parameters for titanium are shown in Table II.

All the results were expressed as ng/ml. Calibration was performed by applying the standard addition method and by using NIST (National Institute of Standards and Tech-

Table III. Comparison (Mann Whitney U test) between the mean ± SEM (median; ng/ml) ion values in ceramic-on-ceramic (group A) and metal-on-metal patients (group B) and the control subjects (group C)

	Group A (n = 23)	Group B (n = 42)	Group C (n = 47)	p value*	p† value	p‡ value
Cobalt	0.18 ± 0.03 (0.13)	1.57 ± 0.26 (0.89)	0.24 ± 0.02 (0.23)	< 0.001	ns§	< 0.001
Range	0.08 to 0.53	0.08 to 7.31	0.08 to 0.50			
Chromium	0.30 ± 0.06 (0.26)	2.10 ± 0.35 (1.20)	0.28 ± 0.04 (0.29)	< 0.001	ns	< 0.001
Range	0.06 to 0.96	0.06 to 8.60	0.06 to 0.93			
Titanium	3.44 ± 0.37 (2.91)	3.66 ± 0.59 (2.91)	3.21 ± 0.15 (2.91)	ns	ns	ns
Range	2.91 to 9.68	2.91 to 11.60	2.91 to 5.39			
Aluminium	5.24 ± 0.64 (4.99)	7.88 ± 1.14 (8.56)	4.59 ± 0.48 (4.11)	ns	ns	< 0.01
Range	1.36 to 12.36	1.36 to 16.31	1.36 to 10.10			

* group A *vs* B
† group A *vs* C
‡ group B *vs* C
§ ns, not significant

nology, Gaithersburg, Maryland) certified standard solutions at three concentrations for each element. Samples (15 μl) were analysed in triplicate, after dilution with 0.1% HNO_3, 0.05% Triton X 100 and magnesium nitrate as the matrix modifier.

Standard reference material 1598 NIST human serum, normal trace elements and high-range trace elements UTAK (UTAK Laboratories Inc., Valencia, California) were employed to validate the accuracy and precision of the methods. Results with a relative standard deviation % (RSD %) higher than 10% were rejected and outliers were excluded by using the Dixon test.[27] The detection limits for the sample matrix were 0.06 ng/ml for chromium, 0.08 ng/ml for cobalt, 2.91 ng/ml for titanium and for aluminium 1.34 ng/ml. All the subjects with ion levels below the detection level were adjusted to the detection limit values.

Statistical analysis. Ion values were expressed as the arithmetical mean and SEM, the range and the median value. The data were processed using StatView 4.5 software (Abacus Concepts Inc., Berkeley, California). Specific differences between the groups were evaluated using the Mann Whitney U test. The correlation between the ion values, as well as between the ion values at follow-up and the age of the patients, was calculated by using the Spearman correlation coefficient. A p value ≤ 0.05 was considered to be statistically significant in all analyses.

Table IV. Spearman's coefficient correlating the serum ion values, the age of the subjects (years), and the time from insertion of the implant (months)

	Group	Correlation coefficient (r)	p value
Cobalt, chromium	A	0.26	ns*
	B	0.85	< 0.001
Cobalt, aluminium	A	0.08	ns
	B	0.22	ns
Chromium, aluminium	A	0.23	ns
	B	0.52	0.05
Aluminium, titanium	A	-0.03	ns
	B	0.31	ns
Chromium, age	A	-0.25	ns
	B	-0.26	ns
Cobalt, age	A	0.13	ns
	B	0.14	ns
Aluminium, age	A	-0.23	ns
	B	0.14	ns
Titanium, age	A	0.04	ns
	B	-0.10	ns
Chromium, follow-up	A	-0.20	ns
	B	0.20	ns
Cobalt, follow-up	A	-0.06	ns
	B	-0.20	ns
Aluminium, follow-up	A	-0.12	ns
	B	0.18	ns
Titanium, follow-up	A	0.12	ns
	B	0.05	ns

* ns, not significant

Results

The serum ion concentrations are given in Table III. The normal reference range was given by the values of group C. The 95th percentile found for each element in the control group was calculated and provided the upper normal reference limit, i.e. 0.53 ng/ml for chromium, 0.40 ng/ml for cobalt, 5.13 ng/ml for titanium and 8.28 ng/ml for aluminium.

Gender did not show a significant relationship to the ion concentrations in groups A and B (Mann-Whitney U test, p > 0.05).

A highly significant increase in the values for chromium, cobalt, and aluminium was observed in group B, compared with those recorded for groups A and C, while no significant difference was found between groups A and C, or between the cobalt-stem and titanium-stem implants of group A (Mann Whitney U test; p > 0.05). The serum concentration of titanium did not show any statistical difference in the groups (Table III). A highly significant positive correlation was found between the cobalt and chromium values in patients with metal-on-metal implants, using the Spearman's coefficient, while no correlation was shown between aluminium and titanium, either in ceramic-on-ceramic or in metal-on-metal implants.

No correlation was shown between the ion concentrations and the age of the patients, or the length of follow-up in groups A or B (Table IV).

Discussion

Our results showed a highly significant release of chromium and cobalt in patients with metal-on-metal bearings compared with ceramic-on-ceramic bearings and the control group. As previously reported, the 95th percentile for each element in the control group provided the upper normal reference limit. We found that 11% of patients in the ceramic coupling group and 76% of patients in the metal-on-metal group had chromium levels which exceeded the control value (0.53 ng/ml). Likewise, 11% in the ceramic coupling group and 90% in the metal-on-metal group had a cobalt concentration greater than the reference limit (0.40 ng/ml). A significant positive correlation between cobalt and chromium levels in the medium term was shown with all metal articulations which were not present in the previous report,[21] probably because of the small number of patients studied. In the metal-on-metal group we measured the levels to see if fretting or corrosion at the modular head/neck connection released these ions from the stem. Additionally, aluminium may have been present if contamination had occurred because of sandblasting of the surface of the implant.

The upper normal reference limit was 5.13 ng/ml for titanium and 8.28 ng/ml for aluminium, respectively. No significant difference between the implanted groups and the control group was shown for titanium, probably because of the high detection limit (2.91 ng/ml) of the method. However, only two patients from the ceramic group A and two in the all-metal group B had detectable levels of titanium in the serum.

It is interesting that the level was highly significant in the metal-on-metal group and that 53% of these patients had values higher than the reference limit. However, in ceramic couplings the aluminium level only exceeded the control reference value in 18% of the patients.

Our findings are in agreement with those of other authors,[28] and suggest that a fretting process may be occurring between the cobalt-chromium-based modular head and the titanium-based neck, disrupting the passivity of the surface and leading to the release of metal ions or debris. The absence of elevated levels in the ceramic-on-ceramic group suggests that fretting corrosion at the junction of the ceramic head and titanium alloy neck did not occur.

Despite the apparent advantage of metal-on-metal coupling, there is concern about the extent and duration of exposure to metal ions. The wide dissemination of metal ions can affect many biological functions with local and systemic effects.[10-15]

Long-term studies on metal corrosion with a variety of designs of implant and under different experimental conditions are needed. Although the measured ion levels were many orders of magnitude below the toxic range, the relevance of chronic low-grade exposure to these ions is unknown and tolerable values in patients with THR have not been well established.[29]

However, the negligible ion release from stable ceramic-on-ceramic implants was clear. These articulations are not immune to wear and surface damage and conditions associated with ceramic wear, including a vertical position to the acetabular component and impingement of some designs, have been described.[30] Clinical results reported in the short- and medium-term indicate that alumina-on-alumina bearings are at least equivalent in their performance to the metal-on-polyethylene design and support the continued use of such types of coupling.[31-33]

In conclusion, it is impossible to demonstrate the overall superiority of any one bearing couple for all THRs. The choice of bearing surface should be individualised, maximising the benefit-to-risk ratio.[34] However, the improvements in ceramic-on-ceramic manufacturing and the absence of concern over increased ion exposure make this option a valid alternative to a metal-on-metal bearing, especially for young and active patients.

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