CHANGES IN CHROMOSOME ABERRATIONS AND METAL LEVELS IN THE PERIPHERAL BLOOD OF PATIENTS AFTER CERAMIC-ON- CERAMIC HIP REPLACEMENT

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Intoduction

A wide variety of materials have been used for prosthetic implants in the human body: metals, ceramic and polymeric synthetic materials. However, as the indications have been extended, it has become apparent that early loosening of the components remains an on-going problem. The metal alloys, which are used in orthopaedic surgery, include potential mutagenic metals such as, chromium, cobalt, nickel and vanadium. It is not known whether there are any relevant clinical effects after very long term exposure to these alloys.

Ceramic-on-ceramic combination represents alternative, more durable bearing surfaces. Ceramic properties such as hardness, brittleness and bioinertness play an important role in reduction of wear debris (1). Despite the superior wear resistance of the surface, the ceramic acetabular component has a 10-year survivor-ship of 89% due to aseptic loosening (2). Cytogenetics biomarker such as chromosome aberration (i.e aneuploidy and chromosomal translocation) can be useful as indicator of exposure to environmental mutagens. FISH (Fluorescence in situ hybridisation) has been introduced as an improvement to classical cytogenetic methods for scoring chromosomal aberration in methaphase cells or in interphase cells (3)

The main aim of this study was a prospective screening of individual patients before and after operation in order to assess if there were changes in chromosome aberrations and metal concentration over time. Furthermore it was of interest to study whether similar changes were occurring compared to those observed in metal-on-metal patients as described previously (4).

Material and methods

A total of 24 patients with the Cerasul® (Zimmer Inc.) ceramic-on-ceramic hip replacement were recruited to provide the data for this study with informed consent and with ethical approval. This prosthesis had the same stem as for the metal-on-metal study (Metasul®, Zimmer Inc.) but had a different cup with titanium shell and a polyethylene inlay. Blood samples were obtained not only immediately prior to operation but also 6 months after (22), 1 year after (16) total hip replacement to allow a successful comparison. Whole blood cultures were initiated by the addition of 5 ml RPMI 1640 medium contained 10% Fetal Bovine Serum, 25mM Hepes, penicillin (100 U/ml) and streptomycin (100 U/ml), 25mM L-glutamine and phytohemagglutinin (1.25%). Duplicate cultures for each patient were carried out 72 hours at 37 ºC.

Fluorescent in situ hybridisation was performed on freshly made slides "aged" with ethanol at 94 ºC. Each slide was evaluated for chromosomal aberrations (translocations and aneuploidy: gain and loss) by simultaneous painting of chromosome 1, 2 and 3. The method was performed with the use of commercial available human painting probes (Cambio, Cambridge, UK) according to the supplier's protocol with some modifications. 300 metaphase spreads were examined per patient.

Whole blood metal measurements, in nanograms/ml (ng/ml), were obtained using high-resolution inductively coupled plasma mass spectrometry of metals, chromium (Cr), cobalt (Co), nickel (Ni) and molybdenum (Mo) as described previously (5). The detection limits were 0.2 ng/ml for Cr, Co, Mo and 1 ng/ml for Ni.

Results

Chromosome aberrations. The changes in chromosome aberrations in whole blood are presented in fig 1. There was a significant increase of chromosome aberrations postoperatively (6 months and 1 year) compared to preoperative values. In the figure are shown values for total aneuploidy, gain and losses of chromosomes. All these values were increased postoperatively. The chromosome translocations were increased postoperatively at 6 months and then decreased at 1year. The increase of aneuploidy was much greater then that of chromosome translocations.

Metal level. The changes in metal level preoperatively and postoperatively in whole blood are shown in fig.2. No significant changes were seen in any of the metals. In some patients the level of nickel were greater at one year post implantation.

Discussion

This study has demonstrated that the level of chromosome aberrations in whole blood of patients after ceramic-on-ceramic hip replacement is increased. No significant increases were found in metal concentration. The pattern and level of chromosomal changes (aneuploidy and translocations) seems to be similar to that which we described in our previous and similar study of patients with metal-on-metal prosthesis (4). This suggests that the increase of chromosome aberrations may have been caused either by the stem of the prosthesis inserted into the bone marrow (the same stainless steel Protasul stem is used in ceramic-on-ceramic and metal on metal implants) or by a small particle effect or by some non specific effect of surgery (but see 6).

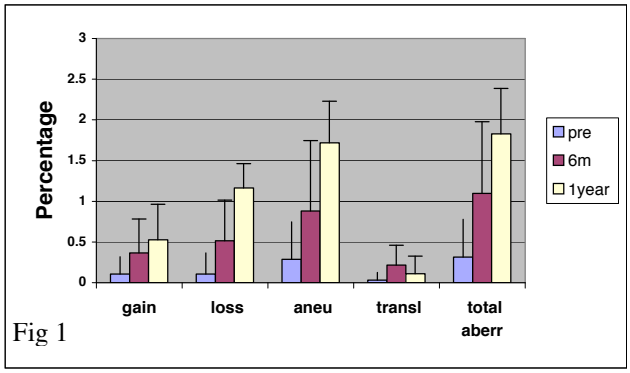

Fig 1

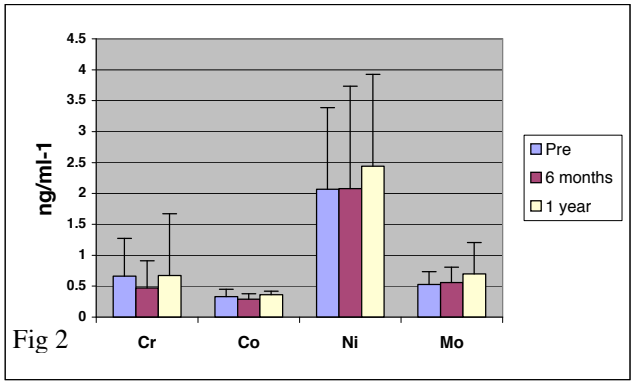

Fig 2

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