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Impact of Raised Serum Cobalt Levels From Recalled Articular Surface Replacement Hip Prostheses on the Visual Pathway

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ABSTRACT

Background: The articular surface replacement (ASR) was recalled in 2010 because of higher than expected revision rates. Patients reported symptoms of neurologic dysfunction including poor vision. This cohort study, using objective measurements, aimed to establish whether a higher incidence of visual function defects exists in ASR patients.

Methods: Thirty-three ASR patients and 33 non-ASR controls (control 1) were recruited. Data were compared with normative population data from the visual electrophysiology database (control 2). Patients underwent investigations for serum cobalt levels, psychophysical visual tests, and extensive electrophysiological visual testing.

Results: After excluding 2 subjects with pre-existing eye disease, data from 33 ASR patients were compared with the 2 control cohorts. The median serum cobalt level in the ASR group (median, 52 nmol/L [interquartile range, 14-151 nmol/L]) was significantly higher than that in the control 1 cohort (median, 7 nmol/L [interquartile range, 5-14 nmol/L]; $P < .0001$). The photoreceptor function of patients with an ASR of the hip showed significantly larger electroretinography mixed rod-cone b-wave amplitudes than both control 1 and control 2 cohorts ($P = .0294$ and .0410, respectively). Abnormalities in macular function as reflected by multifocal and scotopic electroretinography were more prevalent in control 1 ($P = .0445$ and .0275, respectively). Optic nerve pathway measurements using visual-evoked potential latency was significantly longer in the ASR group compared with those in the control 2 cohort ($P = .0201$). There were no statistical differences in visual acuity.

Conclusion: A statistically significant disturbance in visual electrophysiology was found in the ASR group when compared with the control groups. These differences did not translate to identifiable clinical visual deficits. Orthopedic surgeons need to be aware of the possibility of visual dysfunction in patients with ASR and other metal-on-metal hip arthroplasties; however, routine visual testing is not recommended.

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With increasing numbers of younger, more active patients presenting with osteoarthritic hips, the concept of the metal-on-metal (MoM) prosthesis has been revisited. In 2008, they accounted for 35% of the hips replaced in the United States [1].

DePuy introduced the articular surface replacement (ASR) in 2003. The ASR prosthesis is manufactured from a cobalt-chromium alloy. Although these essential elements are required for normal biological function, high concentrations of cobalt and chromium are potentially toxic [2,3]. In well-functioning MoM arthroplasties, the metal ion levels are generally below toxic levels and are usually only slightly higher than those in patients with metal-on-polyethylene implants [4,5].

However, in poorly functioning MoM hips, metal ion levels may be significantly elevated causing local and also possible systemic disease [6]. The normal reference range for cobalt is 0-17 nmol/L [7]. A serum cobalt level of >17 nmol/L indicates excessive cobalt exposure, and levels of >168 nmol/L are likely to have significant implant deterioration [8]. The DePuy ASR was recalled by its manufacturer in 2010 following higher than expected revision rates as reported in the Australian and UK joint registries [9–11]. This prosthesis failure has also been noted in other MoM products on the market [11]. Failure is primarily related to the design of the ASR, which has a reduced "arc of cover" (the angle subtended by the articular surface of the cup) and head-cup clearance, which is believed to increase the likelihood of edge loading and high wear [6,12,13]. Suboptimal component positioning appears to compound these factors [6,12,13].

Systemic complications of acutely elevated chromium levels result in disturbance of renal, hematologic, hepatobiliary, and respiratory systems [14,15]. Chronic exposure to an elevated chromium level is known to be allergenic and carcinogenic with environmental exposure [15]. Reassuringly, a large observational study of close to 300,000 patients showed no increased risk of cancers when comparing MoM prosthesis with alternative bearings [16]. Cobalt neurotoxicity involves memory loss, limb paresthesia, peripheral neuropathy, and nerve deafness [16]. Concerns have also been raised throughout the literature suggesting a correlation between cobalt toxicity and visual loss or dysfunction [17–20]. This cohort study was designed to investigate this concern: aiming to ascertain if there is impairment of visual pathway function in patients with high cobalt levels from the ASR hip system and to establish which components of the visual system are affected.

Methods

Patients

Ethical approval was granted by the Human Research Ethics Committee, Perth, WA, Australia. The study was advertised to local surgeons through seminar presentations, and local surgeons (who were known to have implemented ASR prostheses) were contacted so that ASR patients could be recruited. Thirty-three patients met the eligibility criteria having an ASR of the hip in-situ or recently revised implant. Four of these patients had bilateral ASR of the hip. These patients were compared with 2 groups. Control group 1 (control 1) comprised 33 patients recruited from 3 surgeons with non-MoM hip arthroplasties performed between 2005 and 2011 to frequency match time of surgery. Control group 2 (control 2) was selected from the hospitals electrophysiology normative data set of the Department of Medical Technology and Physics. Both control groups were recruited and was stratified for age and gender to reduce confounding of these variables on eye pathologies. Trained interviewers administered a screening questionnaire to exclude cases with pre-existing significant eye disease or medications known to interfere with the visual pathway.

Protocol

Following provision of informed consent, patients of ASR and control 1 groups underwent serum cobalt analysis and extensive visual testing. Cobalt levels were not obtained from patients in control 2 as this cohort were not known to have undergone hip replacement and assumed to represent cobalt levels in the normal population.

The ASR and control 1 cohort underwent comprehensive battery visual assessments undertaken by an experienced technician. Testing was performed over a 6-hour assessment period or 2 visits of 3 hours depending on patient availability. Multiple tests were needed as many factors can influence overall visual function. Control 2 results were obtained from a database. Results were assessed and categorized by a senior ophthalmologist.

Visual acuity was measured using a standardized early treatment of diabetic retinopathy study chart. Visual fields to assess peripheral vision and contrast sensitivity (ability to see letters of reducing contrast) were also examined. Contrast sensitivity measurement can demonstrate subtle abnormalities of visual function even when acuity is deemed normal.

Electrophysiology assessments involved placing electrodes around the eyes and on the scalp. Retinal function was assessed using electro-oculography to test retinal pigment epithelial cell function, electroretinography (ERG) to test photoreceptors, and pattern ERG to investigate central retina (macula) and optic nerve function. Visual-evoked potentials (VEPs) provided further information about function of the optic nerve and pathway to the visual cortex using recording electrodes on the scalp in response to a visual stimulus (a television monitor with alternating checker pattern). Macular function was determined using multifocal ERG (MFERG) which helps localize abnormalities within the central retinal (macular) field. All tests were performed according to the International Society for Clinical Electrophysiology of Vision standards.

Statistical Analysis

Data were analyzed using the R environment for statistical computing [21]. Percentages (%) are reported for categorical variables, while means ± standard deviations are reported for normally distributed continuous variables or medians and interquartile ranges (IQRs) for non-normally distributed continuous variables.

A 1-way analysis of variance was used to compare age between ASR, control 1, and control 2 groups, and a chi-squared test was used to compare the proportion of males between groups. Independent samples t tests were used to compare (log transformed) serum cobalt levels between ASR and control 1 groups, as well as between normal and abnormal psychophysical visual function.

Chi-squared tests (Fisher exact tests where appropriate) were conducted to investigate relationships between psychophysical and electrophysiology variables (when categorized as either normal or abnormal) between ASR and control 1 groups. This analysis used only patients' worst eye for each variable. Significance was set at the 5% level.

The results were analyzed as categorical variables of normal or abnormal, with abnormal being determined using clinical classifications for psychophysical measures of visual function some of which do not follow normal distribution. Electrophysiological categories were defined based on weighted z-scores for salient response features from age-stratified normal ranges established for the clinic.