Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/jor

Original Article

Differences in concentration of metal debris in blood, serum, and plasma samples of patients with metal-on-metal hip resurfacing arthroplasty

M. Khan [a,*], J.H. Kuiper [a], Christine Sieniawska [b], J.B. Richardson [a]

[a] Institute of Orthopaedics, The Robert Jones and Agnes Hunt Orthopaedic and District Hospital, Oswestry, Shropshire SY10 7AG, United Kingdom
[b] Department of Clinical Biochemistry, University Hospital Southampton NHS Foundation Trust, Southampton SO16 6YD, United Kingdom

ARTICLE INFO

Article history:
Received 24 June 2015
Accepted 4 October 2015
Available online 9 December 2015

Keywords:
Metal ions
Serum
Plasma
Chromium
Cobalt

ABSTRACT

Background/aims: Cobalt and chromium are released from MOM hips and their precise nature (ions/particles) is not known. Their distribution in serum, plasma, and whole blood may help to determine their nature.
Methods: We measured cobalt and chromium concentrations in plasma, serum, and whole blood samples of patients with resurfacing MOM hips.
Results: We found that chromium concentration was highest in plasma, followed by serum and whole blood. Chromium and cobalt concentrations were higher in serum and plasma, compared to whole blood.
Conclusion: We, therefore, suggest that in future cobalt and chromium concentrations shall be reported using plasma samples.

1. Introduction

Patients with metal-on-metal bearing hip arthroplasty have elevated levels of cobalt and chromium in blood and urine. Excess of both elements is toxic to humans, and concerns have been raised about their carcinogenic potential.[1,2]

Several studies have reported cobalt and chromium levels in patients with metal-on-metal bearing hip replacement. The levels can be affected by differences in age, activity level, time since implantation,[3] analytical technique, and implant types.[4]

Most of the metal debris are produced as a result of wear. The commonest mode of wear at the bearing surfaces is adhesive wear, and therefore, it is expected that the wear debris will be in the form of particles. The literature mostly reports the circulatory cobalt and chromium debris as ion levels. We believe that this convention has resulted because of laboratory reporting of the results. In order to calculate the quantity of the individual element in an alloy, the alloy has to be broken down

* *Corresponding author.*
E-mail address: surgeonmunir@hotmail.com (M. Khan).
http://dx.doi.org/10.1016/j.jor.2015.10.006

into constituent elements (cobalt, chromium, etc.). This process occurs in an extremely hot plasma chamber of the machine, and thus at this stage, the elements are present in ionic states, which otherwise cannot be expected because cobalt and chromium are highly reactive, and therefore, do not exist in pure form.

If metal debris exists in the form of particles, then more of these are expected to be outside the red cells, which approximately make about 45 percent of the blood volume. In order to perform analysis of the whole blood concentration of metal debris, the red cells are hemolyzed. This process causes addition of the intracellular water to the extracellular compartment, and results in dilution of the concentration of metal debris in extracellular compartment, and will result in erroneous results. Similarly, some metal debris may be attached to plasma proteins, and therefore, elimination of those proteins can result in dilution of the results in serum samples. Hence, it is important to know which sample will give highest concentration of metal debris, and accordingly use it routinely.

We designed this study to measure the concentration of metal ion debris in whole blood, serum, and plasma, in order to identify the component of blood to which most of the wear debris is added from the hip joint. We tested the null hypothesis that there is no difference in whole blood, serum, and plasma cobalt and chromium levels of the same patient.

2. Material and methods

Patients who had metal-on-metal resurfacing hip replacement were identified from the hospital records. Patients with these implants were sent a postal invitation to take part in the study. The local Research Ethics Committee and the Research Panel in our hospital approved the study. All subjects were informed about the study and provided written consent.

2.1. *Collection of whole blood, serum, and plasma samples*

Plasma, serum, and whole blood samples were taken for analysis of cobalt and chromium levels from patients. The first 3 ml of each blood sample was discarded at collection and two samples (2 ml each) were then collected, one into a metal-free lithium heparin tube (Teklab, Durham, UK), and one into a plain metal-free container. The samples were then centrifuged at 3500 revolutions per minute for 5 min. Serum was isolated from the free metal container and plasma from the lithium heparin centrifuged tube.

2.2. *Sample analysis*

All blood analyses were performed at the SAS Trace Metal Unit at Southampton General Hospital (Southampton, UK). Cobalt was determined using Inductively Coupled Plasma Mass Spectrometry (ICP-MS), and chromium was determined using Dynamic-Reaction Cell ICP-MS. The detection limits for each element were 1 nmol/L. To see differences between blood, serum, and plasma metal ion levels, the analysis was performed separately for each sample. To see the repeatability in sample measurements (precision of repeated measurements), measurements in each sample (blood, serum, and plasma) were taken in duplicate.

2.3. *Statistical analysis*

The two types of statistical analysis[5] used for the purpose were intraclass correlations (ICCs),[6] and Bland and Altman tests.[7] Bland and Altman approach is based on the analysis of differences between measurements. The differences between two measures are plotted against average of the two measurements. The resulting graph shows size of each difference, the range of differences, and their distribution about zero (perfect agreement). Distributions on the graph will show if differences in samples are related to the size of the mean of two samples. In other words, as the mean of two samples increases, so does the difference. The results of Bland and Altman analysis include the mean difference between measures, the 95% confidence intervals, and the reliability coefficient (assuming that the mean difference is zero).

3. Results

There were seventeen patients with two different types metal-on-metal bearing resurfacing hip replacement (Birmingham Hip Resurfacing, Midland Medical Technologies, UK; and Cormet Hip Resurfacing, Corin Medical, UK). Ten participants were male and seven were females with the mean age of 55 years (range 42–80 years). The median time since implantation was 44 months (range 6–96 months).

3.1. *Intersample analysis*

Mean plasma, serum, and whole blood cobalt and chromium levels are shown in Tables 1 and 2. Plasma and serum had high levels of cobalt and chromium, as compared to whole blood.

Table 1 – Mean and standard deviation of the cobalt and chromium levels in plasma, serum, and whole blood.

	Intersample reliability		
	Plasma (nmol/L) (Mean, SD)	Serum (nmol/L) (Mean, SD)	Blood (nmol/L) (Mean, SD)
Cobalt	40 (31.3)	42.2 (34.8)	33.8 (25.7)
Chromium	117 (52.2)	65.9 (39.7)	47.7 (24)

Table 2 – Mean and standard deviation of the cobalt and chromium repeatable measures (nmol/L) in plasma, serum, and whole blood.

Between-measurements repeatability in a sample (measurement 1 and measurement 2)					
Plasma cobalt (nmol/L) (Mean, SD)		Serum cobalt (nmol/L) (Mean, SD)		Blood cobalt (nmol/L) (Mean, SD)	
P1	P2	S1	S2	B1	B2
39.1 (31.1)	39.9 (31.2)	41.8 (34.2)	42.6 (34.5)	33.7 (24.2)	34 (25.3)