Serum Chromium Levels Sampled With Steel Needle Versus Plastic IV Cannula. Does Method Matter?

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Abstract: Purpose: Modern metal-on-metal (MoM) joint articulations releases metal ions to the body. Research tries to establish how much this elevates metal ion levels and whether it causes adverse effects. The steel needle that samples the blood may introduce additional chromium to the sample thereby causing bias. This study aimed to test that theory. Methods: We compared serum chromium values for two sampling methods, steel needle and IV plastic cannula, as well as sampling sequence in 16 healthy volunteers. Results: We found statistically significant chromium contamination from the steel needle with mean differences between the two methods of 0.073 ng/mL, for the first sample, and 0.033 ng/mL for the second. No difference was found between the first and second plastic sample. The first steel needle sample contained an average of 0.047 ng/mL more than the second. This difference was only borderline significant. Conclusion: The chromium contamination from the steel needle is low, and sampling method matters little in MoM populations. If using steel needles we suggest discarding the first sample.

Keywords: blood-material interaction; metal ions; stainless steel; measurement/assessment; cobalt-chromium (alloys)

INTRODUCTION

Metal-on-metal articulations (MoM) in total hip replacement have gained increasing popularity in recent years due to possible greater range of motion,1,2 greater stability of the artificial joint and less linear wear as compared to the standard articulation of polyethylene cup/liner and a metal head.3 However, MoM produces metal ions that can be measured both locally, in urine and in blood. This has raised concerns about local hypersensitivity reactions (ALVAL),4 local toxic effects leading to tissue necrosis and formation of pseudo tumor,5 and possible carcinogenetic effects.4,6–8

When measuring very low concentrations of metal ions, contamination could have a tremendous impact.

A possible source of contamination is the steel needle used to draw the sample. The concern is that chromium bound in the alloy as well as dust from the manufacturing process can be transferred to the blood sample. Flushing the steel needle for metal dust is recommended in order to avoid contamination, but to our knowledge not documented.5 To completely avoid the chrome contact some recent publications have taken to using plastic IV cannulas instead.10–14

We have found the plastic IV cannula method more difficult to handle. Not all patients have veins suitable for placing the plastic cannula, and the lack of a vacuum means that the flow stalls in some patients before all tubes are filled. Many of our patients have also remarked that they find the method more uncomfortable than the steel needle, and given the choice we would prefer using steel needles.

Our aim with the study is to compare serum chromium levels sampled with steel needles to those from plastic IV cannulas, and to compare the metal levels from first to second flush within each method. The null-hypothesis being that there is no difference of either of the purposes.

PATIENTS AND METHODS

Eighteen healthy volunteers (9 men, 9 women) median age 41 yrs (24–58 yrs) from the staff at the orthopedic dept.
were included after informed consent. They had no occupational exposition to chrome and no metal implants. Two volunteers were excluded from the analyzes as the blood flow stopped while sampling using the plastic IV cannula. Institutional board review was obtained 26th of November 2007 (project-ID: S-20070118). Sample size was calculated to 16 based on a power of 90%, a delta SD of 0.03 ng/mL of a MIREDIF of 0.025 ng/mL and a 5% type-one error. Our chosen MIREDIF corresponds roughly to 10% of the serum chromium levels measured in pre 2008 studies of nonimplanted populations,12,15–20our rationale being that anything below 10% variability is a reliable result and hence that difference should be acceptable even in the lowest-chromium populations.

**Design and Materials**

With sealed envelopes we randomized to “plastic cannula first” or “steel needle first”. Two blood samples were drawn from each arm. On one side through the steel needle, and on the other side through the plastic cannula. A cobalt-free steel needle (Nickel 9.2%, Chromium 18.4%, Manganese 1.8%, Iron 69.6%, and Mixed listing1%; Vacutainer® “Safety-Lok Blood collection set” (21 G 0.8 × 19 mm × 304.8 mm)(BectonDickinson, NJ) and a small plastic tube; Venflon Pro (18G-1, 3 × 32 mm) (BectonDickinson, NJ) were used. The blood was collected in 6 mL BD Vacutainer® plus serum plastic tubes (368380) (BectonDickinson, NJ) and allowed to coagulate. The first sample was labeled “Needle/Plastic 1” and the following sample was labeled “Needle/Plastic 2,” depending on method. Powder free vinyl gloves, Sempercare Vinyl (Sempermed, FL) were used during sampling and handling and all pipettes and vials had been soaked for a week in 0.14 M HNO₃ and verified contamination free.

**Analyzing Methods**

Samples were initially handled in a ISO/EN 17025 accredited hospital based trace element lab. The tubes were centrifuged for 10 min at 1500 rpm, and the serum transferred to 3.8 mL acid washed Nunc tubes (Thermo Fisher Scientific, Denmark) and frozen at minus 80°C. The frozen serum samples were analyzed for chrome and chromium content on a Perkin–Elmer, Elan 6100 DRC FI-ICP-MS (Perkin–Elmer, MA) in a ISO/EN 17,025 accredited lab (Danish Technological Institute, Taastrup, Denmark). In order to avoid potential contamination from theoretically higher metal ion concentrations, we analyzed the samples in the following order; 0.14 M HNO₃, Plastic 2, Plastic 1, 0.14 M HNO₃, steel needle 2 and steel needle 1.

Chromium detection limits ranged from 0.04 to 0.08 ng/mL. To measure the chromium content we used a DCR technique with ammonia as the reactive gas, the detection limit was higher for cobalt due to calcium oxide interference, namely 0.2 ng/mL.

**Statistical Methods**

Serum levels below the detection limit were assigned a value of half the detection limit. Total serum values are presented as medians in box plots. Data were compared as means using 95% Limits of agreement (LOA).

Statistical difference was evaluated by using Wilcoxon signed-rank test in STATA 10.0 (StataCorp LP, College Station, Texas). Probability values below 0.05 were considered statistical significant.

**RESULTS**

All cobalt measurements were, as expected, below the detection limit. The chromium levels are presented in Figure 1, and the difference of the means with 95% LOA in Table I. For chromium, there were significant differences between plastic and steel for both the first (p = 0.0006), and the second sample (p = 0.0322). The difference between the first and second plastic samples was not statistically significant (p = 0.585). Although the mean Cr level of the second sample steel needle was 36% percentages lower than the first sample, the 0.047 ng/mL difference was not statistical significant, however, with p = 0.059 it was bordering.

**DISCUSSION**

To our knowledge no publication has compared a plastic versus steel cannula when measuring metal ions in serum.

**TABLE I. Difference of the Mean (95%LOA) Serum Chromium Content**

<table>
<thead>
<tr>
<th></th>
<th>Plastic 1</th>
<th>Needle 2</th>
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</thead>
<tbody>
<tr>
<td>Needle 1</td>
<td>−0.073 (−0.188 to 0.042) ng/mL</td>
<td>−0.047 (−0.220 to 0.127) ng/mL</td>
</tr>
<tr>
<td>Plastic 2</td>
<td>−0.007 (−0.063 to 0.048) ng/mL</td>
<td>−0.033 (−0.135 to 0.068) ng/mL</td>
</tr>
</tbody>
</table>

*Indicates statistical significant difference.
The investigation is highly relevant for studies where low concentrations of metal ions are found. The study demonstrated that the use of a steel needle contaminated the serum with chromium in contrast to the plastic cannula.

The chromium contamination from the steel needle is statistical significant and there is a clear systematic difference between plastic and steel for the first sample in particular. For the second samples the average steel needle contribution of 0.033 ng/mL is in the gray-area around the detection limit.

When monitoring a MoM population this contamination is likely to be of little consequence. The metal levels in these patients have large variations and are manifold greater than the contribution from our needle with median serum levels ranging from 0.91 to 5.5 ng/mL.15,19,21–24

To compare results from different research groups, consensus in handling and analyzing the samples is suggested.9

There are several factors which might influence the measured value of metal-ion concentrations. The medium used (serum, whole blood or erythrocytes)12,23,25–27 contributes significantly to the result, and as the analyzing machines themselves (ICP-MS, High Resolution ICP-MS or GAFFS) have different degrees of precision and detection limits some variability must be accounted for in this link as well.

Compared to that variation, the choice of steel needle versus IV plastic cannula seems of less consequence for the final ion level.

If there was a difference in serum Cobalt we did not demonstrate this due to the high detection limit for cobalt.

There was the option of running the tests again specifically for Cobalt, without using the ammonia gas, but as the steel needle used in the study is a cobalt-free alloy and previous testing of 10 steel needles all yielded cobalt levels below a detection limit of 0.03 ng/mL, we are satisfied that the needle does not add cobalt to the samples. We therefore refrained from running the tests again.

We were not able to reject our null-hypothesis for the “first flush” procedure. The first steel needle sample was only borderline significantly different from the second needle sample. We may have underpowered our study though. Our calculated sample size was based on a SD of 0.03 ng/mL. In reality it was double that, 0.06 ng/mL for the first steel needle sample. As our found difference of 0.047 ng/mL was twice the size of our designed MIREDEL of 0.025 ng/mL it seems fair to speculate that a larger sample size would have lead to a statistically significant difference.

That, combined with the slightly larger variation within the first steel needle sample, leads us to support the continued use of the “first flush” procedure for the steel needle.

One cannot help speculating if the trocar from the plastic cannula, like the steel needle, in some cases could leave behind some metal dust from the manufacturing process. The first plastic sample did display some outliers and had double the variation of the second sample, but overall there was very little chromium difference from the first to second sample and, although flushing the system with an extra blood sample imposes little inconvenience, we have not demonstrated a need when using the IV plastic cannula.

We used a specific brand of steel needles for this study and whether the results can be extrapolated to other steel needles cannot be concluded. Previous contamination testing of 10 needles using demineralised water and 0.14 M HNO₃ and a DL of 0.02 ng/mL found median chromium levels of 0.092 ng/mL range 0.01–0.51. It seems reasonable to assume that other needles matching these levels can be used in the same way.

In conclusion, stainless steel needles, in contrast to IV plastic cannulas contaminated the serum samples. The importance of measuring the “true” chromium value must be weighed very high in scientific investigations and according to our study, we should chose the plastic cannula. However, in MoM- studies there are no clinical relevance of the difference we found and that has to be weighted against patient discomfort and the risk of not getting the sample at all or changing the sampling method in some patients. For metal-on-metal studies we suggest that the researcher should examine whether contamination is a problem if using a steel needle. If using a steel needle we suggest discarding the first flush. When measuring in low-chromium populations (e.g. occupational health testing) the steel needle could influence the “true” value, and in these cases we suggest using the IV plastic cannula as standard to minimize contamination.

REFERENCES


