Association of Urine-Cobalt, Blood-Cobalt, and Exposure-Duration to Cobaltism Symptoms: A Prospective studS of 230 Post-Arthroplasty Patients

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INTRODUCTION:

Cobalt toxicity afflicts metabolically active organs, most significantly the brain and heart.[1, 2] The resulting toxidrome, known as cobaltism, was first noted sixty years ago from vocational exposure, cobalt-chloride hematemics, or cobalt laced beer.[1] Jones[3] described systemic dissemination of cobalt from 1970s-era metal-on-metal hip implants.

Cobaltism from modern primary hip replacement was first reported in Alaskans[4] in 2010 then Australians[5] in 2011. Data from an Australian joint-replacement registry spurred the first of a hip because and risked risk of revision because of cobalt related complications.[6] Any cobalt-chromium orthopaedic component may result systemic cobalt exposure from wear or corrosion placing tens of millions at-risk for cobaltism.[2, 4, 7-16]

Cobalt from orthopaedic implants accumulates in the brain, nerves, heart, liver, kidney, and cerebrospinal fluid.[1, 3, 4, 8, 9] Advanced cobaltism is a catastrophic illness that can manifest as Parkinsonism,[13] blindness, deafness, numbness, weakness, or heart failure.[1, 7-9] Unfortunately, cobaltism may escape diagnosis until irreversible neurologic impairment, heart transplantation, or death occurs.[1, 8, 9, 13] Prodromal cobaltism symptoms are non-specific and easily misattributed to primary psychopathy, aging, idiopathic cardiomyopathy, or dementia.[2, 4, 5, 8-13] Early cobaltism appears to be largely reversable,[2, 4, 5, 8, 11-13] rendering diagnosis at this stage essential.

The relationship between cobaltism severity and urine-cobalt, blood-cobalt, and exposure-duration lacks prospective investigation. We therefore screened post-arthroplasty patients for cobaltism symptoms with a directed history and physical and a spot urine-cobalt. We adapted an industrial cobaltism questionnaire,[15] and inventories used for systematic literature reviews,[8, 9] into a healthcare provider administered and scored instrument. We then related scores from this survey to cobalturia, cobaltemia, and exposure-duration.

We investigate whether urine-cobalt of ≥1.0 or blood-cobalt of ≥0.4 ppb and exposure-duration to chrome-cobalt orthopaedic-implants relate to cobaltism symptoms.

METHODS:

Prospective study of 230 patients post hip, knee, or shoulder arthroplasty with cobalt-chromium component(s) presenting to one community surgeon.

Subjects were assigned a Cobaltism-Symptom-Inventory-Score (CSIS) based on a protocolized interview and examination followed by a spot urine-cobalt or blood-cobalt determination.

RESULTS:

A total of 129 (56%) subjects were cobalturic (U[Co] ≥1.0 ppb) or cobaltemic (B[Co] ≥0.4 ppb). The product of years exposed to a cobalt-chromium implant and urine-cobalt or blood-cobalt significantly positively associates with the CSIS. In total, 122 (53%) of subjects had a CSIS of >2, this status significantly associates with cobalturia or cobaltemia. Median [IQR] urine-cobalt in the subjects with a CSIS >2 was 4.1[1.1-17.0] compared to 0.5[0.5-1.4] in subjects with CSI score ≤ 2. Cobalturia has a sensitivity of 0.69, a specificity of 0.77, and a positive predictive value of 0.74 for prodromal cobaltism as defined as a CSIS of >2.

DISCUSSION AND CONCLUSION:

We find the Cobalt-Symptom-Inventory-Score significantly positively correlates with the product of exposure-duration and urine-cobalt or blood-cobalt indicating a dose-response-relationship. Cobalturia or cobaltemia is specific, sensitive, and positively predictive of early cobaltism as defined as a CSIS of >2. These findings are consistent with other studies with a similar degree of cobalturia or cobaltemia finding quantitative brain hypometabolism,[2] brain atrophy,[14] retinopathy,[18] Obstructive-Sleep-Apnea,[19] and quantitative audiovestibular dysfunction.[20]

The large at-risk population with orthopaedic cobalt-chromium implants,[16] the treatability of early cobaltism,[2, 11, 12, 21] and the severity and irreversibly of the severe cobaltism,[8, 9, 13] position orthopaedic-implant cobaltism as an ideal malady for screening. Patients with severe cobaltism or those with periprosthetic toxicity benefit from revision of wearing or corroding implants to cobalt-free alternatives and delay in revision surgery may result in irreversible neurologic and cardiac pathology.[9, 10] OTC N-acetylcysteine may benefit cobalturic or cobaltemic patients.[2, 11, 12, 21]

Cobaltism should be considered in the differential diagnosis for at-risk patients experiencing cognitive decline, constitutional deterioration, or progressive neurologic, psychiatric or cardiovascular pathology with or without periprosthetic symptoms because orthopaedic-implant cobaltism is both common and treatable.[2, 4, 5, 8-12, 18, 20, 21] Further implantations of cobalt-chromium orthopaedic-implants should be tempered given known safer materials.

Table 1. Cobaltism-Symptom-Inventory Score criteria

Fatigue	Forgetfulness	Disordered Mood	Disordered Sleep	Imbalance or Weakness	Numbness Extremities	Deafness or Tinnitus	Thermal Neurovisitor	Non-refractive Visual Dysfunction	Generalized Pain
0 Expected 1 Excessive	0 Expected 1 Excessive	0 Expected 1 Excessive	0 Expected 1 Excessive	0 Expected 1 Excessive	0 None 1 Minor 2 Moderate 3 Severe	0 Expected 1 Excessive	0 None 1 Minor 2 Moderate 3 Severe	0 Expected 1 Excessive	0 Expected 1 Excessive
Non-zero score only recorded if patient noted symptom onset or worsening after cobalt-chromium containing joint-replacement implantation and if patient considered symptom beyond his/her expectation for aging.									

Figure 3. Blood-cobalt and urine-cobalt in subjects with CSIS ≤ 2 or > 2

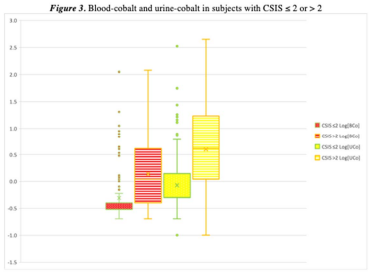

Figure 4. Blood-Cobalt-Years or Urine-Cobalt-Years by Quartiles of CSIS