Blood Nickel Concentrations in Patients with Stainless-Steel Hip Prostheses*

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ABSTRACT

Nickel concentrations were analyzed by electrothermal atomic absorption spectrophotometry in serum and whole blood specimens from patients 9 to 15 years after unilateral (N = 11) or bilateral (N = 2) hip arthroplasty. The hip prostheses were of the "Charnley" or "TR-28" (metal-to-plastic) types, fabricated of stainless-steel (14 to 16 percent Ni) with polyethylene acetabular cups. In 12 of the 13 patients, nickel concentrations (± SD) averaged 0.30 ± 0.25 µg per L (range 0.05 to 0.85) in serum and 0.36 ± 0.20 µg per L (range 0.11 to 0.67) in whole blood; these values did not differ significantly from the corresponding nickel concentrations in specimens from 30 healthy controls (0.28 ± 0.24 µg per L, range <0.05 to 1.08, in serum; 0.34 ± 0.28 µg per L, range <0.05 to 1.05, in whole blood). The remaining patient, a 78-year-old man with bilateral hip arthroplasty, had nickel concentrations of 3.1 µg per L in serum and 2.3 µg per L in whole blood; renal insufficiency apparently contributed to hypernickelemia in this patient. The arthroplasty patients were asymptomatic with respect to their joint replacements; X-rays at the last follow-up examinations did not reveal bone resorption around the implants. This study shows that patients with stainless-steel hip prostheses of the metal-to-plastic types do not develop hypernickelemia in the apparent absence of corrosion, local complications, or systemic conditions, such as renal insufficiency.

Introduction

Metal-induced hypersensitivity, local toxicity, and carcinogenesis have been implicated as iatrogenic hazards in patients with long-term exposures to metal alloys in orthopedic prostheses.20,24,30 Cutaneous or systemic allergic reactions to Ni, Co, and/or Cr have been reported in numerous recipients of implanted orthopedic devices.2,19,32,35,37,39,45,47 Corrosion of metal implants leads to accumulation of alloy-
specific metals in the surrounding soft tissues,14,21,22,25,29,34,48 and contributes to inflammation, necrosis, and susceptibility to infection in the vicinity of implants.4,7,9,10,12,13,17,40 Eight patients have been reported who developed malignant soft-tissue tumors near the implantation sites of bone plates or joint prostheses that contained carcinogenic metals (Ni, Cr, or Co).1,11,15,16,31,38,44,46 Several studies have indicated that analyses of trace metal concentrations in serum or whole blood can be used to monitor the release of metals from orthopedic prostheses.6,14,23,24,36 To test this suggestion, nickel concentrations were determined in serum and whole blood specimens from 13 patients with stainless-steel hip prostheses.

Methods

Blood specimens were collected with polyethylene intravascular cannulas, polypropylene syringes, and polyethylene test tubes, with stringent precautions to avoid nickel contamination.8,28,42 The blood specimens were collected, without fasting, at various times during the workday. Nickel-free heparin from bovine lung* was used as the anticoagulant.28 Nickel concentrations in serum and whole blood were analyzed by electrothermal atomic absorption spectrophotometry, as described by Sunderman et al,42 using a model 5000-Z spectrometer with automatic sampler, pyrolytic graphite tubes, and Zeeman background correction system.† The detection limit for nickel was 0.05 µg per L; coefficients of variation for replicate nickel analyses averaged 3.8 percent (within-run) and 8.1 percent (day-to-day); recovery of nickel added in concentration of 8 µg per L to 16 serums averaged 97 percent (SD ± 3 percent); recovery of nickel similarly added to 13 samples of whole blood averaged 103 percent (SD ± 6 percent). Nickel concentrations in 30 serums, measured by the method of Sunderman et al,42 did not differ significantly (corr. coef. = 0.980) from results obtained by the IUPAC reference method.8

The healthy control subjects were 30 asymptomatic residents of central Connecticut (15 men, 15 women, age 23 to 84 years), who were not taking medications and who had no occupational exposures to nickel. The patients (table I) were 13 residents of central Connecticut (8 men, 5 women, age 35 to 78 years) who had received unilateral (N = 11) or bilateral (N = 2) hip prostheses 9 to 15 years previously. Nine of the patients had prostheses of the “Charnley” type; the other four patients had prostheses of the “TR-28” type.‡ The femoral heads were fabricated of Zimmer certified stainless steel (14 to 16 percent Ni); the acetabular sockets were made of polyethylene. One of the authors (H.R.G.) performed all of the arthroplasty operations and followed the patients regularly during the ensuing years. At the last follow-up examinations in 1984, the patients were asymptomatic with respect to their prostheses; X-rays did not reveal bone resorption around the implants. The patients were generally in good health, except No. 6 (male, age 78), who suffered from mild renal insufficiency. At the last follow-up examination, his serum concentration of urea nitrogen was 40 mg per 100 mL (normal = 8 to 18 mg per 100 mL) and his serum creatinine concentration was 1.5 mg per 100 mL (normal = 0.6 to 1.2 mg per 100 mL).

Results

In serum specimens from 30 healthy adults, nickel concentrations (± SD)
TABLE I
Clinical Parameters of the Patients with Hip Arthroplasty

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Year of Birth</th>
<th>Joint Disease</th>
<th>Year of Surgery</th>
<th>Type of Prosthesis</th>
<th>Years After Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>1913</td>
<td>Rheumatoid arthritis</td>
<td>1969</td>
<td>Charnley</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>1916</td>
<td>Osteoarthrosis</td>
<td>1975</td>
<td>Charnley</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>1917</td>
<td>Osteoarthrosis</td>
<td>1971</td>
<td>Charnley</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>1921</td>
<td>Osteoarthrosis</td>
<td>1969</td>
<td>Charnley</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>1923</td>
<td>Osteoarthrosis</td>
<td>1974</td>
<td>Charnley</td>
<td>10</td>
</tr>
<tr>
<td>6*</td>
<td>M</td>
<td>1906</td>
<td>Rheumatoid arthritis</td>
<td>1976</td>
<td>Charnley</td>
<td>9</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>1909</td>
<td>Osteoarthrosis</td>
<td>1976</td>
<td>TR-28</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>1910</td>
<td>Osteoarthrosis</td>
<td>1976</td>
<td>Charnley</td>
<td>9</td>
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<tr>
<td>9</td>
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<td>1913</td>
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<td>1976</td>
<td>Charnley</td>
<td>9</td>
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<tr>
<td>10</td>
<td>M</td>
<td>1914</td>
<td>Osteoarthrosis</td>
<td>1976</td>
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<td>9</td>
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<tr>
<td>11</td>
<td>M</td>
<td>1916</td>
<td>Osteoarthrosis</td>
<td>1976</td>
<td>TR-28</td>
<td>9</td>
</tr>
<tr>
<td>12†</td>
<td>M</td>
<td>1936</td>
<td>Rheumatoid arthritis</td>
<td>1975</td>
<td>TR-28</td>
<td>9</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>1949</td>
<td>Rheumatoid arthritis</td>
<td>1976</td>
<td>Charnley</td>
<td>9</td>
</tr>
</tbody>
</table>

*Patient No. 6 had bilateral hip arthroplasty; he subsequently developed mild renal insufficiency.
†Patient No. 12 had bilateral hip arthroplasty in 1975 and bilateral knee arthroplasty in 1976.

Averaged 0.28 ± 0.24 μg per L (range < 0.05 to 1.05). In specimens of whole blood from the same healthy subjects, nickel concentrations averaged 0.34 ± 0.28 μg per L (range < 0.05 to 1.05). The concentrations of nickel in whole blood specimens from healthy subjects were slightly lower than previously reported, owing to the use of heparin that contained no detectable nickel.

Nickel concentrations in serum and whole blood specimens from 13 patients with hip arthroplasty are listed in table II. In 12 of the patients, nickel concentrations in serum and whole blood averaged 0.30 ± 0.25 and 0.36 ± 0.20 μg per L, respectively, which did not differ significantly from the corresponding values in the healthy controls. In the initial samples from patient No. 6, nickel concentrations in serum and whole blood were 3.1 and 2.3 μg per L, respectively. When repeat blood samples were obtained from patient No. 6 three weeks later, nickel concentrations in serum and whole blood were 2.4 and 2.1 μg per L, respectively. X-ray examinations of the bilateral hip arthroplasties in patient No. 6 gave no indication of bone resorption around the implanted stems. Interrogation of patient No. 6 and his internist disclosed no exogenous sources of nickel.

**Discussion**

This study shows that only one of 13 patients with stainless-steel hip prostheses had elevated concentrations of nickel in serum and whole blood specimens that were obtained 9 to 15 years post-arthroplasty. The patient with positive results (No. 6) had none of the conditions that are known to be attended by hypernickelemia, viz., myocardial infarction and unstable angina pectoris, cerebral stroke, thermal burns, renal hemodialysis, disulfiram therapy of chronic alcoholism, intravenous infusion of human albumin concentrates, and occupational or environmental exposures to nickel compounds. The present authors speculate that the bilateral hip prostheses are the probable
source of hypernickelemia in patient No. 6, with impaired renal clearance of nickel as a contributory factor. This study indicates that asymptomatic patients with stainless-steel hip prostheses, without X-ray signs of local complications or clinical evidence of renal insufficiency, do not have elevated concentrations of nickel in serum or whole blood after long-term exposure.

At first glance, the positive results of previous studies of nickel concentrations in body fluids and tissues of prosthesis recipients\textsuperscript{6,14,23,24,36} seem incongruent with the predominantly negative outcome of this study. Dobbs and Minski\textsuperscript{14} observed increased concentrations of nickel in lung, liver, and kidney samples obtained at autopsy of an 81-year-old woman who had bilateral hip prostheses. Tissue adjacent to one of the prostheses, a Stanmore "Mk-1" metal-on-metal joint, was heavily laden with metal wear debris; tissue adjacent to the second prosthesis, a Stanmore "Mk-7" metal-on-plastic joint, was relatively free of debris. Hildebrand et al\textsuperscript{23,24} found increased nickel concentrations in plasma or whole blood specimens from 8 of 9 patients 2 to 18 years after implantation of various nickel-containing osteosynthesis plates, intramedullary nails, or total hip prostheses. In four of these patients, plasma nickel concentrations exceeded the limit of 7.5 \( \mu \text{g} \) per L that has been recommended for workers in nickel refineries;\textsuperscript{3} in one patient, the plasma nickel concentration reached 60 \( \mu \text{g} \) per L.\textsuperscript{23} Several of the patients studied by Hildebrand et al\textsuperscript{23,24} had severe inflammatory or allergic reactions to the metal prostheses. Black et al\textsuperscript{6} reported two-fold increase of mean nickel concentrations in serum specimens from 15 patients during three to six months after implantation of total hip prostheses of the Charnley or Charnley-Mueller types, fabricated of unspecified Co-Cr-Ni alloys and polyethylene. Black et al\textsuperscript{6} presented their results as means and confidence intervals; they did not specify the number of prosthesis recipients with hypernickelemia; the plot of their data suggests that the apparent increase of mean nickel concentrations was statistically insignificant. Pazzaglia et al\textsuperscript{36} found two-fold increases of mean nickel concentrations in plasma, whole blood, and urine specimens from 20 patients 10 to 13 years after implantation of hip prostheses of the Charnley type, fabricated of stainless-steel and polyethylene.\textsuperscript{*} Conditions favorable to corrosion of the prostheses, such as bone resorption around the stem, were present in 12 of these patients. Pazzaglia et al\textsuperscript{36} presented their results as means ± SD; they did not specify the number of prosthesis recipients with hypernickelemia or hypernickeluria.

Upon careful scrutiny, the present findings do not contradict the previous reports; the metal alloys in prostheses used in previous studies were evidently more subject to corrosion than the stainless-steel prostheses implanted in this investigation. Hypernickelemia in pa-

* Thackray Ltd., model "Mk-1S".
tients with metal prostheses appears to be indicative of corrosion, allergic, or inflammatory complications, or the presence of contributory systemic conditions, such as renal insufficiency.

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References

26. Hopper, S. M., Linden, J. V., Crisostomo,


