Arthroplasty (joint replacement surgery) is a surgical procedure designed to restore the function of a joint by replacing damaged joint surfaces with artificial components. The longevity and biocompatibility of arthroplasty implants are of utmost importance. However, all implants are subject to biological processes, which result in corrosion of the implant components. Since neurotoxic effects have been observed for certain metals, such as titanium, cobalt, and vanadium, which are frequently used in arthroplasty, the authors from Germany investigated the concentrations of arthroplasty-relevant metals in the blood and cerebrospinal fluid (CSF) of patients who had undergone major joint replacement.

Modern arthroplasty implants consist of up to ten metals, which leads to uncertainties regarding their potential systemic effects after long-term exposure. The authors emphasized previous studies on degradation products of arthroplasty implants, which have shown their negative effects on bone and soft tissue surrounding the prosthesis, contributing to implant loosening and other forms of implant failure. As some studies have shown a higher prevalence of neurodegenerative diseases and psychiatric disorders in patients with arthroplasty implants, increasing concerns have recently been raised about possible systemic toxic effects of metals released from arthroplasty implants. However, the results of studies on brain structural changes possibly caused by exposure to cobalt and chromium entering the bloodstream from arthroplasty implants are contradictory.



About the study

The NeuroWear pilot study was a single-center, hospital-based, cross-sectional study. It prospectively included patients with at least one major artificial joint (i.e., an arthroplasty implant of the hip, knee, ankle, shoulder, or elbow joint). Age- and sex-matched arthroplasty-naïve patients served as the control group.

Standard cannulas for blood and CSF collection had previously been tested for any metal

relevant to this study to exclude contaminations.

The CSF, whole blood, and serum levels of aluminum, cobalt, chromium, molybdenum, nickel, niobium, tantalum, titanium, vanadium, and zirconium were quantified by inductively coupled plasma mass spectrometry (ICP-MS). Results represent the means of three measurements each. Serum levels of S-100B protein, as a marker of the blood-brain barrier integrity, were analyzed by an automated chemiluminescent immunoassay (CLIA).

The primary endpoint assessed CSF metal concentrations, and the secondary endpoints assessed S-100B serum levels and the CSF-to-whole blood ratio and CSF-to-serum ratio of the aforementioned metals.



Results

A total of 204 participants were included in the study; 102 participants were assigned to each group (the implant or control group). 118 were women and 86 were men. The median age was 69.4 years (ranging from 21.3 to 93.1 years), and patients in the implant group were significantly older than control participants. Baseline and medical characteristics at enrollment were similar between groups. Spearman's correlation analysis revealed a positive correlation between age and the whole blood levels of molybdenum and a negative correlation between age and serum levels of vanadium.

Metal quantification

Compared with controls, participants from the implant group had higher whole blood concentrations of cobalt, chromium, titanium, niobium, tantalum, and zirconium and higher serum concentrations of cobalt, chromium, nickel, titanium, vanadium, niobium, and

zirconium.

Only patients with elevated whole blood or serum levels of any metal were included in the CSF analyses. Cobalt levels in the CSF were higher in the implant group than in the control group and correlated with cobalt levels in the whole blood and serum. According to the authors, cobalt CSF levels can be predicted based on a linear correlation identified between cobalt levels in whole blood and CSF.

Interestingly, patients who reported pain in the index joint at the time of sampling had higher CSF cobalt concentrations, whereas this increase was not observed in patients with pain-free joints. In addition, the results showed that patients with knee arthroplasty implants had particularly high levels of cobalt in their bloodstream.

Patients with elevated whole blood and serum chromium concentrations did not have higher CSF chromium levels. Likewise, participants with elevated whole blood concentrations of titanium, niobium, or zirconium did not have higher concentrations of these metals in the CSF, but their CSF concentrations of titanium, niobium, or zirconium were significantly higher than in control subjects. As for chromium, levels of these metals did not correlate between serum and CSF. The authors stated that zirconium dioxide (ZrO_2) released from bone cement could explain elevated systemic zirconium levels. Remarkably, despite the notable prevalence of aluminum in arthroplasty as a component of titanium-aluminum-vanadium and titanium-aluminum-niobium alloys, which are frequently used for implant components, no significantly elevated aluminum concentration was detected in any of the compartments studied.

Subdivision of the implant group and correlation analyses implied that arthroplasty implants are the source of such exposure. Cobalt and chromium levels in whole blood, serum, and CSF were higher in patients with at least one cobalt-chromium-molybdenum implant component than in the matched controls. This suggests that using cobalt-chromium-molybdenum implant components carries a risk of the central nervous system’s exposure to arthroprosthetic metals. In contrast, patients with cobalt-chromium-molybdenum-free implants had higher whole blood and serum nickel and titanium levels. However, higher concentrations of any metal were not detected in their CSF samples.

The quantification of S-100B, a marker of the integrity of the blood-brain barrier, showed that serum levels of S-100B were lower in the implant group than in the control group. This indicates that compromised barrier functions most likely did not contribute to an increase in metal concentrations in the CSF. In participants with elevated cobalt or zirconium concentrations in the CSF, S-100B concentrations were lower than in the control group, while in participants with elevated chromium concentrations in the CSF, S-100B concentrations were not affected.

Conclusion

This cross-sectional study showed that chronic exposure to arthroplasty implants was associated with increased blood levels of cobalt, chromium, titanium, niobium, and

zirconium. Arthroprosthetic cobalt, chromium, titanium, niobium, and zirconium seemed to cross the blood-brain barrier and accumulate in CSF.

The authors concluded that future studies should investigate whether metal concentrations in CSF correlate with objective measures of neurotoxic effects. Given the known neurotoxic potential of cobalt, but also of titanium and niobium, this could be particularly relevant in patients with new-onset or deteriorated neurological or psychiatric disorders following arthroplasty.

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