THE MEDICAL BULLETIN OF
SISLI ETFAL HOSPITAL

DOI: 10.14744/SEMB.2022.22587
Med Bull Sisli Etfal Hosp 2022;56(2):212–219

Original Research

Long-Term Effects of Metal-on-Metal Cobalt-Chromium-Containing Prostheses Used in Total Knee Arthroplasty on Hearing and Tinnitus

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Abstract

Objectives: We aimed to determine the long-term effects of metal-on-metal (MoM) cobalt (Co)-chromium-containing prostheses used in total knee arthroplasty (TKA) on hearing and tinnitus.

Methods: A total of 88 patients with the normal otoscopic examination and normal blood B12 levels, consisting of 44 patients who had been using MoM Co-chromium-containing total knee prosthesis for more than 5 years, and 44 non-implanted patients with similar demographic characteristics, were randomly selected and included in the study. Patients with previous ear surgery, chronic middle ear disease, or conductive hearing loss were excluded from the study. All participants were evaluated with pure-tone audiometry (PTA), distortion product otoacoustic emission (DPOAE), tinnitus handicap inventory (THI), and tinnitus reaction questionnaire (TRQ).

Results: The mean age of the 88 patients was 67.22±10.4 years. The mean age of 44 patients who underwent TKA at least 5 years ago was 72.89±7.18 years, 75% of these patients had bilateral prostheses, and the mean prosthesis duration was 11.00±5.08 years (range 5–25). The two groups were compared statistically using PTA, DPOAE, THI, and TRQ scores. When the patient groups with and without prostheses were compared in terms of hearing and tinnitus, we did not find a significant difference between the two groups ($p>0.05$).

Conclusion: In our study, we observed that the long-term use of MoM Co-chromium total knee prostheses did not have an ototoxic effect, contrary to what was believed. We also found that prolonged prosthesis duration or undergoing bilateral surgery did not worsen hearing and tinnitus.

Keywords: Arthroplasty, cobalt, hearing loss, ototoxicity, tinnitus

Please cite this article as "Ozdemir O, Baris A, Cagliyan A, Yigit O. Long-Term Effects of Metal-on-Metal Cobalt-Chromium-Containing Prostheses Used in Total Knee Arthroplasty on Hearing and Tinnitus. Med Bull Sisli Etfal Hosp 2022;56(2):212–219".

Cobalt (Co) is an essential trace element for humans and is in the structure of cobalamin (Cbl), the functional unit of Vitamin B12 necessary for mammals. The B12 content in food is very low. Its greatest abundance is in meat, fish, and milk products. Cbl acts as a cofactor for methionine synthase and methylmalonyl-CoA mutase in humans. The most important disease known to be caused by B12 deficiency is pernicious anemia.[1]

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Submitted Date: April 19, 2022 **Accepted Date:** June 06, 2022 **Available Online Date:** June 28, 2022

Prostheses containing trace elements such as Co and chromium are used in many areas, especially in total knee arthroplasties (TKA) and total hip arthroplasties (THA). Metal-on-metal (MoM) prostheses are predominantly comprised Co (64%) and chromium (Cr) (28%) and these prostheses corrode over time and can trigger systemic metallic ion release.[2] Especially, some MoM TKA and THA configurations have been correlated with high Co and Cr levels, local adverse reactions, pseudotumors, vasculitis-associated lesions, systemic allergic reactions, hypersensitivity, and skin reactions.[3-6]

Co overexposure has been shown to cause a variety of adverse health effects. Internal exposure through MoM orthopedic implants and oral intake of Co supplements deliver the highest systemic Co concentrations.[7] In some cases, the increase in free ionic Co has been associated with a decrease in serum carrier proteins (90–95% binds with albumin) and monitoring of the Co^{2+} free fraction is recommended for future risk assessment. Renal failure, iron deficiency, sepsis, malnutrition, alcoholism, or drug intake may reduce Co-albumin binding, thereby increasing free Co^{2+} ions, resulting in toxic manifestations at low doses.[8] Several factors can lead to higher metal ion levels: Suboptimal surgical positioning of the implant, different types of prosthesis, excessive number of modular connections, impaired kidney function, and bilateral implantation.[6,9]

High blood Co levels are mainly associated with neurological, cardiovascular, and endocrine problems. These systemic effects have been expressed as the "arthroprosthetic cobaltism" syndrome.[10] There are a variety of symptoms related to hearing and balance, vision, cognitive function, and sensory-motor performance. Furthermore, these symptoms often coincide with polyneuropathy.[10-13] Hearing loss is always sensorineural and usually progressive. Furthermore, hearing impairment is mostly bilateral and more severe at higher frequencies. In addition, patients may complain about tinnitus and vertigo.

Exposure to Co can cause increased oxidative stress and DNA damage induced by free radicals.[14] The ototoxic effects of Co are due to the production of reactive oxygen species and its effect on basal outer hair cells.[15] Loss of hair cells in the cochlea usually presents as sensorineural hearing loss and tinnitus.

The main hypothesis of this study was to examine the ototoxic effects of MoM Co-chromium-containing prostheses used in TKA on hearing and tinnitus.

Methods

Ethical Approval

The study was approved by the Local Ethics Committee (No.2906/13.08.2021). All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. There were no animals involved in this study.

Patients and Study Design

A total of 88 patients with normal otoscopic examination and blood B12 levels, similar body mass index (BMI; kg/m^2), ethnicity, and age were included in this study. All patients were evaluated by otomicroscopic examination. Patients with the previous ear surgery, chronic middle ear disease, or conductive hearing loss were excluded from the study.

The patients were divided into two groups as patients with total knee replacement for more than 5 years (range 5–25) and the control group. All implanted 44 patients were operated under spinal anesthesia by a single-experienced surgeon using the same technique and surgical instruments. Anteroposterior and lateral control knee radiographs were taken before hearing and tinnitus evaluations of all patients with prostheses (Fig. 1).

Forty-four patients in the control group were randomly selected from patients of similar age and comorbid disease history, who presented to our ear, nose, and throat outpatient clinic with complaints other than hearing loss and tinnitus. All 88 patients were evaluated with, pure-tone audiometry (PTA) test, otoacoustic emission test (OAE), tinnitus handicap inventory (THI), and tinnitus reaction question-

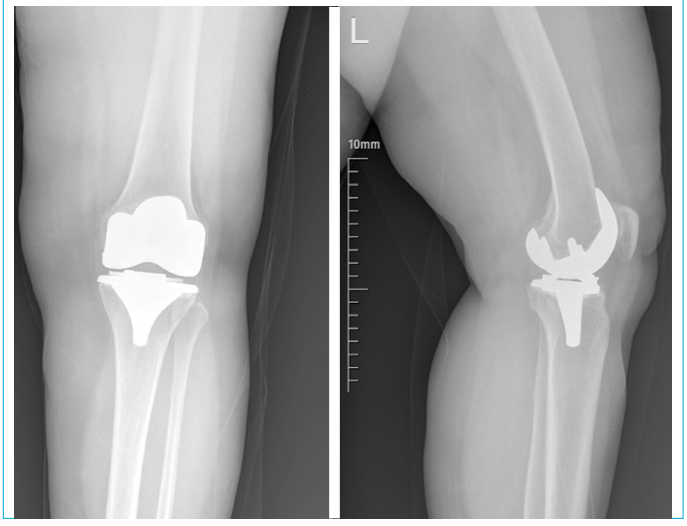

Figure 1. Prosthesis control with anteroposterior and lateral knee radiographs.

naire (TRQ). Hearing levels and tinnitus scores of the two groups were compared.

When calculating the prosthesis duration of patients with bilateral prostheses, prosthesis durations were added. For example, the prosthesis period of a patient who had the first prosthesis surgery 7 years and the second prosthesis surgery 3 years ago was evaluated as 10 years.

Surgical Technique

All patients were operated by a single-experienced orthopedic specialists in our institute. The procedure was performed with the patient in supine position under spinal anesthesia. All patients received a primary cemented cruciate retaining implants (Vanguard Complete Knee System; Zimmer, Biomet, Indiana, USA) using the standard medial parapatellar approach. Soft-tissue releases were performed if needed. The patella was not resurfaced. A tourniquet was used to control bleeding during the surgery and a drain was placed to monitor post-operative bleeding.

Patient Evaluation

Forty-four patients who had been using MoM total knee prostheses for at least 5 years were included in the study. After otomicroscopy, PTA and distortion product otoacoustic emission (DPOAE) measurements of prosthesis patients without chronic ear disease were performed. After these measurements, patients filled out THI and TRQ, and tinnitus scores were recorded. As the control group, 44 patients without prosthesis, who presented to the otolaryngology outpatient clinic with a complaint other than tinnitus, had normal otomicroscopy, had similar demographic and comorbid characteristics, and were randomly selected. These two groups, consisting of equal numbers of patients, were compared with each other in terms of PTA, DPOAE, THI, and TRQ.

Statistical Analysis

In the data obtained from the study of Leyssens et al. using the G Power 3.1.9.7 (Franz Faul, Germany) program, "The ototoxic potential of cobalt from metal-on-metal hip implants: a pilot study on the patient-reported auditory, vestibular, and general neurological outcome," the effect size is assumed to be d: 0.397. In the calculations for the determining effect size, 95% power, 10% margin of error, and one-way statistical significance, it was determined that there should be a total of at least 88 samples.

Statistical analysis was performed using the IBM SPSS Statistics 23.0 package program (SPSS Corp; Armonk, NY, USA). Kolmogorov–Smirnov test was used to determine whether the variables were normally distributed. Descriptive statistics of the data are presented with n (%) and normal distributions are shown as mean±SD. The Mann–Whitney U-test was used when evaluating non-parametric variables between the two groups. The benferroni multiple comparison test was used while investigating the reason for the significant difference between the groups. Analysis of categorical variables was carried out with the Chi-square (Exact) Test. Spearman correlation test was used to evaluate the relationships between quantitative variables. $P<0.05$ was considered statistically significant.

Results

A total of 88 patients, 61 male and 27 male, were included in the study. The mean age of the participants was 67.22±12.23 years (range 32–86). Of the 88 people participating in the study, 51 (57.95%) had hypertension and 19 (21.59%) had diabetes mellitus. About 75% of the patients had bilateral prostheses and the mean prosthesis time was 11.00±5.08 years (range 5–25) (Table 1).

Participants with and without prostheses were compared in terms of PTA test, tinnitus handicap index, and TRQ.

Table 1. Demographic characteristics of the patients

	MoM patients		Control subjects	
	n	%	n	%
Gender				
Female	41	93.18	20	45.45
Male	3	6.82	24	54.55
Age (mean±SD)	72.89±7.18		61.55±13.62	
Comorbidity				
Hypertension	18	40.90	13	29.55
Diabetes	9	20.45	7	15.90
BMI (mean±SD)	27.79±6.29		28.20±3.34	

MoM: Metal-on-metal; BMI: body mass index; SD: standard deviation.

There was no statistically significant difference between the two groups (p>0.05, Table 2). In addition, both groups were compared in terms of 1k, 2k, 4k, 6k, and 8k Hertz DP-OAE measurements, and similar results were obtained (p>0.05, Table 3).

In the prosthesis group, patients were compared in terms of PTA test, tinnitus handicap index, and TRQ, depending on whether they had prosthesis on one or both sides. However, no statistically significant difference was found between them (p>0.05, Table 4). When the patients were compared in terms of 1k, 2k, 4k, 6k, and 8k Hertz DP-OAE measurements depending on whether they had prosthesis on one or both sides, no statistically significant correlation was found (p>0.05, Table 5).

There was no statistically significant relationship between prosthesis duration and PTA test, tinnitus handicap index, and TRQ (p>0.05, Table 6). In addition, there was no statistical difference between prosthesis duration and DP-OAE scores (p>0.05, Table 7).

Discussion

Co is an essential trace element for humans and is in the structure of Cbl, the functional unit of Vitamin B12 necessary for mammals. Cbl is a cofactor of the enzymes methylmalonyl-Coenzyme A mutase and methionine synthase, and specific proteins are involved in all steps of Cbl transport (such as intrinsic factor and haptocorrin). In Vitamin B12 deficiency, clinics such as methylmalonic aciduria, hyperhomocysteinemia, megaloblastic anemia, and Cbl neuropathy may occur.[1,16] Deficiency is rare in people fed with meat, fish, and milk products, and Vitamin B12 deficiency was not detected in our study patients.

Knee replacement surgery is one of the most common procedures for knee osteoarthritis.[17] Since the mid-1990s, Co-chromium-containing MoM prostheses have been widely used in arthroplasty. In the following years, increases in Co and Cr metal ions were observed, mostly due to wear caused by malpositioned components.[18] Although wear in the TKA consists mainly of polyethylene debris, recent studies have demonstrated that abrasive and corrosive damage can occur in the femoral component of total knee replacements.[19] Abrasive damage to the surface of the femoral component, inflammatory cell-induced corrosion, and mechanically assisted crevice corrosion can cause the release of metal ions from the implant bulk.[20] Cadosch et al. showed that metal ions are able to induce the expression of different chemotactic cytokines in macrophages and osteoclasts, which may ultimately stimulate periprosthetic osteolysis and implant loosening.[21] However, when we evaluated our patients with direct anteroposterior and lateral knee radiographs in our study, we did not see periprosthetic osteolysis.

Today, apart from diet and occupational exposure, the most common cause of Co elevation is MoM implants.[22] Various studies show that Co levels will peak in the first 12 months postoperatively, after which the ion concentration will decrease to a steady-state.[23,24] Lons et al. found significantly higher blood Co and Cr levels 1 year after TKA, consistent with the literature.[25] Although elevated serum Co has been detected, particularly in the 1st year after MoM implants, the existing literature shows conflicting evidence of a dose-response relationship between Co level and systemic toxicity.[26-28] Therefore, objective auditory outcome tests were preferred in our study.

Tower defined systemic Co toxicity effects as arthropros-

Table 2. PTA,THI, and TRQ comparison of groups with and without prosthesis

	MoM patients (n=44)		Control subjects (n=44)		p
	Mean±SD	Median	Mean±SD	Median	
PTA 500 Herzt R (dB)	18.07±14.68	15.00	20.34±15.30	20.00	0.455
PTA 1000 Herzt R (dB)	21.02±16.76	20.00	21.36±17.76	22.50	0.983
PTA 2000 Herzt R (dB)	31.02±16.66	30.00	28.75±21.27	30.00	0.5781
PTA 4000 Herzt R (dB)	33.86±16.35	35.00	34.20±22.90	32.50	0.9361
PTA 500 Herzt L (dB)	18.30±14.18	15.00	20.11±17.24	20.00	0.782
PTA 1000 Herzt L (dB)	21.14±15.77	20.00	22.05±18.81	20.00	0.916
PTA 2000 Herzt L (dB)	29.09±16.22	27.50	29.55±21.21	30.00	0.9101
PTA 4000 Herzt L (dB)	33.30±17.39	35.00	36.25±22.36	40.00	0.4911
Tinnitus Handicap Inventory	9.09±10.62	5.50	8.48±7.89	8.00	0.938
Tinnitus Reaction Questionnaire	12.25±14.90	7.50	12.70±11.08	15.00	0.560

MoM: Metal-on-metal; PTA: Pure-tone audiometry; THI: Tinnitus handicap inventory; TRQ: Tinnitus reaction questionnaire; R: Right; L: Left; dB: Desibel; SD: Standard deviation, independent two sample test[1].

Table 3. DPOAE comparison of groups with and without prosthesis

	MoM patients (n=44)		Control subjects (n=44)		p
	n	%	n	%	
1k Herzt DPOAE R					
–	41	93.18	37	84.09	0.314
+	3	6.82	7	15.91	
2k Herzt DPOAE R					
–	34	77.27	36	81.82	0.792
+	10	22.73	8	18.18	
4k Herzt DPOAE R					
–	40	90.91	36	81.82	0.352
+	4	9.09	8	18.18	
6k Herzt DPOAE R					
–	40	90.91	40	90.91	1.000
+	4	9.09	4	9.09	
8k Herzt DPOAE R					
–	44	100.00	41	93.18	0.241
+	0	.00	3	6.82	
1k Herzt DPOAE L					
–	39	88.64	35	79.55	0.383
+	5	11.36	9	20.45	
2k Herzt DPOAE L					
–	35	79.55	35	79.55	1.000
+	9	20.45	9	20.45	
4k Herzt DPOAE L					
–	37	84.09	37	84.09	1.000
+	7	15.91	7	15.91	
6k Herzt DPOAE L					
–	43	97.73	40	90.91	0.360
+	1	2.27	4	9.09	
8k Herzt DPOAE L					
–	44	100.00	42	95.45	0.494
+	0	.00	2	4.55	

MoM: Metal-on-metal; DPOAE: Distortion product otoacoustic emission; R: Right; L: Left.

thetic cobaltism.[10] Arthroprosthetic cobaltism is mainly associated with neurological, cardiovascular, and endocrine problems. Neurological symptoms are usually related to auditory and vestibular complaints (e.g., hearing loss, tinnitus, and imbalance).[29] Gessner et al. detected these symptoms in 52% (13/25) of the cases in their study on patients with MoM hip implants.[26] Ho et al. detected tinnitus in 26% (8/31) patients and hearing loss in 29% (9/31) patients with MoM hip implants.[27] Although MoM Co-Cr total implant studies were generally performed on hip prostheses in the literature, we did not detect a significant difference in the study and control groups in terms of auditory and vestibular aspects in our study of total knee prostheses.

Li et al. in their experimental rat study to reveal the auditory damage of Co, they concluded that high-dose Co damaged outer hair cells more than inner hair cells, and the damage was more at the base of the cochlea.[30] In our study, we used PTA and DPOAE measurements to objectively evaluate hair cell functions. In addition, we evaluated the neurological effects of Co with commonly used tests and did not detect a significant difference in tinnitus scores between the two groups.

The main limitation of the present study was that a limited number of patient populations were included in the study. Further studies with larger case numbers are needed. In addition, evaluation of patients with serum Co and Cr levels may increase the value of the study.

Conclusion

In our study, we found similar results in hearing and tinnitus evaluations in patient and control groups with similar demographic characteristics. From this, we can conclude that long-term or bilateral use of MoM Co-chromium-con-

Table 4. PTA, THI, and TRQ comparison of unilateral and bilateral prosthesis surgery groups

	Unilateral (n=11) prosthesis		Bilateral (n=33) prosthesis		p
	Mean±SD	Median	Mean±SD	Median	
PTA 500 Herzt R (dB)	15.00±12.65	15.00	19.09±15.33	15.00	0.538
PTA 1000 Herzt R (dB)	17.73±16.49	20.00	22.12±16.96	20.00	0.437
PTA 2000 Herzt R (dB)	31.82±19.01	25.00	30.76±16.11	30.00	0.873
PTA 4000 Herzt R (dB)	36.36±18.99	35.00	33.03±15.61	30.00	0.470
PTA 500 Herzt L (dB)	18.18±17.79	15.00	18.33±13.09	15.00	0.728
PTA 1000 Herzt L (dB)	20.91±18.00	20.00	21.21±15.26	20.00	0.810
PTA 2000 Herzt L (dB)	33.18±19.27	30.00	27.73±15.16	25.00	0.376
PTA 4000 Herzt L (dB)	38.18±20.77	40.00	31.67±16.14	30.00	0.283
Tinnitus handicap ınventory	7.64±9.49	5.00	9.58±11.06	8.00	0.810
Tinnitus reaction questionnaire	11.73±13.81	7.00	12.42±15.45	8.00	0.979

PTA: Pure-tone audiometry; THI: Tinnitus handicap inventory; TRQ: Tinnitus reaction questionnaire; R: Right; L: Left; dB: decibel; SD: standard deviation.

Tablo 5. DPOAE comparison of unilateral and bilateral prosthesis surgery groups

	Unilateral (n=11) prosthesis		Bilateral (n=33) prosthesis		p
	n	%	n	%	
1k Herzt DPOAE R					
–	9	81.82	32	96.97	0.150
+	2	18.18	1	3.03	
2k Herzt DPOAE R					
–	8	72.73	26	78.79	0.692
+	3	27.27	7	21.21	
4k Herzt DPOAE R					
–	11	100.00	29	87.88	0.558
+	0	.00	4	12.12	
6k Herzt DPOAE R					
–	10	90.91	30	90.91	1.000
+	1	9.09	3	9.09	
8k Herzt DPOAE R					
–	11	100.00	33	100.00	–
+	0	0.00	0.0	0.00	
1k Herzt DPOAE L					
–	9	81.82	30	90.91	0.586
+	2	18.18	3	9.09	
2k Herzt DPOAE L					
–	9	81.82	26	78.79	1.000
+	2	18.18	7	21.21	
4k Herzt DPOAE L					
–	9	81.82	28	84.85	1.000
+	2	18.18	5	15.15	
6k Herzt DPOAE L					
–	11	100.00	32	96.97	1.000
+	0	0.00	1	3.03	
8k Herzt DPOAE L					
–	11	100.00	33	100.00	–
+	0	0.00	0.0	0.00	

DPOAE: Distortion product otoacoustic emission; R: Right; L: Left.

Tablo 6. Relationship between PTA, THI, TRQ, and prosthesis duration

	PTA 500 Hz. R	PTA 1000 Hz. R	PTA 2000 Hz. R	PTA 4000 Hz. R	PTA 500 Hz. L	PTA 1000 Hz. L	PTA 2000 Hz. L	PTA 4000 Hz. L	THI	TRQ
Prosthesis duration										
r	−0.040	−0.064	−0.050	0.010	0.016	0.020	−0.028	0.055	0.074	0.113
p	0.799	0.682	0.748	0.948	0.920	0.897	0.859	0.723	0.632	0.466

PTA: Pure tone audiometry; THI: Tinnitus handicap inventory; TRQ: Tinnitus reaction questionnaire; R: Right; L: Left; Hz: Hertz.

taining prostheses does not have an ototoxic effect. However, the increased Co effect revealed in some studies that may be due to conditions that decrease Co-albumin binding, such as renal failure, iron deficiency, sepsis, malnutrition, alcoholism, or drug intake.

Table 7. Relationship between DPOAE and prosthesis duration

	Prosthesis duration (years)		p
	Mean±SD	Median	
1k Herzt DPOAE R			
–	11.10±5.18	10.00	0.792
+	9.67±4,16	11.00	
2k Herzt DPOAE R			
–	11.06±5.34	10.00	0.901
+	10.80±4.37	11.00	
4k Herzt DPOAE R			
–	11.10±5.30	10.00	0.984
+	10.00±2.16	10.50	
6k Herzt DPOAE R			
–	11.30±5.18	10.50	0.165
+	8.00±2.94	8.00	
8k Herzt DPOAE R			
–	11.00±5.09	10.00	–
+	–	–	
1k Herzt DPOAE L			
–	11.21±5.27	10.00	0.667
+	9.40±3.29	11.00	
2k Herzt DPOAE L			
–	10.57±5.01	10.00	0.156
+	12.67±5.32	12.00	
4k Herzt DPOAE L			
–	11.38±5.36	10.00	0.377
+	9.00±2.71	10.00	
6k Herzt DPOAE L			
–	10.95±5.14	10.00	0.545
+	13.00±0.00	13.00	
8k Herzt DPOAE L			
–	11.00±5.09	10.00	–
+	–	–	

DPOAE: Distortion product otoacoustic emission; R: Right; L: Left; SD: Standard deviation.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee (No.2906/13.08.2021).

Peer-review: Externally peer-reviewed.

Funding: There was no funding from either public, private, or third sector sources.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Authorship Contributions: Concept – O.O., O.Y.; Design – O.O., O.Y.; Supervision – O.O., O.Y.; Data collection &/or processing – O.O., A.B., A.C., O.Y.; Analysis and/or interpretation – O.O., A.B., A.C., O.Y. Literature search – O.O., A.B., A.C.; Writing – O.O, A.B., A.C.; Critical review – O.O, A.B., A.C., O.Y.

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