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Effect of Nickel-Containing Metallic Restorations on Liver and kidney blood tests

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Abstract

Objective: This study aimed to assess the effect of Nickel-containing metallic restorations on liver and kidney blood tests. **Methods:** Twenty patients were selected from the Fixed Prosthodontics clinic, Faculty of Dentistry, Tanta University, to be included in this study. Ten patients who never had metallic restorations were studied as a control group (group I). The other group included 10 patients with old porcelain fused to metal (PFM) or metallic restorations (group II). Liver, kidney, and serum Nickel (Ni) level tests were measured for all at the beginning of the study. For group II patients, the metallic restorations were replaced with Zirconia then liver, kidney, and serum Ni level tests were repeated six months after insertion of the new restorations. **Results:** At the beginning of the study, liver and kidney tests were significantly worse in patients of group II than in group I. But, there was no significant difference as regards blood cell counts between both groups. Six months after replacement with Zirconia restorations for group II patients, there was a significant improvement in their liver and kidney function tests, a decrease in WBCs count, and a slight increase in hemoglobin level than baseline. Also, the serum Nickel test significantly dropped after the replacement of metallic restorations. **Conclusion:** within the limitations of this study, Nickel released from metallic restorations has a negative impact on liver and kidney blood tests, especially those with multiple restorations or prolonged durations.

Keywords: PFM, Zirconia, serum nickel level test, liver, and kidney blood tests.

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Introduction

Metal ceramic restorations have a combination of the esthetic properties of ceramics and the extraordinary mechanical properties of metals.[1] Some metals used as restorative materials in dentistry may cause a problem for some patients. One of these problems is the release of metallic ions into the gingival tissue and the gingival fluid.[2-6]

Dental materials should perform its desired function without causing any unwanted local or systemic effects in the recipient.[7] Although most of dental materials are considered as inert materials, the heterogeneous composition of dental ceramics and also combination with metal can affect the inertness. The degradation of dental materials may be occurred because of mechanical force or solubility in oral fluids. The released ions can generate unwanted biological and mechanical effects.[8,9]

The use of Nickel (Ni) containing alloy in dentistry has been questioned because of the biological liabilities of Ni and the release of Ni ions from dental appliance into oral cavity. Nickel ions have negative effects on the normal function of bone marrow and may cause liver damage by producing peroxidation of membrane lipids.[10] It was also found that subcutaneous administration of nickel chloride on rats induced a significant decrease in maternal body weight and anemia two days after administration. In addition, significant increase in plasma aspartate aminotransferase and in plasma alanine aminotransferase were observed. Alternation of hepatic histoarchitecture was also observed.[11]

Nickel ions can produce pulmonary inflammation and increase gene expression of inflammatory markers in cardiovascular tissue. These inflammations may adversely affect the number and function of endothelial progenitor cells (EPCs) which are responsible for repair of cardiovascular endothelium resulting in cardiovascular diseases.[12]

Methodology

This study was conducted as a prospective, randomized clinical trial. Ethical approval for the study was granted by the Research Ethics Committee, Faculty of Dentistry, Tanta University, Egypt No. FP-1-20-2.

Power analysis. The sample size was estimated by using the following formula:

$$\text{Sample size} = (Z^{2*}(P)^{*}(1-P))/C^{2}$$

(where z= z value (1.96 for 95% confidence level), p=percentage picking a choice, expressed as a decimal, c= confidence interval, expressed as a decimal). It was calculated that 10 patients per group would provide 95% power with a significance level (0.05).

This study was conducted from January 2021 to April 2022 at the out clinics of the faculty of dentistry, Tanta University, Egypt. The purpose of the study was explained to the patients and informed consents were obtained. Twenty patients (11 females and 9 males) aged 30-60 years were selected and divided into: group I (Control Group) included 10 patients without any metallic fixed restorations. Group II included 10 patients had PFM or metallic fixed restorations. Patients of group II were further subdivided into 2 groups: group II a which describe data of patients at the beginning of the study and group II b which include patients' data at the 6 months interval after cementation of the new restorations.

Inclusion criteria. Age 30-60 years, the ability to read and sign the informed consent document, medically free, having at least four units PFM or metallic fixed restorations for two years or more ago and the ability to return for follow-up examinations and evaluation.

Exclusion criteria. Patient with chronic liver disease (liver cirrhosis, metabolic liver diseases, viral hepatitis), uncontrolled systemic disease (hypertensive patient or diabetic patient), heavy smokers, having certain medications, recent PFM or metallic restorations for less than two years and patients with all ceramic restorations.

Preoperative preparation. Some preoperative steps were performed to all the patients which are complete blood picture (CBC), ultrasound examination for the abdomen, serum nickel level test, liver and kidney blood tests including alanine transaminase (ALT), Aspartate aminotransferase (AST), Gamma-glutamyl transpeptidase (GGT), serum albumin, serum bilirubin (direct and indirect), Alkaline phosphatase (ALP), blood urea and serum creatinine.

Assessment of old restorations and re-treatment. For group II, all the old restorations were removed using pneumatic crown and bridge removal (Dent-corp, Georgia) after injection of local anesthesia (Artinibsa, insiba, Spain) (Fig. 1). The prepared teeth were evaluated and the preparations adjusted for zirconia restorations. The preparations criteria for anterior teeth were incisal reduction (1.8- 2.0 mm) using rounded tipped tapered diamond bur with 0.8mm in diameter (Komet Dental, Germany) and chamfer finish line with a reduction (0.8-1.0) mm at the gingival margin. Facial surface was reduced into two planes. Lingual fossa was prepared with football diamond bur. For posterior teeth, anatomical occlusal reduction was prepared to provide at least 1.5 to 2 mm clearance. Axial walls were prepared to provide circumferential deep chamfer finish line with 1.0 mm thickness and all the undercuts were removed.[13] Final impressions were taken using addition silicon impression material (Elite HD, Zhermack, Badia Polesine, Italy) and interim restorations were cemented.

Scanning and designing of the final restorations. After pouring the final impression, the prepared teeth were blocked out by scanning spray (Calidia San Spray, Whitepeaks dental solutions GmbH&Co.KG, Germany) in order to avoid laser beam reflections which might interfere with proper surface scanning procedure. The teeth were scanned by Dental wings7 series 3D scanner. After that merging and saving of information as Standard Tessellation Language (STL) file. Designing of the restoration was done by using Exocad 2015 software

(Exocad GmbH, Darmstat,Germany) by choosing the design and the corresponding tooth number.

Milling of zirconia restorations. This was done by choosing the shade of milling blanks of Zirconia (Katana, kuraray noritake dental Inc, Germany) then introduced them to the five-axis milling machine (imes-icore 250i) and dry milling was done. After milling, the restoration was dried before sintering by using heat lamp (Drying lamp, Zirkonzahn, Italy) then the restoration was placed in a sintering tray to be introduced into the oven (Sintering furnace, Zirkonzahn, Italy). The recommended sintering temperature was 1530° C as recommended by the manufacture to achieve dense zirconia. For proper sintering, ensured that the oven reached 1530° C and this temperature was held for 2.5 hours then the oven was allowed to cool sufficiently to safely remove the restoration.[14,15]

Finishing and glazing of the restorations. Finishing was done using low pressure or water-cooled grinding instruments (Diamond tool, China) to reach the final anatomical shape. Then the restoration was glazed and stained to reach the desired shade.

Cementation of final restorations. Interim restorations and residual cement were removed. Then the teeth were rinsed, dried and partially isolated. Zirconia restorations were tried and cemented in the patient mouth using glass ionomer cement (Medicem, Promedica, Germany) that mixed according to manufacturer instructions (Fig.2).[13]

Study end point. After six months from the restoration's insertion, serum Ni level, CBC, liver and kidney blood tests were repeated.

Statistical analysis. It was performed using Statistical Package for Social Sciences (SPSS version 26). Independent t-test was used to compare difference between groups, paired sample t-test was used to compare difference between before removal and after insertion of new restoration in the same group.

Results

Regarding to CBC test, the level of Hb was significantly higher in group (II b) when compared with control group (P-value=0.042). The level of white blood cell (WBCs) was significantly decreased after six months (P-value=0.049) as presented in Table 1. Liver and kidney tests were significantly worse in patients of group II than in group I at the beginning of the study. Six months after replacement with Zirconia restorations for group II patients, there was significant improvement in their liver and kidney function tests. Demographic data of comparing liver, kidney function and serum nickel level tests before and after treatment showed that all these tests were higher at the beginning of the study and decreased after six months as represented in Table 2 and 3. There was significant difference in each test and highly significant regarding to serum nickel level as presented in Table 4.

Discussion

Conventional feldspathic porcelains have higher percentage of glass matrix which made them very weak, brittle and subjected to fracture under low tensile stresses. Combination with metal in PFM restorations solve these problems due to adequate mechanical properties of metals.

Different types of noble and base metal alloys are used to fabricate the substrate of PFM restorations. Cobalt-chromium (Co-Cr) and nickel chromium (Ni-Cr) are the most common alloys have been used because of higher mechanical properties and corrosion resistance of them.[16]

The development of polycrystalline ceramics with suitable fillers such as alumina and zirconia have the advantage of increased strength without using a metal substrate. The appearance of translucent and ultra-translucent types of zirconia made them also have adequate esthetic properties.[17]

Patients only with multiple old restorations were selected to participate in this present study. To expect that there was a chronic effect on the liver, the patients were selected to have at least four units fixed restorations either crowns or bridges. Also, these fixed restorations must be for two years ago at least.

In this study, the number of WBCs were significantly decreased after six months in group II (p value=0.049). This could be due to leaching of ions from the metal present in the old PFM restorations. These metal ions were considered as foreign bodies. White blood cells are the first line of defense so WBCs increased at the beginning and decreased after removal of the metallic restorations.

This come in accordance with **Mcginley et al** who analyzed the histology, viable cell count, oxidative stress, cytokine expression and toxicity of keratinocyte and fibroblast cell after exposed to (Co-Cr) and (Ni-Cr) base metal alloy. The results of the old study showed that there was increase in the level of inflammatory cytokines and oxidative stress in case of (Ni-Cr) alloys.[18]

Also this study showed that the level of blood hemoglobin (Hb) was significantly increased group II after six months when compared with control group (p value=0.042). This may be due to increase in the level of the released metal ions at the beginning of the study which may affect the peripheral blood cell count. This coincide with **Liberda et al** who found that inhalation of Ni nanoparticles caused pulmonary inflammation that affect cardiovascular function, reduce number and function of bone marrow endothelial progenitor cells.[12]

According to the results of this study, liver and kidney blood tests were high in group II at the beginning of the study but without reaching the diseased level and significantly decreased after six months. This may be occurred due to accumulation of metal ions which may impair the kidney and liver function. **Strauss et al** found that exposure to low levels of Ni and Cr and for long duration may result in an accumulation in the kidney and lead to renal dysfunction.[19]

Serum nickel level in patients of group II was higher at the beginning of this study but it didn't reach the toxic level and also significantly decreased after replacement of the restorations. Row data of serum nickel level was directly proportional to the number of restorations present in the

patient's mouth and how long were there. This mean that the patients having large number of restorations and for several years had high serum nickel level but without toxicity.

Liu et al found that Ni and Cr are released from porcelain fused to Ni-Cr crowns in the oral environment and serum Ni concentration increase with prolongation of restoration time which coincide with the results of the current study.[20]

Increasing the level of nickel may compromise liver, kidney and bone marrow function which appeared in the results of this study. Several studies agreed with that the released nickel from dental alloys may aggregate in cells over the period of time and results in several adverse effects on them that include leukocyte chemotaxis suppression, changing in DNA synthesis and enzymes activity.[21]

Elshahawy et al who cultured fibroblasts cells in salt solution and calculate viable cell in each element. They found that Ni and copper are considered the highly toxic elements released from prosthodontics materials.[22] These results also support the results of the present study.

Yu Pan et al who placed nickel chromium (Ni-Cr), cobalt chromium (Co-Cr) and titanium in the cheek pouches of hamsters. They found that trace metal released from these dental alloys and titanium. These results in accordance with the results of the present study. On the other hand, the present study found that the traces accumulated in liver, blood and kidney had no effect on histopathology of liver or kidney. However, **Yu Pan et al** found that the function of liver and kidney were compromised. This may be due to acute and rapid accumulation of released ions in the liver and kidney in the last study.[23]

On the other side several researches proved the biocompatibility of dental zirconia and considered it as biomaterial of choice. Zirconia has the ability to produce bone formation by stimulating osteoblastic aggregation when its used as dental implant.[24,25] **Sharanraj et al** cultured zirconia that used as dental implant with mouse fibroblast cells. MTT assay was used to measure the cell activities with mitochondrial dehydrogenases. The results showed that zirconia had the highest cell growth with zero grade of toxicity.[26]

Conclusions

Based on the results of this present study, the following conclusions were drawn:

1- The serum nickel level of all the cases was high at the beginning of the study and decreased after replacement of metallic restorations.

2- Increase the level of serum nickel had bad effect on liver, kidney function and peripheral blood cell count but without toxicity.

3- Ceramic restorations are better to the body health than metal-ceramic or metallic materials.

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Table 1. Comparison of CBC parameters of group II before and after treatment.

CBC tests			
Tests	Group II a	Group II b	p-value
Hb (Hemoglobin)	12.81 ± 1.19	13.21 ± 0.86	0.307
MCV	84.21 ± 4.39	84.64 ± 3.03	0.786
MCHC	31.97 ± 1.97	32.59 ± 0.31	0.354
WBC count	7.65 ± 3.11	5.34 ± 0.55	0.049*
Platelets count	256 ± 73.73	214.26 ± 72.66	0.115

Table 2. Comparison of kidney function tests of group II before and after treatment.

Kidney Functions			
Tests	Group II a	Group II b	p-value
Serum Creatinine	1.18±0.16	0.899±0.15	0.011*
Blood Urea	32.30±6.02	25.02±7.26	0.048*

Table 3. comparison of liver function tests of group II a and group II b

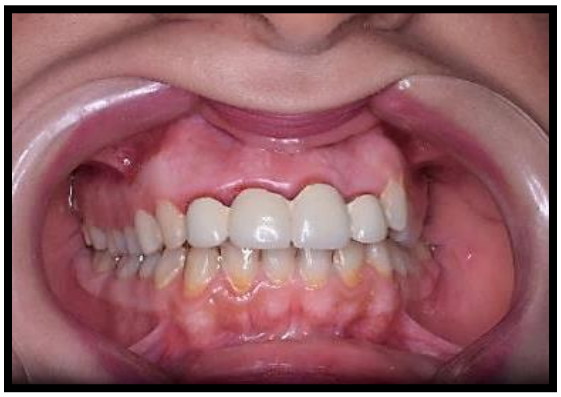
Liver Functions			
Tests	Group II a	Group II b	p-value
ALP (Alkaline Phosphates)	165.60±12.62	106.58±36.44	0.001*

Serum Albumin	4.96±0.46	3.95±0.55	0.001*
SGOPT (Alanine Aminotransferase)	27.80±7.19	20.36±6.83	0.049*
SGOT (Aspartate Aminotransferase)	27.30±5.44	18.17±4.20	0.000**
GGT (G-Glutamyl Transpeptidase	26.90±4.91	16.22±4.14	0.001*
Total Bilirubin	1.09±0.27	0.676±0.09	0.003*
Direct Bilirubin	0.229±0.05	0.149±0.03	0.001*

Table 4. Comparison of serum nickel level of all the studied groups.

Group I	Group II a	Group II b
2.72±1.07	6.40±2.59	3.45±1.91
P1-<0.001*	P2->0.303	P3-<0.000**

P1: p-value of comparing group I and group II a.
P2: p-value of comparing group I and group II b.
P3: p-value of comparing group II a and group II b.



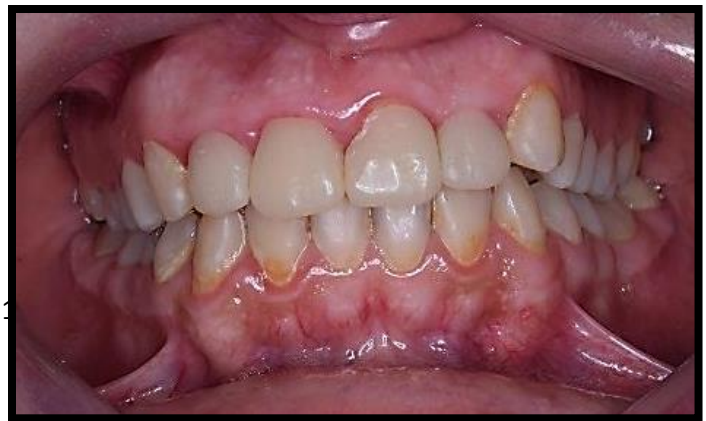


Figure (1) anterior porcelain fused to metal bridge before its removal.

Figure (2) cementation of anterior zirconia crowns.

Figure legend

Figure (1) anterior porcelain fused to the metal bridge before its removal.

Figure (2) cementation of anterior zirconia crowns.