



Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Nickel-based (Ni–Cr and Ni–Cr–Be) alloys used in dental restorations may be a potential cause for immune-mediated hypersensitivity

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ARTICLE INFO

Article history:

Received 7 April 2009

Accepted 18 April 2009

Available online xxxx

SUMMARY

Although nickel-based (Ni–Cr and Ni–Cr–Be) alloy prosthesis is widely used in orthodontics, its potential biologic hazards, hypersensitivity in particular, are still uncertain as yet. And only a few studies *in vivo* have considered the biocompatibility. However, several case reports show adverse effects of immunologic alterations, such as urticaria, respiratory disease, nickel contact dermatitis, microscopic hematuria and proteinuria, and even exacerbated to hepatocyte injury and renal injury. So nickel-based alloy used in dental restorations may be a potential cause for immune-mediated hypersensitivity. The metal surface would occur electrochemical corrosion as metal edge of porcelain-fused-to-nichrome crown exposed to oral cavity rich in electrolytes after restoration, and metal ion would release to oral cavity then come into contact with cells and tissues in the immediate environment, or be distributed throughout the body, mainly to the intestine canal. Once these ions are not biocompatible, the human system may be injured (toxicity and risk of sensitization) if they are absorbed in sufficient quantity. Thus, it is necessary to determine the long-term biocompatibility properties of nickel-based alloy, reduce sensitization, and grasp the information of individual differences in the appearance of adverse reactions in further research.

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Background

Clinical application of dental nickel-based alloys

With the development of oral repair techniques, porcelain-fused-to-metal prosthesis is approved by patients because of its strength of metal and beautiful outlook of porcelain. For clinical dental applications, there are currently hundreds of alloys available for prosthodontic restorations. Among them, nickel-based (Ni–Cr and Ni–Cr–Be) alloy prosthesis is widely used (especially in developing countries) in the inner crown of casting crown and bridge and porcelain-fused-to-metal crown and bridge owing to its simple fabrication process, low cost, and additionally, improvement of castability and oxidizability. However, the oxidizability increment is accompanied by an increment of the corrosion rate, which has the disadvantage to release nickel (which presents an allergen character), chromium (able to be present as toxic chromate) and beryllium (high toxicity) in the human system. Nickel might activate monocytes and endothelial cells, suppressing or promoting the expression of intercellular adhesion molecule-1 (ICAM-1) by endothelial cells, depending on the ionic concentration [1]. Nickel complexes in the form of arsenides and sulphides are also known to be carcinogenic, allergenic, and mutating substances, whereas nickel at nontoxic concentrations is found to in-

duce DNA alterations, mainly by base damage and site-specific DNA strand scission [2,3]. The mutative action of nickel might derive from its effect on inhibiting several enzymes known to restore DNA breaks, promoting microsatellite mutations, and increasing total genomic methylation, thereby contributing to genetic instability [4]. At the same time, it was confirmed by epidemiological survey that in workers worked in factories produced dichromate by chromium ore incidence of lung cancer was high, and this kind of cancer was called “chromium lung cancer”. Chromium toxicity is correlated with its existing form. Toxicity of metal chromium is the minimum, toxicity of Cr²⁺ and Cr³⁺ is higher, and toxicity of Cr⁶⁺ is the maximum [5]. Moreover, the potential risks of beryllium used in the dental industry have been recognized for some time. The case series study demonstrates that dental technicians exposed to beryllium are at high risk of developing chronic beryllium disease and other lung diseases [6]. As we know, the oral cavity is a dynamic environment, subjecting to changes in pH and temperature, a continuous flow of saliva, microbiological activity, occlusal load, diet, unconscious regular contact with metal ions (contact with jewelry and cooking utensils or living in a nickel-contaminated region), as well as many other factors. However, only a few *in vivo* studies have considered the biocompatibility of nickel-based alloys in orthodontics. Accordingly, with the increasing of health consciousness, dental material of nickel-based alloy which was used predominantly for crowns and bridges, has elicited significant concern among dentists and patients, because of its local and systemic toxic, immunogenic, mutagenic, and chemotactic

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effects [7–9]. But as yet, the potential biologic hazards – hypersensitivity in particular – from nickel-based dental alloys are still uncertain.

Clinical case reports associated with dental nickel-based alloys

There are several case reports on hypersensitive reactions made from nickel-based alloy in dental restorations. According to statistics, approximately 10% of women and 1% of men are sensitive to nickel-based alloys. Back in 1985, Strauss and Eggleston [10] reported a patient with documented IgA nephropathy in whom microscopic hematuria, proteinuria and hypertension first occurred after placement of nickel alloy base dental crowns. Progressive proteinuria culminating in nephrotic-range proteinuria occurred parallel to increased nickel placement and dramatically resolved following nickel alloy removal. The patient may represent an example of nickel-induced sensitization and associated IgA glomerulopathy. And recently, in China, a health status report of patients who obtained nickel-based alloys for dental restorations attracted a great deal of concern online. As a result of nickel alloy exposure, adverse effects of immunologic alterations present in 55 cases, with the common occurrence of nickel contact dermatitis, urticaria, respiratory disease, and even exacerbated to hepatocyte injury and renal injury.

Hypotheses

In light of the above, we can make the hypotheses that nickel-based alloy used in dental restorations may be a potential cause for immune-mediated hypersensitivity. Corrosion in the mouth is continuous, because the metal ions are removed with the abrasion of foods, liquids and toothbrushes, mainly with an electrochemical mechanism. The metal surface would occur electrochemical corrosion as metal edge of porcelain-fused-to-nichrome crown exposed to oral cavity rich in electrolytes after restoration. And metal ion would release to oral cavity then come into contact with cells and tissues in the immediate environment, or be distributed throughout the body, mainly to the intestine canal. If these ions are not biocompatible, then the organism may be injured (toxicity and risk of sensitization) if they are absorbed in sufficient quantity. The former experiment *in vitro* showed that dental alloy would educe metal ion into the fluid after placing in artificial saliva or cell culture fluid for a period of time, scanning electron microscope revealed that the alloy surface was corroded [11]. Additionally, it was found *in vivo* that dental alloy could educe metal ion in oral envi-

ronment. Metal ion educed from alloy was found in gingiva after wearing full metal crown and the concentration of corresponding metal ion in saliva elevated [12]. The transport and distribution of nickel in the body depend on the site of absorption, the rate and concentration of nickel alloys exposure, the solubility of the nickel compound, and the physiologic status of the body. Nickel alloys are mainly transported in the blood by binding with serum and, to a lesser degree, histidine [13]. The alloy ion can also bind with body proteins to form a nickel-rich metalloprotein [14]. Thus, it needs further research to determine the long-term biocompatibility properties of this material, reduce sensitization to nickel-based alloy and allergies, and grasp the information of individual differences in the appearance of adverse reactions. Once a patient has a positive history of confirmed nickel allergy, or once such hypersensitivity to dental restorations is suspected, alternative metal alloys may be used.

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