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Hypothesis Open Access

Diagnostic Specificity of Nickel Nano-Particles in Allergic Contact Dermatitis

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Abstract

Metal allergy is mainly an environmental disorder. Nickel is present everywhere. Exposure to nickel is a major cause of Allergic Contact Dermatitis, which respectively is an inflammatory, cellular type delayed hypersensitivity immuno response induced by antigen specific T cells. However, there is no standardized method to assess trace to moderate nickel diagnostic accuracy. The actual antigen is the nickel ion that can only penetrate skin epidermis in soluble form as ion metal hapten, leading to sensitization. Standard nickel sulfate molecule 5.0% w/v in petroleum, as contactant in patch test, evokes clinical global data which are inconclusive and disputable. Such limited antigenic surface recognition does not disclose in full subsequent immuno bio-responses.

Nanoparticles have much larger surface area to unit mass ratios which has more powerful and specific foreign signal ability to activate human immune system responses, indeed. Increased immunogenicity with subsequent enhanced immuno-recognition of unrestrictedly exhibited surface antigenicity toward nickel nanoparticles is consistent with presented working hypothesis. Those unique, most effective, super sensitive surface nano-antigens are regulating with extreme precision; recognition, cellular binding and intra-cellular interactions comprising immuno-biological responses toward nickel nano-particles. On the basis of patients under the study with Allergic Contact Dermatitis, and control group the distinctive diagnostic definition of nickel nano molecules will be formulated.

Keywords: Nickel nano-particles; Allergy skin patch test; Allergic contact dermatitis

Introduction

Allergic Contact Dermatitis (ACD) to nickel is a frequently encountered problem and can be the cause of significant morbidity, particularly in patients with chronic hand eczema, which can lead to inability to work, a decrease in quality of life and significant healthcare expenses [1,2]. Sources of nickel sensitizations involve environmental exposure toward either by exogenous skin contact and/or endogenous endanger by inhalation or oral ingestion [2]. It is well established that nickel allergy is more frequent among women than man, and depends of certain occupations and geographical location [3]. A genetic predisposition possibly plays a role. The women who become sensitized to nickel have a higher prevalence of histocompatibility HLA-B35 and BW22 tissue antigens. Documented loss of function mutations in the filaggrin gene are likely to increase the risk of nickel allergy [2,4]. ACD should be always investigated using skin prick test for immediate, humoral type IgE mediated hypersensitivities and skin patch test, to diagnose cellular, delayed-type hypersensitivity [5]. To detect cellular, delayed-type hypersensitivity reactions to environmental haptens like nickel, the patch test is the golden standard in clinical assessment of impending symptomatology. To establish clinical diagnosis of nickel ACD, a detailed history should investigate possible source of exposure, including daily activities, environmental conditions, past and current occupations and elements of products exposure. Primary skin eruptions observed among patients with nickel ACD, are characterized by recurrent eczematous lesions on the site of direct contact with the items that release nickel, such as use of pierced earrings in earlobes, wrist use of watches, neck use of necklaces, and umbilical region exposed to metallic jeans button. The face and scalp may be involved from contact with cellular phones, piercing and hair claps. Secondary generalized eruptions which can be eczematous or not, reveals the maculopapular exanthema with flexural involvements presented as a symmetrical eruptions of the neck, face, eyelids, elbow and forearms flexures, hands, inner thighs, and anogenital regions [2]. Multiple sensitizations to metals can easily occur in clinical setting and require differential diagnostic tests applications. Cross reactivity between nickel and palladium sensitive patients provides evidence that 96% of palladium reactive individuals exhibit also nickel allergy [1]. Palladium is a precious metal used in dental alloys and jewelry. Such metal cross sensitivity was due to similar stereo chemical arrangements [1,2].

Clinical Materials and Proposed Methodology

Study design

The aim of our working hypothesis is to provide evidence that nickel-nanoparticles, like the ones obtained using sodium borohydride, are diagnostically, specifically and precisely superior from standard nickel sulfate 5.0% w/v in petroleum, *in vivo* comparative patch testing. Apparently, many antigenic properties of nano sized elements are not present in their bulk states [6].

Nano-probes characterization

The physicochemical properties of nano particle probes will be measured with appropriate X-ray and atomic methods.

Precise determination of elemental composition of entire nanoparticles will be assessed with the Grazing Incidence X-Ray Fluorescence (GIXRF) method. Oxidation state of nickel atoms

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will be determined from X-ray Absorption Spectroscopy (XAS) measurements.

Surface properties of nanoparticles can drastically differ from the bulk. Elemental composition and chemical state of the surface atoms can be reviled with the X-ray Photoelectron Spectroscopy (XPS). This technique provides detailed information on composition and chemical state of the nanoparticle shell.

The size and shape of nanoparticles will be determined with the use of Atomic Force (AFM) and Transmission Electron Microscopy (TEM). These techniques can provide spatial resolution in nanometer to Ångströms range, e.g., corresponding to a size of single atoms.

Detailed nano-characteristics of surface and bulk of different nano-probes will provide a credible reference to clinical results and varying immune response patterns among patients.

Clinical materials

Approximately 25 subjects, 20 females and 5 males, age from 18 to 55 y.o. and respectable 10 control group subjects consisting 7 females and 3 males, will be enrolled to the study.

Patients with ACD will be recruited from Dermatology Departments of Medical Schools in Lausanne-Switzerland and Zabrze Rokitnica-Poland. They all will have previously confirmed positive patch skin reaction toward nickel sulfate 5.0% w/v in petrolatum. Patch testing

Patch test can be considered as biological provocation test and it can be postulated that locally induced skin symptoms like erythema, scaling and itching were considered as immune responses toward nickel sulfate in general and nickel-based nanoparticles in particular [7,8].

Patch testing is the established method to prove contact sensitization

The study strips will be attached for 2 days and reactions will be examined on day 2 and day 3; negative (-) no visible reaction, questionable (?) erythema no infiltrations, follicular (f) only discrete follicular papules in the test area, weak (+) erythema infiltrations with possible slight papules, moderate (++) erythema infiltrations papules vesicles, strong (+++) erythema infiltrations with confluent vesicles. To compare the strengths of reactions, numerical values were allocated to distinct reactions, as follows: 0 to negative reaction; 0.5 to questionable, irritant and follicular reactions; 1 to + reactions; 2 to ++ reactions; and 3 to +++ reactions [9]. The test strips either with nickel sulphate and/or nanosized nickel particles, using sodium borohydride will be applied on forearm skin [6,10]. Ethical committee approvals and informed consent from participants will be obtained.

Statistical evaluation

The sign test will be used for statistical evaluation, $p<0.05$ will be considered to indicate a statistically significant difference.

Anticipated Results

There is no standardized method to assess trace to moderate nickel exposure [11]. Selective and critical application in patch test of nickel nanoparticles among ACD patients has been never reported before.

We hypothesize that cellular, delayed type hypersensitivity induced by bulk nickel sulfate in ACD, can be diagnostically refined in its precision by using nickel nano-particles. Such proposed super antigen, specific optimization ligand is representing the most reliable and adequate new surface epitope immuno-biomarkers [12].

Our concept study will develop a novel, more accurate approach to increase diagnostic sensitivity of immuno-reactivity responses among nickel susceptible populations.

To determine false negative and false positive results of nickel nanoparticles diagnostic outcome, traditional techniques of nanoparticles interferences will be applied [13].

Discussion

The possible origin, mechanisms, diagnosis, treatment and prevention of nano-quantum material related diseases expressed and induced by skin contactants are inconclusive and disputable [14].

The immunological system response to hostile and disturbing agents is the most sophisticated, ultra sensory signaling network demonstrated among altered environmental factors.

The immuno-response parameters detects instantly aberrant nano-particles in our surroundings like inhalants (nickel containing dust), ingestants (food containing nickel), and contactants metals like nickel. However, different people on different continents will show different clinical symptoms induced by the same offending agent.

With this respect, uniform well established standard methodology in the assessment of given eco-toxic factors must be applied via proposed molecular profiling of applicable nickel nano-particles, more specific and more precise diagnostic patch tests positive responses will culminate in protective management of our home environment, expressed as Environmental Syndrome [15].

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