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**Effects of TIO NICKEL in patients with ACD and SNAS:
experience on 700 patients in Italy**

Running head: **TIO NICKEL in patients with ACD and SNAS**

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The nickel is causes of allergic contact dermatitis (ACD) and of "systemic nickel allergy syndrome" (SNAS). From 2009 to 2015 a very large number of patients with allergies, presented to our Department of Dermatology and Allergology at Sant'Andrea Hospital in

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Rome; 700 of these showed an allergic reaction to nickel with a double clinical manifestation, skin and gastrointestinal symptoms, between 25 and 60 years old. Regarding the skin manifestation, the diagnosis was confirmed by Patch Test SIDAPA standard series. The results were positive for nickel sulphate with +2 to +3, using the ICDRG scoring system, and also to others allergens (Table 1).

A questionnaire was administered to 700 patients with suspected Systemic Nickel Allergy Syndrome (SNAS) in which they were asked what type of gastrointestinal manifestation they were suffering from and to describe the eczema's severity on a scale from 1 to 10. To objectify the gastrointestinal involvement, 10 patients were subjected to biopsy of the small intestine which showed a marked inflammatory infiltrate, especially lymphoplasmacellular, intestinal villi's deformation and deepening of crypts: an aspect very similar to the one of celiac disease but with a negative antibody profile. If the patients follow a nickel restricted diet, the symptoms improve but they couldn't follow it for more than a month, since this metal is ubiquitous.

The inclusion criteria of this study were: age > 18 aa, a moderate (++) or severe (+++) reaction for nickel sulphate to Patch Test SIDAPA standard series, and skin and gastrointestinal symptoms associated.

We thus selected a sample of 700 patients who had been treated with the oral hypo-sensitization therapy (TIO NICKEL- LOFARMA, Milan, Italy). It consisted of the use of capsules containing nickel sulphate (NiSO_4), administered in increasing doses. During the first phase, which lasted 6-weeks, we administered a 10 ng capsule 3 times per week for the first two weeks, 100 ng 3 times per week in the third and fourth week and 500 ng capsules 3 times per week in the fifth and sixth week. During this period the patient was required to

observe a nickel restricted diet, since nickel was assumed already with oral therapy. After these first six weeks, we switched to the maintenance phase with a 500 ng tablet 3 times per week for three years, and it was possible again to resume an unrestricted diet.

Patients underwent clinical evaluations at one, three and six months and at the end of maintenance therapy; the Patch Test SIDAPA standard series continued to show a positive result to nickel sulphate but with minor positivity than that performed before oral therapy (Table 2). After the first four weeks of treatment, the patients already reported a decrease or absence of clinical symptoms, both cutaneous and gastrointestinal, and a complete remission at the end of therapy.

Besides, the patients with allergy to nickel showed high levels of pro-inflammatory cytokines in the serum before of the treatment, as TNF, IL-15, IL-5 and IFN. After the vaccine, we have determined the concentration of these same cytokines with Elisa method, and we saw that their levels were significantly reduced.

Our results show that patients have had benefit from the vaccine already after few months and 1 year, 2 and 3 years after starting the treatment. Its effectiveness is still valid on both gastrointestinal and skin symptoms. This leads us to continue the hyposensitizing oral therapy which seems to have good feedback also in some patients who are positive to cobalt chloride.

References

1. Mahdi G, Israel DM, Hassal E. Nickel dermatitis and associated gastritis after coin ingestion. J Pediatr Gastroenterol Nutr 1196;23:74-80.

2. Cempel M. Effect of nickel chloride on iron content in rat organs after oral administration. Biol Trace Elem Res. 2004;102(1-3):189-198.
3. Latunde-Dada GO, Shirali S, McKie AT, et al. Effect of Transition metal ions (cobalt and nickel chlorides) on intestinal iron absorption. Eur J Clin Invest. 2004;34(9): 626-630.
4. Falagiani P1. Nickel hyposensitization: a literature review. Int J Immunopathol Pharmacol. 2005 Oct-Dec;18(4 Suppl):3-5.
5. Tsoumbaris P, Tsoukali-Papadopoulos H Heavy metals in common foodstuff: quantitative analysis. Bull Environ Contam Toxicol 1994; 53:61-66.
6. Mario Di Gioacchino, Luisa Ricciardi, Ornella De Pità, Mauro Minelli, Vincenzo Patella, Susanna Voltolini, Valerio Di Rienzo, Marina Braga, Enzo Ballone, Rocco Mangifesta, Domenico Schiavino Nickel oral hyposensitization in patients with systemic nickel allergy syndrome Annals of Medicine, 2014;46:31-37.
7. Braga M, Quecchia C, Perotta C, Timpini A, Maccarinelli K, Di Tommaso L, Di Gioacchino M, Systemic nickel allergy syndrome: nosologic framework and usefulness of diet regimen for diagnosis, Int J Immunopathol Pharmacol. 2013 Jul-Sep;26(3):707-16.
8. Schiavino D, Nucera E, Patriarca G. A clinical trial of oral hyposensitization in systemic allergy to nickel. Int J Immunopathol Pharmacol 2006;19:593-600.
9. Tuchman M, Silverberg JI, Jacob SE, Silveberg N., Nickel contact dermatitis in children, Clin Dermatol. 2015 May-Jun;33(3):320-6
10. Tamaro A., De Marco G., Persechino S., Narcisi A., Camplone G., Allergy to nickel: first results on patients administered with an oral hyposensitization therapy, Int J Immunopathol Pharmacol. 2009 Jul-Sep;22(3):837-40.

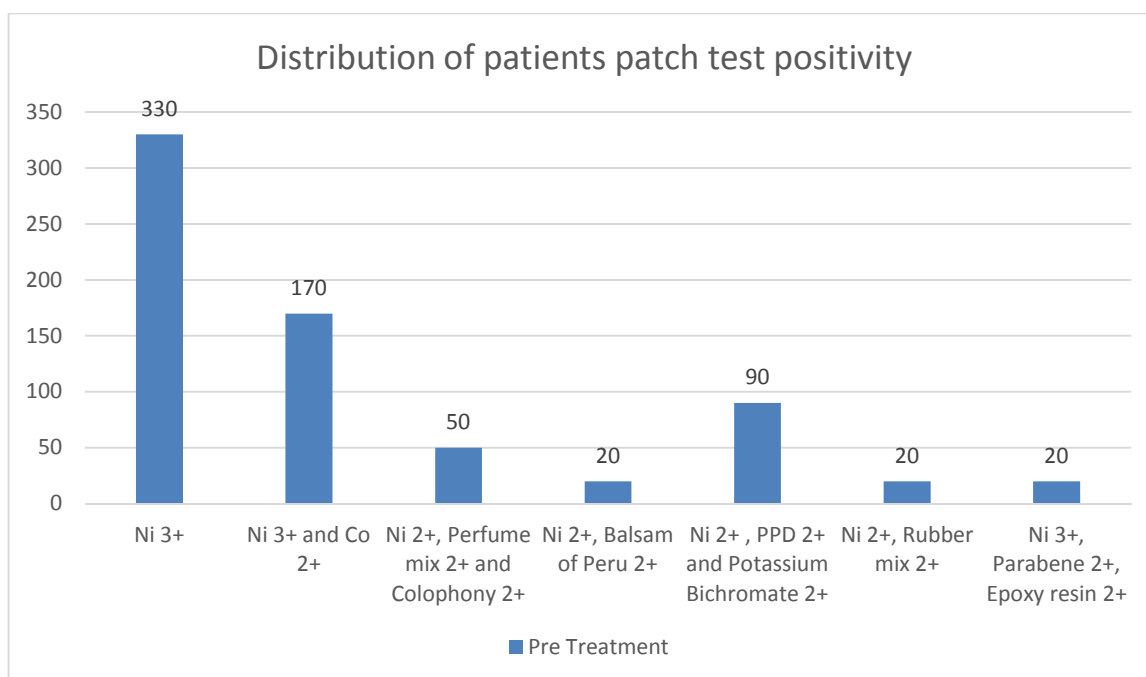


Table 1: Distribution of patients on basis of positive to patch test before the treatment.

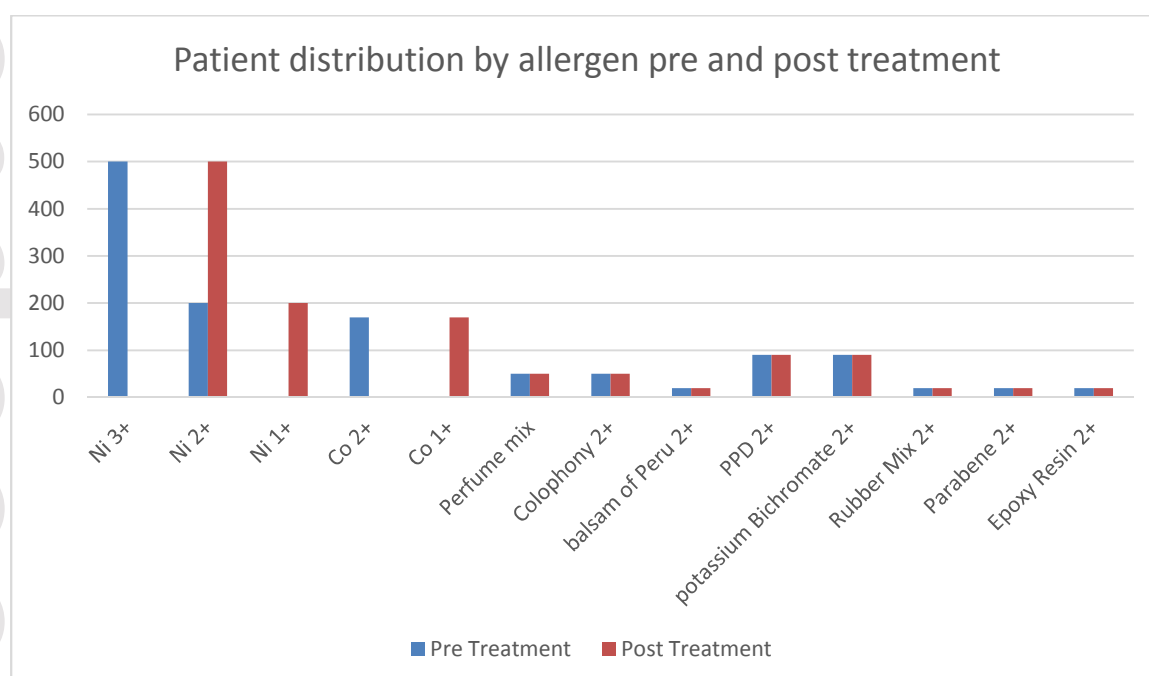


Table 2: Comparison of positive to patch test pre and post treatment.