Immune changes are observed after radioiodine treatment for hyperthyroidism in Graves' disease patients

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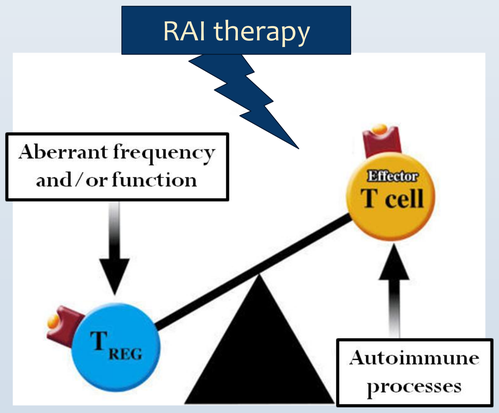
Introduction

Graves' disease (GD) involves autoimmunity against thyrotropin receptor (TSHR) bearing cells, leading to hyperthyroidism and often orbitopathy. When hyperthyroidism is treated with radioactive iodine (RAI), exacerbation of the orbital disease can occur.

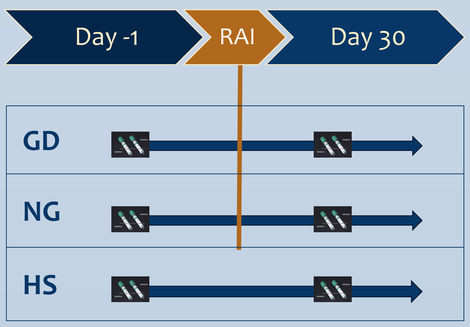
Hypothesis

We hypothesized that RAI has immune effects affecting the balance between auto-reactive T cells and T cells with regulatory properties.



Objectives

We monitored lymphocyte populations in peripheral blood of 24 GD patients, 5 patients with non-autoimmune goiter (NG), and 19 healthy subjects (HS).



Methods

- **Identifying TSHR peptide sequences targeted by auto-reactive T cells**

Circulating T cell interferon gamma (IFN-γ) production in the presence of TSHR peptides was measured by ELISPOT assay.

- **Monitoring lymphocyte populations**

  - Regulatory $CD4^+CD25^{high}FOXP3^+$ (Treg) and Natural Killer $V\alpha24^+V\beta11^+CD3^+$ (NKT) T cells were counted by flow cytometry.

  - Treg immunossuppressive property in inhibiting non-specific proliferation of dye-labeled responder T cells was assessed by *in vitro* co-culture assay.

Data analysis

All data were expressed as the mean ± SEM. Statistical comparisons were performed using One-way ANOVA (Figure 1, 2A et 4), Kruskall-Wallis ANOVA (Figure 2B) and F Test (Figure 3). P values < 0.05 were considered to be statistically significant; **P < 0.01; *** P < 0.001; NS, Not significant).

Results

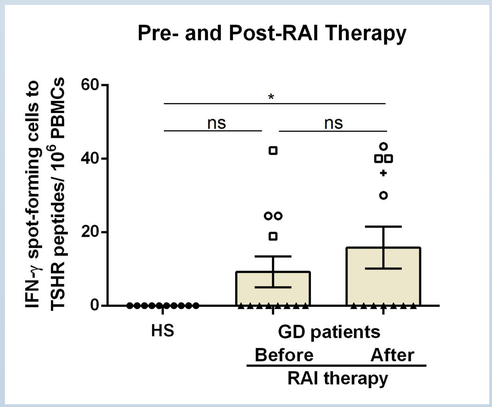
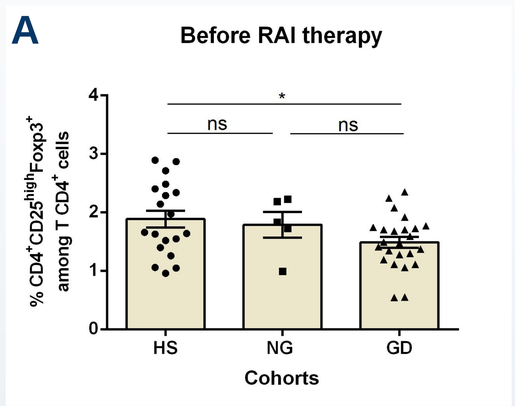


Figure 1. RAI therapy has a mild effect on auto-reactive T cells specific to thyroid peptides. T cell IFN-γ production in the presence of TSHR peptides was measured in 10 GD patients and in 10 HS. Significant response to at least one peptide was measured in 2/10 (○ and □) and 3/10 (○, □ and +) GD patients before and after RAI therapy, respectively, and in none of the controls.

Results



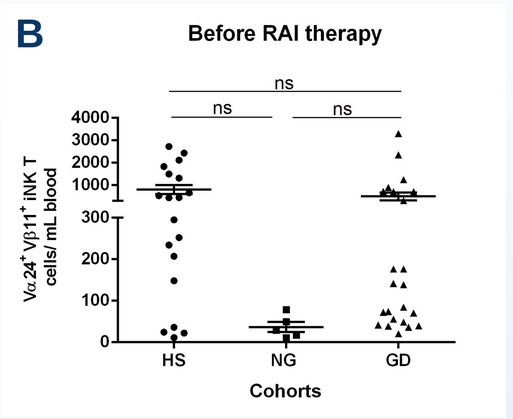
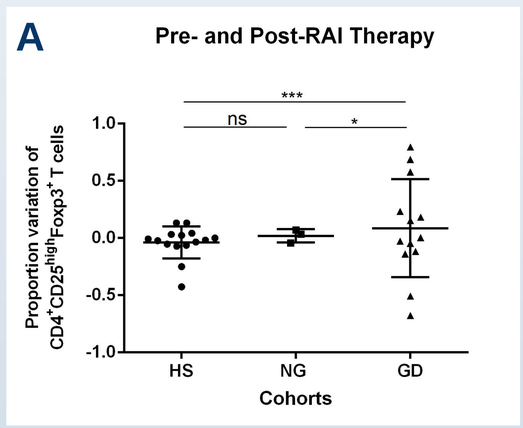


Figure 2. There is a decrease in frequency of Treg but not NKT cells before RAI treatment in GD patients. Treg **(A)** and NKT **(B)** cells were counted in 24 GD patients and in 5 NG patients before RAI treatment, as well as in 19 untreated HS over the same time period.



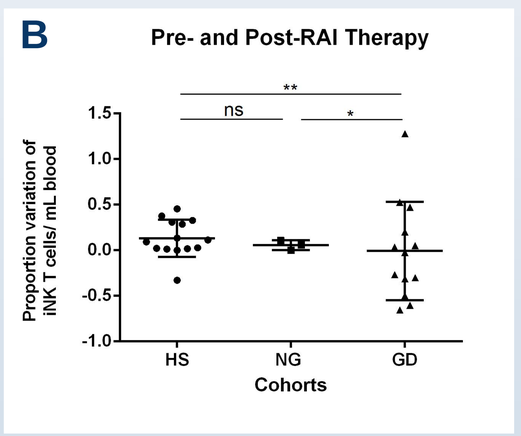


Figure 3. Numerical variation of Treg and NKT cells after thyroid radiation appears to be greater in GD patients. Proportion variation of Treg **(A)** and NKT **(B)** cells were analysed in 13 GD patients and in 3 NG patients before and one month post-RAI treatment, as well as in 15 untreated HS over the same time period.

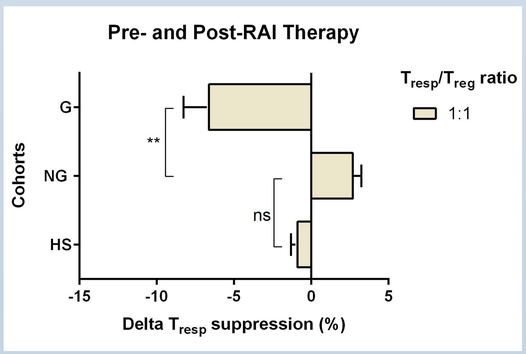


Figure 4. RAI therapy induces a decrease in the suppressive function mediated by Treg in GD patients. Suppressive capacity of Treg was assessed in 9 GD patients and in 3 NG patients before and one month post-RAI treatment, and in 9 HS over the same time period. Responder T cells *from the pre-treatment sample* were co-cultured with Treg.

Conclusion

RAI therapy in GD patients induces :

- **Changes in frequency of peripheral T cells with regulatory properties**
- **A decreased suppressive function mediated by Treg.**

These effects may be involved in the exacerbation of autoimmune processes observed following radiation damage to the thyroid gland.

Targeting Treg could be a promising approach in controlling autoimmune processes following this treatment.