

The immune status peculiarities depending on the level of thyroid peroxidase antibodies in Graves' disease

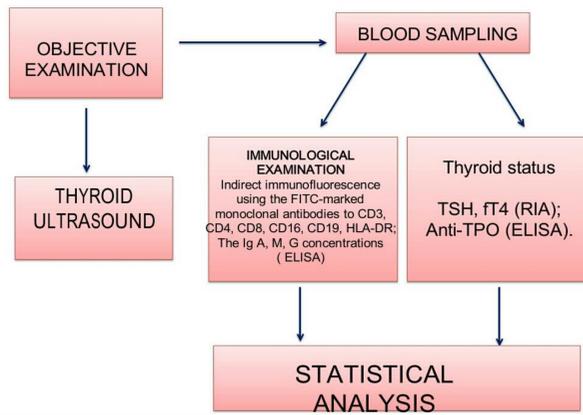
Margarita A. Dudina, Sergey A. Dogadin, Andrey A. Savchenko

Krasnoyarsk State Medical University named after prof. V. F. Voyno-Yasenetsky
Institute for Medical Problems of the North, Siberian Division, Russian Academy of Medical Sciences
Krasnoyarsk regional clinical hospital, Krasnoyarsk, Russian Federation

OBJECTIVES

It is known that thyroid peroxidase is expressed on the apical surface of thyrocytes, where catalyze the iodination of thyroglobulin and may, also, be a surface-cell antigen, which involves in the complement-dependent cytotoxicity reactions. Objective: to study the immune status indices depending on thyroid peroxidase (anti-TPO) antibodies in patients with Graves' disease (GD).

Study design



The level of TSH and thyroid hormones in blood from patients with GD depending on the level of anti-TPO (Me, C₂₅-C₇₅)

| Indicies | Control (n=45) | | Patients with GD (n=35) | | | |
|-----------------|----------------|----------------------------------|--------------------------|-------------|------------------------|-------------|
| | Me | C ₂₅ -C ₇₅ | < 100 мЕд/л n=20 2 | | >100мЕд/л n=15 3 | |
| TSH, mU/l | 1,19 | 0,90-1,56 | 0,09 | 0,06-0,12 | 0,08 | 0,07-0,10 |
| | | | p ₁ <0,001 | | p ₁ <0,001 | |
| fT4, pmol/l | 14,90 | 13,80-15,60 | 49,55 | 42,32-66,33 | 49,20 | 39,70-70,15 |
| | | | p ₁ <0,001 | | p ₁ <0,001 | |
| anti-TPO, IU/ml | 1,0 | 0,0-3,5 | 18,5 | 2,5-45,5 | 292,0 | 187,0-751,0 |
| | | | p ₁ <0,001 | | p ₁ <0,001 | |

* p₁-statistically significant differences with the control values.

CONCLUSIONS

The most significant changes of immunological indices in GD were found in patients with more than 100 IU/ml anti-TPO level. In the case of anti-TPO level less than 100 IU/ml the immunopathogenesis of GD is characterized by the appearance of positive relationships anti-TPO with B-, and negative with T-cell immunity indices. Thus, the immunopathogenesis of GD is characterized by positive correlation in AT-TPO and indicators of b-cell immunity, and negative – with the parameters of T-cell immunity, regardless of thyrocytes peroxidase autoantibodies concentration.

Correspondence: Margarita Dudina,
email: margo85_@bk.ru

METHODS

The study included 35 women aged from 18 to 55 years, mean age of 39.1±7,2, with manifestations of GD, before antithyroid therapy. Concentrations of thyroid hormones were measured by RIA. Anti-TPO concentrations was assessed by ELISA. The analysis of lymphocytes subset pattern were performed by indirect immunofluorescence using the FITC-marked monoclonal antibodies to CD3, CD4, CD8, CD16, CD19, HLA-DR. The Ig A, M, G concentrations were determined by ELISA. The CD4⁺/CD8⁺ T cell ratio and the relative synthesis of IgA (IgA /CD19⁺), IgM (Ig M/CD19⁺) and IgG (IgG/CD19⁺) were also calculated. Results. The patients with more than 100 IU/ml anti-TPO level were characterized by an increase in absolute lymphocytes, relative and absolute number of CD19⁺ and HLA-DR⁺cells, CD3⁺ and CD8⁺cells, compared to the control range and patients with anti-TPO less than 100 IU/L.

RESULTS

Fig. 1. Lymphocytes subset pattern from patients with GD (n=35) and control group (n=45).

The phenotypic composition of lymphocytes in the blood from patients with GD depending on the level of anti-TPO (Me, C₂₅-C₇₅)

| Indicies | Control (n=45) | | Patients with GD (n=35) | | | |
|---------------------------------|----------------|----------------------------------|--------------------------|-----------|------------------------|-----------|
| | Me | C ₂₅ -C ₇₅ | < 100 мЕд/л n=20 2 | | >100мЕд/л n=15 3 | |
| Leucocytes, 10 ⁹ /l | 5,80 | 4,80-7,00 | 5,05 | 4,55-6,15 | 6,00 | 4,50-8,20 |
| Lymphocytes, % | 37,0 | 31,0-41,0 | 41,0 | 35,0-48,5 | 43,0 | 32,0-54,0 |
| | | | p ₁ <0,05 | | p ₁ <0,05 | |
| Lymphocytes, 10 ⁹ /l | 2,16 | 1,76-2,64 | 2,13 | 1,85-2,79 | 2,78 | 1,85-3,08 |
| | | | p ₁ <0,05 | | p ₁ <0,05 | |

* p₁ - statistically significant differences with the control values.

Fig. 2. The immunological coefficients from patients with GD (n=35) and control group (n=45).

The coefficients characterizing the cellular and humoral immunity, from patients with GD depending on the of anti-TPO level (Me, C₂₅-C₇₅)

| Indicies | Control (n=45) | | Patients with GD (n=35) | | | |
|--|----------------|----------------------------------|--------------------------|-------------|------------------------|-------------|
| | Me | C ₂₅ -C ₇₅ | < 100 мЕд/л n=20 2 | | >100мЕд/л n=15 3 | |
| Leucocytes/CD3 ⁺ | 3,99 | 3,37-5,03 | 4,10 | 3,19-4,66 | 3,35 | 2,89-4,31 |
| | | | p ₁ <0,05 | | p ₁ <0,05 | |
| Leucocytes/CD19 ⁺ | 22,41 | 16,8-28,83 | 18,40 | 13,81-28,26 | 17,36 | 12,20-21,93 |
| | | | p ₁ <0,01 | | p ₁ <0,01 | |
| HLA-DR ⁺ /CD19 ⁺ | 1,42 | 1,17-1,80 | 1,38 | 1,21-2,00 | 1,51 | 1,41-1,87 |

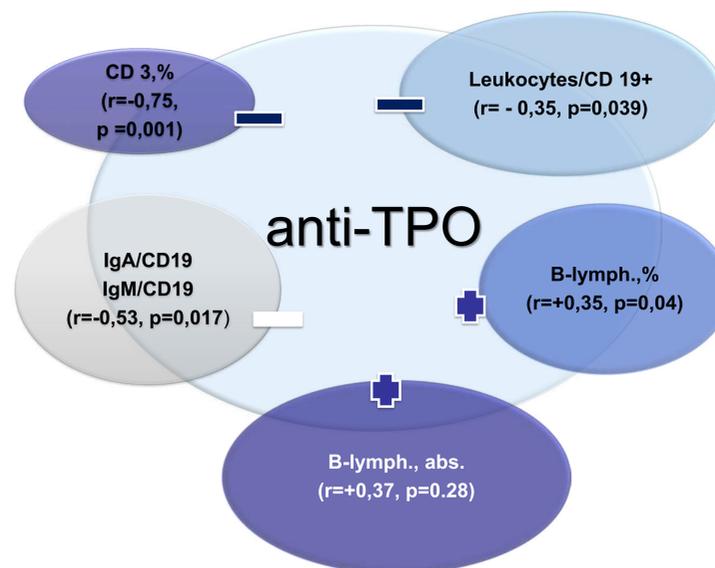
| Indicies | Control (n=45) | | Patients with GD (n=35) | | | |
|---------------------------------------|----------------|----------------------------------|--------------------------|-----------|------------------------|-----------|
| | Me | C ₂₅ -C ₇₅ | < 100 мЕд/л n=20 2 | | >100мЕд/л n=15 3 | |
| CD3 ⁺ , % | 67,0 | 59,0-72,0 | 66,0 | 61,0-68,0 | 67,0 | 63,0-72,0 |
| CD3 ⁺ , 10 ⁹ /l | 1,43 | 1,11-1,65 | 1,43 | 1,05-1,72 | 1,79 | 1,35-2,00 |
| | | | p _{1,2} <0,05 | | p _{1,2} <0,05 | |
| CD4 ⁺ , % | 38,0 | 34,0-40,0 | 39,0 | 35,0-41,0 | 38,0 | 30,0-44,0 |
| CD4 ⁺ , 10 ⁹ /l | 0,82 | 0,61-1,00 | 0,86 | 0,70-0,98 | 0,93 | 0,74-1,22 |
| CD8 ⁺ , % | 30,0 | 21,0-33,0 | 27,5 | 24,5-31,5 | 32,0 | 26,0-36,0 |
| CD8 ⁺ , 10 ⁹ /l | 0,60 | 0,42-0,78 | 0,64 | 0,48-0,73 | 0,86 | 0,62-0,98 |
| | | | p _{1,2} <0,05 | | p _{1,2} <0,05 | |

* p₁ - statistically significant differences with the control values; p₂ - statistically significant differences in the rate of patients with GD with anti-TPO level < 100 IU/l

| Indicies | Control (n=45) | | Patients with GD (n=35) | | | |
|-----------------------------------|----------------|----------------------------------|--------------------------|-------------|------------------------|-------------|
| | Me | C ₂₅ -C ₇₅ | < 100 мЕд/л n=20 2 | | >100мЕд/л n=15 3 | |
| Ig A, r/l | 1,46 | 1,04-2,36 | 1,54 | 1,00-2,76 | 1,76 | 0,91-3,10 |
| Ig M, r/l | 1,46 | 0,99-1,58 | 1,41 | 1,01-1,77 | 0,94 | 0,80-1,75 |
| Ig G, r/l | 5,79 | 4,94-8,60 | 6,78 | 5,50-9,43 | 7,05 | 5,79-13,10 |
| Ig A/CD19 ⁺ ng/cell | 6,91 | 4,98-12,23 | 5,49 | 4,15-9,18 | 4,41 | 2,72-6,33 |
| | | | p ₁ <0,01 | | p ₁ <0,01 | |
| Ig M/CD19 ⁺ ng/cell | 5,45 | 4,03-8,09 | 4,89 | 3,40-7,29 | 2,19 | 1,86-6,19 |
| | | | p ₁ <0,05 | | p ₁ <0,05 | |
| Ig G/CD19 ⁺ ng/cell | 28,44 | 19,7-44,52 | 25,18 | 15,59-39,84 | 19,12 | 12,57-49,09 |
| ЦИК, о.е. | 5,00 | 3,00-6,00 | 6,00 | 5,00-9,00 | 8,00 | 2,00-11,00 |

* p₁ - statistically significant differences with the control values; p₂ - statistically significant differences in the rate of patients with GD with anti-TPO level < 100 IU/l

Fig.3. The relationship between anti-TPO level and immunological indices in patients with GD.



| Indicies | Control (n=45) | | Patients with GD (n=35) | | | |
|--|----------------|----------------------------------|--------------------------|-----------|------------------------|-----------|
| | Me | C ₂₅ -C ₇₅ | < 100 мЕд/л n=20 2 | | >100мЕд/л n=15 3 | |
| CD16 ⁺ , % | 16,5 | 12,0-22,0 | 20,0 | 14,5-23,5 | 19,0 | 16,0-21,0 |
| CD16 ⁺ , 10 ⁹ /l | 0,38 | 0,27-0,51 | 0,37 | 0,30-0,57 | 0,54 | 0,22-0,61 |
| CD19 ⁺ , % | 12,0 | 9,0-15,0 | 12,0 | 9,0-17,0 | 15,0 | 12,0-17,0 |
| | | | p ₁ <0,05 | | p ₁ <0,05 | |
| CD19 ⁺ , 10 ⁹ /l | 0,25 | 0,18-0,34 | 0,30 | 0,19-0,39 | 0,37 | 0,29-0,56 |
| | | | p ₁ <0,05 | | p ₁ <0,05 | |
| HLA-DR ⁺ , % | 18,0 | 14,0-21,0 | 19,0 | 16,0-25,0 | 23,0 | 20,0-27,0 |
| | | | p ₁ <0,001 | | p ₂ <0,05 | |
| HLA-DR ⁺ , 10 ⁹ /l | 0,37 | 0,29-0,46 | 0,43 | 0,33-0,53 | 0,62 | 0,52-0,74 |
| | | | p ₁ <0,001 | | p ₂ <0,05 | |

* p₁ - statistically significant differences with the control values; p₂ - statistically significant differences in the rate of patients with GD with anti-TPO level < 100 IU/l

References

- 1) Khoury EL, Hammond L., Bottazzo GF et al. Clin Exp Immunol 1981;(45): 316-328.
- 2) Anvari M, Khalilzadeh O, Esteghamati A. et al Endocrine 2010;37(2): 344-348.
- 3) Wang HC, Klein JR. Crit Rev Immunol 2001;21(4): 323-337.