REVIEW

Prolactin and interleukin 2 concentrations before and after i.v. TRH application in primary hypothyroidism and in controls

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Abstract

The authors evaluated serum level of prolactin (PRL) and interleukin 2 (IL-2) before and after i.v. application of tyreoliberin (TRH) 0.2 mg in 10 women as controls and 10 women with primary hypothyreoidism. In controls, there was a significant increase of IL-2 20 min following application of TRH (IL-2 0 min: 17.95±11.69, IL-2 in 20 min: 33.36±17.73 fmol/l), in patients with hypothyreoidism the serum level of IL-2 decreased (IL-2 0 min: 31.32±19.0, IL-2 in 20 min: 19.11±17.8 fmol/l). The basal concentration of IL-2 in patients with hypothyreoidism was significantly higher as in controls ($p<0.01$). The presented finding indicated relation between the neuroendocrine and immune system but its value is not yet apparent. ***(Tab. 4, Fig. 1, Ref. 7.)***

Key words: thyreoliberin, TRH, interleukin 2, IL-2.

Interleukin 2 is a potent cytokine that activates proliferation and differentiation of T and B lymphocytes. Regulation of IL-2 production and secretion is very complicated and complex. A significat role in this proces is played by neuroendocrine system (Trejbal et al., 2001). Komorowski et al. (1994) found that serum concentrations of IL-2 in healthy persons are influenced by i.v. application of synthetic thyreoliberin (TRH). IL-2 increase after TRH is parallel with an increase of thyrotropin (TSH) and prolactin (PRL). PRL plays a role in immunity regulation and may stimulate IL-2 production in experiment (Viselli, 1991). Increased PRL concentrations were described by a number of authors in patients with various autoimmune disorders (Trejbal, 2001). A significant PRL increase was found mainly in patients with autoimmune thyroiditis and resulting primary hypothyroidism (Komorowski, 1994).

The aim of our study was to follow paralel IL-2 and PRL response to i.v. TRH application in patients with untreated primary hypothyroidism and in controls.

Material and methods

Serum IL-2 and PRL concentrations before and 20 min after TRH application were studied in 10 healthy women (mean age 31, range 22—45 yrs) and in 10 women with primary hypothyroidism (mean age 34, range 22—55 yrs).

Method: Blood samples for determination of IL-2 and PRL were taken after overnight fasting at 7 a.m. Synthetic thyreoliberin (TRH Berlin-Chemie 0.2 mg) was then given intravenously and next samples were obtained after 20 minutes. Basal free thyroxine (FT4) and TSH were also examined in all hypothyroid patients (Tab. 1).

IL-2 was determined by immunoenzymatic method using kits manufactured by Immunotech, PRL was examined by chemoluminiscent method with kits fy. Imunolite.

Results

Individual serum PRL and IL-2 concentration before and after TRH in hypothyroid patients and in controls are in Tables 2 and 3, mean values are in Table 4. Basal as well as stimulated PRL values were significantly higher in hypothyroid patient than in controls ($p>0.01$). Also basal IL-2 values were higher in hypothyroid patients than in controls ($p>0.01$) but after TRH there were seen two different types of response: an elevation was pre-

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Tab. 1. Serum TSH and fT4 concentrations in patients with primary hypothyroidism.

Patient	Age	TSH (mU/l)	fT4 (pmol/l)
1	22	20,46	7,5
2	29	37	4,35
3	55	41	6,32
4	28	149,15	3,5
5	40	16,7	7,7
6	27	50	5,43
7	35	45,2	5,87
8	31	26,6	7,87
9	30	15,4	8,6
10	42	25,11	5,4

Tab. 2. Individual PRL and IL-2 concentrations before and after TRH application in patients with hypothyroidism.

Patient	Age	PRL (ng/ml)		IL-2 (fmol/ml)	
		0 min	20 min	0 min	20 min
1	22	14,04	86,9	47,07	5,07
2	29	16,7	69,7	72,99	69,25
3	55	9,8	131	22,66	9,32
4	28	21	135	32,36	11,44
5	40	14,1	83,5	1,5	8,11
6	27	5,73	62,5	19,66	9,15
7	35	13,08	48,5	32,76	18,97
8	31	16,1	85,2	17,21	12,96
9	30	19,1	26,3	21	21
10	42	50,2	84,2	46	25,8

Tab. 3. Individual PRL and IL-2 concentrations before and after TRH application in control subjects.

Patient	Age	PRL (ng/ml)		IL-2 (fmol/ml)	
		0 min	20 min	0 min	20 min
1	34	7,14	30,36	64,18	63,29
2	22	14,6	34,6	3,26	4,47
3	23	12,84	45,62	14,78	43,28
4	30	7,95	51,5	1,44	15,99
5	34	11	44,31	36	41,46
6	31	4,83	16,9	19,63	45,1
7	45	4,32	64,42	14,08	40,08
8	20	7,24	62,12	19,6	45,1
9	27	6,8	53,9	6,9	11
10	41	12,3	36,7	29,66	23,8

sent in controls and a decline of IL-2 concentrations was characteristic for hypothyroid patient (Fig. 1).

Discussion

Increase in IL-2 concetrations after TRH was originaly described by Komorowski et al. (1994). It is known, that basal PRL concentrations are significantly higher in hypothyroid patients

Tab. 4. Serum PRL and IL-2 mean concentrations and standard deviations in hypothyroidism.

Group Number Average age	TRH 0,2 mg i.v.			
	PRL (ng/ml)		IL-2 (fmol/ml)	
	0 min	20 min	0 min	20 min
Control n=10 31 y	8,9 ±3,36	44,04 ±14,02	17,59 ±11,69	33,36 ±17,63
Primary hypothyreoses n=10 34 y	17,99 ±11,51	81,28 ±31,63	31,32 ±19	19,11 ±17,8

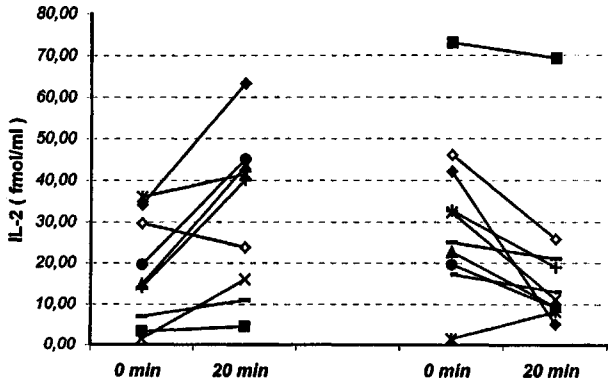

Fig. 1. IL-2 response to TRH stimulation in the primary hypothyroidism and in controls.

than in healthy persons and PRL response to TRH stimulation in this group is exaggerated. Viseli (1991) also found that PRL may stimulate IL-2 production in experimental animals. Generaly a paralel elevation of IL-2 and PRL levels after TRH could be expected. Observed decline of IL-2 concentrations after TRH application was from this aspect a surprise.

Komorowski (1994) found that increase in PRL after metoclopramid is higher than after TRH stimulation but there was no IL-2 response to metoclopramid . He concluded that PRL had no effect on IL-2 production. However, Perez-Castro et al. (1999) observed that for optimal function of immunocompetent cells optimal intracellular TRH/PRL ratio is inevitable. Application of sheep erytrocytes to experimental rats caused an increase of TRH production in hypothalamus and elevated PRL concentration in the serum. Intracereberal application of TRH blocking oligonucleotides blocked production of corresponding antibodies.

Mentioned decrease in IL-2 concentration may result from their decreased production or may be a result of increased periferal clearence on the receptor level. Increased concentration of solubile IL-2R was observed by Loviselli et al. (1994). TRH and

PRL may stimulate IL-2 expressivity, but from this aspect more research is needed.

Intravenous application of TRH causes a significant increase in healthy people and a decrease in IL-2 production in hypothyroid. Mechanism and significance of this finding is unclear.

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