

## Comparative effects and side effects of short-term and long-term treatment of hyperthyroidism, with methimazol and propylthiouracil.

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**Abstract: Methods:** Meta-Analysis of the methods used in this study and number of 35 Articles was found from Pubmed and Cochrain motor search. **Results:** The main finding of this study was: 1- euthyroid duration 2-the number of people who achieve euthyroid. 3-amont of TSH average euthyroid duration of long was 65/207 month, and in short was 18/273 months and ratio of euthyroid groups to the total cases in the long was 0/443 and in short was 0/623. TSH levels in long was: 1/83 IU and in short was 1/048 IU. **Discussion:** According to the results of the Meta-Analysis software, the long term has better effect than short term in increase length of euthyroid duration, but short term treatment is better than long term in number euthyroids and in decrease of TSH amount. So we can conclude that short term is more effective than long term.

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**Key words:** hyperthyroidism, methimazol, propylthiouracil, long term, short term

### It state:

Due to the different treatment solution that there are for hypertiroidism disease and considering to drug effects on the patients and also with regard. That many criteria fallows after treatment such as:

Life guality-cost benfit-expenditures-severdrugs side effects hepatitis, agran, locitosis therefore there aren't unitheory. about long term and short term which method is perferible.

A team of researchers that study on short term considered this method is more appropriated (Donald 1980 duma DJ 1982).

Some researchers from this group believe that there aren't significant different between these type but short term is preferred for treatment duration and low side effect (Tajiri and Etal 1991) And others prefer long-term treatment (Shizumek 1978, Tadzer 1989, Azizi 2005).

In this study we want to find the better way for treatment by study on articles evaluation and extract their data and we will use from meta-analysis we hope to find which method is preferable for patient (with lowest duration treatment-lowest side effect and safer.)

### Review of literature:

Short term treatment with anti-thyroid drugs a team of researchers who have studied this type of treatment is considered more appropriate (Buma DJ, 1982)

Mr. Donald in 1980 in pervious study found similar results in other studies.(2)

Some researchers from this group believe that there aren't significant different between these type of treatment but short term is preferred because

low duration and low side effects. (Tajiri and Etal 1991)(3)

And other researchers preferred long term treatment (Tazder and etal,1989)(4),(azizi,2006)(5)

And in the other study long term treatment like previous study has been approved(6)

In a study of long term treatment for hyperthyroidism has not been good(taskatsk,1999)(7)

Mr. Vansosberg in 1992 in a study determined that long term treatment with methimazol in multinodular goiter in not useful because it has relaps over 95% so replacement therapy with I and operation is offered.(8)

However, an article in 1989 by Mr.Tazder and his colleagues has performed and the results was opposite of last article and determined that long term treatment with methimazol is better than I and operation (9).

In a study short term therapy with methimazol for graves and small goiter showed that this method is effective(10).

In a study by long term treatment with methimazol for graves is better that propylthiouracil because it has lower side effect and upper remission(11)

In another study 55 patient were treated with methimazol single daily dose 30 mg in 17 weeks,46 patients were euthyroid that is placed in short term group(12).

### Method:

In this study number of 1200 object of article from pubmed and cochrain evaluated and the number of 300 abstracts extracted.

And 67 articles has chosed from them but the articles which has written by other language

except English or their object was about animals was excluded, and finally 35 full text of articles related was include and the articles data was entered in meta analysis soft war.

To assess the long term and short term treatment of hyper thyroidism with anti thyroid drugs, the following were examined:

Agranolocytois- hepatitis-length of euthyroid-level of serum TSH-cost benefit-quality echocardiography-lipid profil-LDL-HDL -the size of goiter (clinical and ultrasound)

Anti bodies (TSH. Receptor anti body- tpo AB-TGA) T3-T4 and hip , Spin Score  $Z > 2.5$

Papers was evaluated by two methods: short term and long term.

Long term had tow subgroup: 1-treated up to 25 months 2—after 25 months. There was lack of information so two above group were evaluated in one group.

In short term 3 aims was proposed:

1-who were euthyroid after cessation.

2-who relapsed after discontinue and were euthyroid by I.

3-who relapsed after cissionation and were hypo thyroid by I and were euthyroid by T4.

All of above group due to lack of data in literature were assessed in one group.

The following table details the number of cases found in the article are (Table 1):

Table 1. Details the number of cases

Group Variable	Long term	Short term
Agranolocytois	4	1
Hepatitis	3	-
Eutyroid length	15	16
Serum TSH	7	9
Cost	4	-
Quality	3	-
Echocardiography	1	-
lipid	IDI	-
	HDI	-
Goiter size	clinical	-
	sono	-
AB	TG AB	5
	TPO AB	1
	TSH REC AB	7
BMI	HIP	-
	SPIO	-
T3	12	13
T4	10	14

Those article that has just mean and has not varians or standard deviation (SD) Has omitted from evaluation.

**Results:**

The results for the four factors: 1-number of eutyroid; 2- euthyroid length; 3- serum TSH; 4-serum T4 and average remaining in both group were examined separately the following results were obtained:

**TSH comparison in two methods Long Term and Short Term**

long term		pooled mean	LCI95%	UCI95%	number of stydies	
	random effect	65.207	43.632	86.783	9	
	fixed effect	40.122	36.4	43.844	9	
short term		pooled mean	LCI95%	UCI95%	number of stydies	
	random effect	18.273	12.885	23.661	9	13.82 بدون مطالعه اول
	fixed effect	5.387	5.142	5.632	9	

**Euthyroid ratio to total in both methods SHORT TERM and LONG TERM**

long term		pooled mean	LCI95%	UCI95%	number of stydies
	random effect	1.832	0.386	3.279	3
	fixed effect	1.764	1.597	1.932	3
short term		pooled mean	LCI95%	UCI95%	number of stydies
	random effect	1.048	0.376	1.721	4
	fixed effect	1.032	0.585	1.479	4

**Euthyroid Length in two methods SHORT TERM and LONG TERM**

long term		pooled prev	LCI95%	UCI95%	number of stydies
	random effect	0.443	0.313	0.576	22
	fixed effect	0.285	0.267	0.302	22
short term		pooled prev	LCI95%	UCI95%	number of stydies
	random effect	0.623	0.495	0.742	24
	fixed effect	0.575	0.542	0.609	24

**T4 comparison in two methods SHORT TERM and LONG TERM**

**LONG TERM**

T4		pooled mean	LCI95%	UCI95%	number of stydies
	random effect	13.957	9.423	18.491	4
	fixed effect	10.800	10.627	10.983	4

**Four factor mean in LONG TERM**

**SHORT TERM**

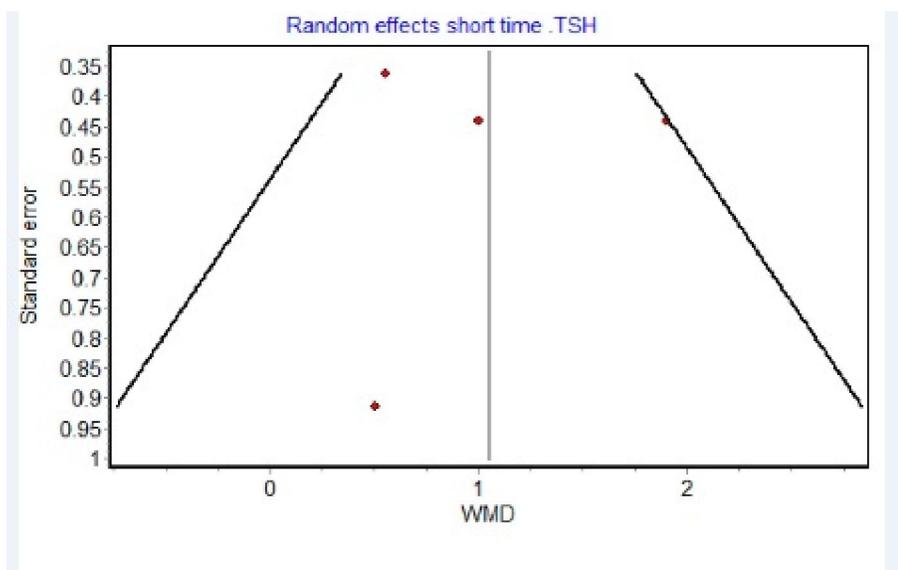
T4		pooled mean	LCI95%	UCI95%	number of stydies
	random effect	41.4	34.674	48.126	16
	fixed effect	7.126	6.804	7.448	16

**SHORT TERM**

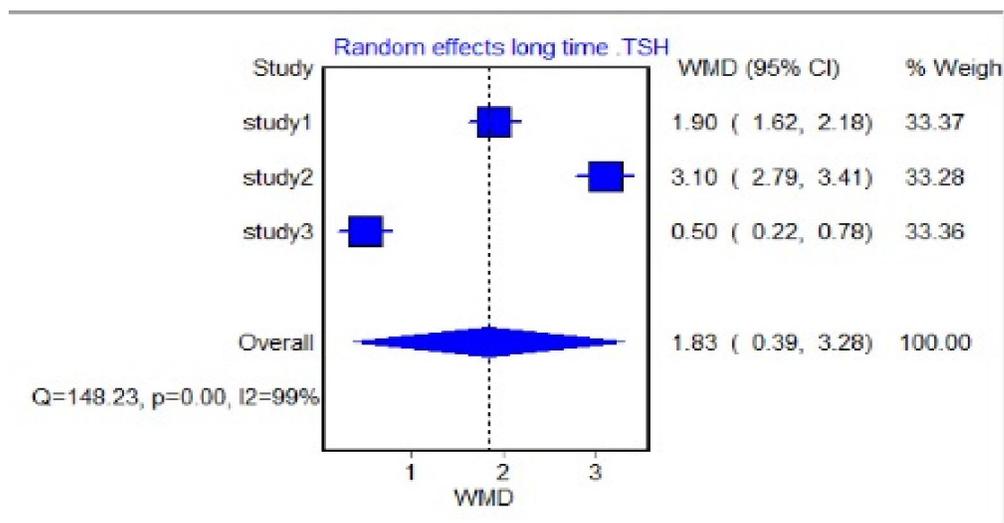
TSH rec ab		pooled mean	LCI95%	UCI95%	number of stydies
	random effect	30.737	18.51	42.964	6
	fixed effect	24.956	23.631	26.281	6
T3		pooled mean	LCI95%	UCI95%	number of stydies
	random effect	5.075	3.445	6.706	8
	fixed effect	4.341	4.09	4.591	8

just weighted mean	
cost	654.084
quality	51.663
size	33.64
tg ab long	41.254

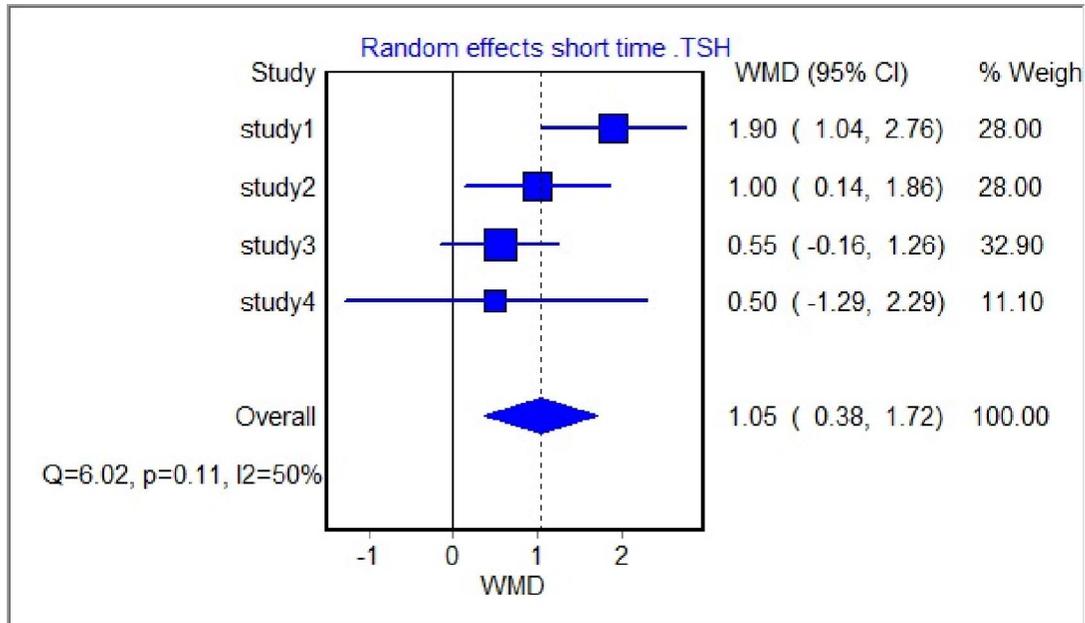
### Funnel Plot



### Forest plot



## Forest plot



### Conclusion:

According to results that obtained from meta analysis we can conclude that long term method is effective in increase of euthyroid length but short term is more appropriated in increase number of euthyroid patient and decrease serum TSH.

However their confidens has overlap together. So we can't determine p value for it.

So there are three comment: if euthyroid length is more important than serum TSH Level or number of euthyroid patient then long term is effective than short term, but if these two factor is important than euthyroid length therefor short term is better than long term.

Here there are some forest and funnel plat about study.

### REFERENCES:

1. Bouma DJ, Kammer H, Greer MA. Follow-up comparison of short-term versus 1-year antithyroid drug therapy for the thyrotoxicosis of Graves' disease. *J ClinEndocrinolMetab* 1982; 55: 1138-42.
2. Bouma DJ, Kammer H. Single daily dose methimazole treatment of hyperthyroidism. *West J Med* 1980; 132: 13-5.
3. Tajiri J, Noguchi S, Morita M, Tamaru M, Murakami N. Antithyroid drug therapy for Graves' hyperthyroidism: is long-term administration of a small maintenance dose necessary? *EndocrinolJpn* 1991; 38: 223-7.
4. Tadzer I, Simova N, Karanfilski B, Korubin V, Serafimov N, Miceva S, Loparska S, Vaskova O. Extended long-term drug monotherapy of Graves' disease. *Acta Med Jugosl* 1989; 4:181-7.
5. Azizi F. The safety and and efficacy of antithyroid drugs. *Expert Opin Drug Saf.* 2006 Jan;5(1):107-16.
6. Roti E, Gardini E, Minelli R, Bianconi L, Braverman LE. Sodium ipodate and methimazole in the long-term treatment of hyperthyroid Graves' disease. *Metabolism* 1993; 42: 403-8.
7. Takáts KI, Szabolcs I, Földes J, Földes I, Ferencz A, Rimanóczy E, Góth M, Dohán O, Kovács L, Szilágyi G. The efficacy of long term thyrostatic treatment in elderly patients with toxic nodular goitre compared to radioiodine therapy with different doses. *ExpClinEndocrinol Diabetes* 1999; 107: 70-4.
8. vanSoestbergen MJ, van der Vijver JC, Graafland AD. Recurrence of hyperthyroidism in multinodular goiter after long-term drug therapy: a comparison with

- Graves' disease. *J Endocrinol Invest* 1992; 15: 797-800.
9. Tadzer I, Simova N, Karanfilski B, Korubin V, Serafimov N, Miceva S, Loparska S, Vaskova O. Extended long-term drug monotherapy of Graves' disease. *Acta Med Jugosl* 1989; 4:181-7.
  10. Bouma DJ, Kammer H. Single daily dose methimazole treatment of hyperthyroidism. *West J Med* 1980; 132: 13-5.
  11. Sato H, Minagawa M, Sasaki N, Sugihara S, Kazukawa I, Minamitani K, Wataki K, Konda S, Inomata H, Sanayama K, Kohno Y. Comparison of methimazole and propylthiouracil in the management of children and adolescents with Graves' disease: efficacy and adverse reactions during initial treatment and long-term outcome. *J PediatrEndocrinolMetab* 2011; 24: 257-63.
  12. Mashio Y, Beniko M, Matsuda A, Koizumi S, Matsuya K, Mizumoto H, Ikota A, Kunita H. Treatment of hyperthyroidism with a small single daily dose of methimazole: a prospective long-term follow-up study. *Endocr J*. 1997; 44:553-8.
  13. Toft AD. Is long-term methimazole therapy as effective as radioiodine for treating hyperthyroidism? *Nat ClinPractEndocrinolMetab* 2005; 1: 14-5.
  14. Mazza E, Carlini M, Flecchia D, Blatto A, Zuccarini O, Gamba S, Beninati S, Messina M. Long-term follow-up of patients with hyperthyroidism due to Graves' disease treated with methimazole. Comparison of usual treatment schedule with drug discontinuation vs continuous treatment with low methimazole doses: a retrospective study. *J Endocrinol Invest* 2008; 31: 866-72.(pdf-Key)
  15. Azizi F, Ataie L, Hedayati M, Mehrabi Y, Sheikholeslami F. Effect of long-term continuous methimazole treatment of hyperthyroidism: comparison with radioiodine. *Eur J Endocrinol*2005 ; 152: 695-701.
  16. Benker G, Reinwein D, Kahaly G, Tegler L, Alexander WD, Fassbinder J, Hirche H. Is there a methimazole dose effect on remission rate in Graves' disease? Results from a long-term prospective study. The European Multicentre Trial Group of the Treatment of Hyperthyroidism with Antithyroid Drugs. *ClinEndocrinol (Oxf)* 1998; 49: 451-7.
  17. Roti E, Gardini E, Minelli R, Bianconi L, Braverman LE. Sodium ipodate and methimazole in the long-term treatment of hyperthyroid Graves' disease. *Metabolism* 1993; 42: 403-8.
  18. Takács IK, Szabolcs I, Góth M, Dohán O, Kovács L, Szilágyi G, Földes J.Consensus statement on management of hypothyroidism and hyperthyroidism. Longterm treatment is not safe in elderly patients with toxic nodular hyperthyroidism. *BMJ* 1996; 313:1487.
  19. Barrio R, López-Capapé M, Martínez-Badás I, Carrillo A, Moreno JC, Alonso M. Graves' disease in children and adolescents: response to long-term treatment. *ActaPaediatr* 2005; 94: 1583-9.
  20. Takata K, Kubota S, Fukata S, Kudo T, Nishihara E, Ito M, Amino N, Miyauchi A.Methimazole-induced agranulocytosis in patients with Graves' disease is more frequent with an initial dose of 30 mg daily than with 15 mg daily. *Thyroid* 2009; 19: 559-63.
  21. Laurberg P, Berman DC, Andersen S, Bülow Pedersen I. Sustained control of Graves' hyperthyroidism during long-term low-dose antithyroid drug therapy of patients with severe Graves' orbitopathy. *Thyroid* 2011; 21: 951-6.
  22. Choo YK, Yoo WS, Kim DW, Chung HK. Hypothyroidism during antithyroid drug treatment with methimazole is a favorable prognostic indicator in patients with Graves' disease. *Thyroid* 2010; 20: 949-54.
  23. Shiroozu A, Okamura K, Ikenoue H, Sato K, Nakashima T, Yoshinari M, Fujishima M, Yoshizumi T. Treatment of hyperthyroidism with a small single daily dose of methimazole. *J ClinEndocrinolMetab* 1986; 63: 125-8.
  24. Jorde R, Ytre-Arne K, Størmer J, Sundsfjord J. Short-term treatment of Graves' disease with methimazole in high versus low doses. *J Intern Med* 1995; 238: 161-5.
  25. Meng W, Meng S, Männchen E, Hampel R, Kirsch G, Dannenberg J, Krabbe S. Effect of therapy duration and low and highly dosed thiamazole treatment in Basedow's-Graves' disease. *ExpClinEndocrinol* 1991; 97: 257-60.
  26. Lippe BM, Landaw EM, Kaplan SA. Hyperthyroidism in children treated with long term medical therapy: twenty-five percent remission every two years. *J ClinEndocrinolMetab* 1987; 64: 1241-5.
  27. Sun MT, Tsai CH, Shih KC. Antithyroid drug-induced agranulocytosis. *J Chin Med Assoc* 2009; 72: 438-41.
  28. Okamoto Y, Tanigawa S, Ishikawa K, Hamada N. TSH receptor

- antibody measurements and prediction of remission in Graves' disease patients treated with minimum maintenance doses of antithyroid drugs. *Endocr J.* 2006 Aug;53(4):467-72.
29. Guntekin U, Gunes Y, Simsek H, Arslan S. P wave duration and dispersion in patients with hyperthyroidism and the short-term effects of antithyroid treatment. *Indian Pacing Electrophysiol J.* 2009 Sep 1;9(5):251-9.
  30. Vali DM, Elfarra AA, Panciera DL, Hutson PR. Pharmacokinetics and short-term clinicopathologic changes after intravenous administration of a high dose of methimazole in dogs. *Am J Vet Res.* 1994 Nov; 55(11):1597-601.
  31. Ford HC, Feek CM, Delahunt JW. Once daily, low dose, low dose, short term antithyroid drug treatment of Graves' disease is followed by an unacceptably high relapse rate. *N Z Med J.* 1991 Mar 13;104(907):97-8.
  32. Orrego H, Blake JE, Blendis LM, Compton KV, Israel Y. Long-term treatment of alcoholic liver disease with propylthiouracil. *N Engl J Med.* 1987 Dec 3;317(23):1421-7.
  33. Orrego H, Kalant H, Israel Y, Blake J, Medline A, Rankin JG, Armstrong A, Kapur B. Effect of short-term therapy with propylthiouracil in patients with alcoholic liver disease. *Gastroenterology.* 1979 Jan;76(1):105-15.
  34. Orrego H, Blake JE, Blendis LM, Compton KV, Volpe R, Israel Y. long-term treatment of alcoholic liver disease with propylthiouracil. Part 2: Influence of drop-out rates and of continued alcohol consumption in a clinical trial. *J Hepatol* 1994;20:343-9.
  35. Wiberg JJ, Nuttall FQ. Methimazole toxicity from high doses. *Ann Intern Med.* 1972 Sep;77(3):414-6.

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