POSTER# CO64

Systematic Review of Methimazole in Grave's Disease Management: Treatment Variations and Efficacy Outcomes

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BACKGROUND

- **Grave's disease (GD)** is the most common form of hyperthyroidism, and is characterized by the overproduction of thyroid hormones due to autoimmune stimulation of the thyroid gland[1]
- **Methimazole (MMI),** an antithyroid medication, is commonly used to inhibit thyroid hormone synthesis and control symptoms. However, treatment protocols vary widely, including differences in dosing regimens, treatment durations, and the criteria for evaluating treatment efficacy. These variations can impact patient outcomes and complicate clinical decision-making[2]

OBJECTIVES

- To consolidate literature on the effectiveness of MMI, assess the implications of different treatment variations, and identify best practices for managing GD

METHODS

- MEDLINE® and Embase® were systematically searched, as per the Population, Intervention, Comparator, Outcome, and Study design (PICOS) criteria (Table 1)
- The title and abstract of each publication retrieved from the database search were initially screened by two independent reviewers. Any uncertainty regarding inclusion was checked by a third independent reviewer. Data were extracted by one reviewer and quality checked against the source by another independent reviewer

Table 1. PICOS criteria

Population	Interventions/Comparators	Outcomes	Study design
Adults with Grave's disease	▪ Methimazole ▪ Levothyroxine ▪ Dexamethasone ▪ Methylprednisolone ▪ Hydrocortisone ▪ Thiamazole	No limits	RCTs only

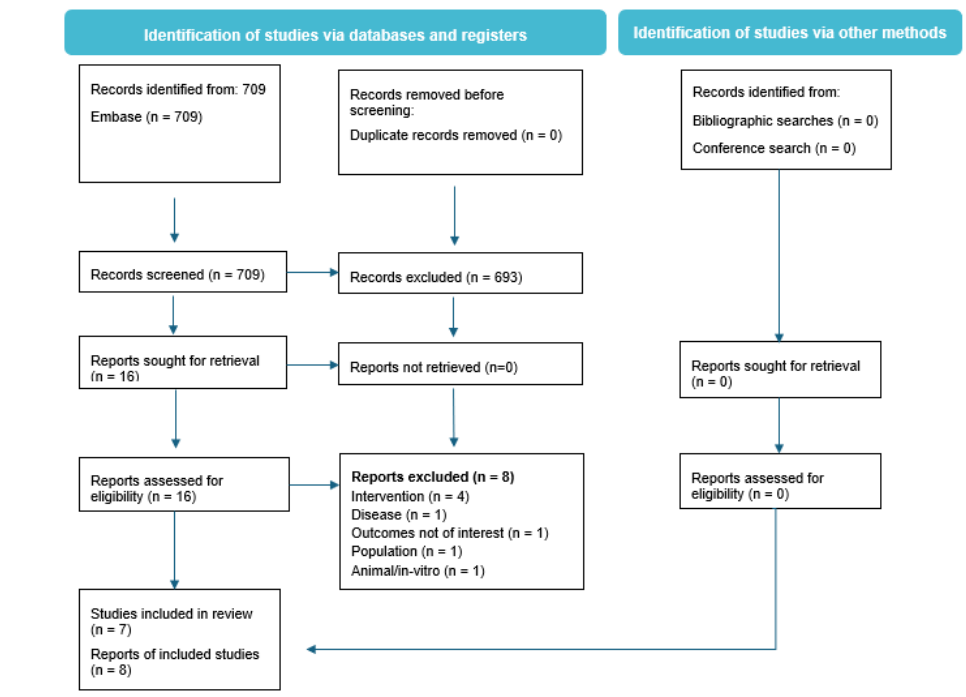
Key: PICOS, Population, Intervention, Comparator, Outcome, and Study design; RCT, randomized controlled trial.

RESULTS

Summary of evidence

- Of the 709 records identified from the electronic database search performed on 28 May 2024, the final review included eight studies (see Figure 1)
- 693 records were excluded in the primary screening, leaving 16 records for secondary screening
- Full-text screening excluded eight reports, leaving eight reports (seven studies) for data extraction
- The seven included studies were randomized control trials (See Table 2). Five studies were conducted in a single centre, while one study was in multiple centres.[9] Study setting was not reported in one study.[10] Three studies were conducted in China[8], Denmark[10] and Iran[4], and the country of study conduct was not reported in four studies
- Mean (SD) age ranged from 38 (13.3) years[9] to 42.8 (13.3) years.[4] The proportion of female patients was higher than males in all studies

Figure 1. PRISMA diagram



KEY EFFICACY FINDINGS

- Results of the included studies are presented in Table 3

Serum hormone levels (T3, T4 and TSH)

- Kocak et al. 2019[9] found that T3 and T4 levels decreased while TSH levels increased in both the propylthiouracil (PTU) and MMI groups (all $p < 0.001$). The changes were more pronounced in the PTU group, indicating that it may be more effective
- In Xu et al. 2019[8], adding selenium (Se) to MMI significantly improved T3 ($p = 0.003$) and T4 ($p = 0.037$) levels compared with MMI alone, with no significant difference in TSH levels ($p = 0.773$) between the groups
- In Zhao et al. 2020[6], both treatment groups showed lower hormone levels after treatment compared to pre-treatment levels. The MMI/PTU group had significantly lower T3, T4, and TSH levels than the PTU alone group ($p < 0.01$)

Relapse rates

- In Karmisholt et al. 2019[10], a fixed low-dose antithyroid drug treatment (FLATD) regimen was associated with a significantly higher relapse rate compared with the observation group ($p < 0.003$)
- In comparing short-term and long-term MMI, Saadat et al. 2024[4] reported a higher relapse-free rate in short-term MMI, and Azizi et al. 2019[7] reported a higher relapse rate for short-term MMI and a much lower rate for long-term MMI

Table 2. Key study and patient characteristics

Study name	Intervention/ Comparator	Sample N	Age, Mean (SD)	Gender, n (%) Male Female	Serum hormone levels at baseline, mean (SD)		
					T3	T4	TSH
Azizi 2019[7]	Short-term MMI	121	38.1 (12.5)	32 (26) 89 (74)	407 (143) ng/dL	37.8 (8.2) pmol/L	< 0.1 IU/L
	Long-term MMI	119	41.3 (13.9)	23 (19) 96 (81)	393 (120) ng/dL	37.9 (9) pmol/L	< 0.1 IU/L
Karmisholt 2019[10]	FLATD	33	43 (37-53)*	3 (10) 30 (90)	1.7 (1.4–1.8) nmol/L*	97 (83.5–111.5) nmol/L*	NR
	Observation	33	46 (36-53)*	9 (27.3) 24 (72.7)	1.7 (1.4–2) nmol/L*	104 (87.5–112) nmol/L*	NR
Kocak 2019[9]	PTU	30	41.1 (12.7)	9 (30) 21 (70)	7.88 (4.22) pg/ml	3.6 (7.1) ng/dL	0.01 (0.01) mIU/L
	MMI	30	38 (13.3)	21 (70) 19 (63.7)	10.21 (7.42) pg/ml	4.53 (7.63) ng/dL	0.01 (0.02) mIU/L
Lertwattanarak 2022[5]	Discont. MMI	90	39.9 (10.9)	13 (14.4) 77 (85.6)	108.6 (73.8) ng/dl	1.22 (0.24) ng/dl	2.15 (1.47) mIU/L
	Cont. MMI	83	42.2 (14.9)	13 (16.25) 70 (83.75)	112.4 (62.5) ng/dl	1.26 (0.18) ng/dl	2.26 (1.35) mIU/L
Saadat 2024[4]	Short-term MMI	128	39.7 (12.6)	34 (27) 94 (73)	130 (21) ng/dl	16.9 (3.2) ng/dl	1.7 (1.2) mIU/L
	Long-term MMI	130	42.8 (13.3)	26 (20) 104 (80)	133 (19) ng/dl	16.7 (2.5) ng/dl	2.1 (1.8) mIU/L
Xu 2019[8]	MMI	50	40.2 (12.63)	19 (38) 31 (62)	28.42 (14.76)	66.14 (26.52)	0.006 (0.001)
	MMI + Se	44	38.89 (11.59)	14 (31.8) 30 (62)	27.93 (10.82)	70.97 (29.12)	0.004 (0.002)
Zhao 2020[6]	MMI/ PTU	46	38.02 (1.23)	23 (50) 23 (50)	9.52 (2.03) pmol/L	18.41 (4.05) pmol/L	5.43 (1.52) pmol/L
	PTU	46	37.86 (1.66)	22 (47.8) 24 (52.2)	9.46 (2.01) pmol/L	18.26 (4.12) pmol/L	5.36 (1.49) pmol/L

Key: FLATD, fixed low-dose antithyroid drug treatment; IQR, inter-quartile range; MMI, methimazole; NR, not reported; PTU, propylthiouracil; RCT, randomized controlled trial; SD, standard deviation; Se, Selenium; TSH, thyroid stimulating hormone.
Note: * Median (IQR).

Recurrence and remission rates

- Azizi et al. 2019[7] found that short-term MMI treatment had a significantly lower remission rate than long-term MMI treatment ($p < 0.001$)
- Lertwattanarak et al. 2022[5] reported significantly lower cumulative recurrence rates in continued MMI treatment compared with discontinued MMI treatment ($p < 0.01$). Additionally, patients with continued low-dose MMI treatment had higher recurrence-free survival than those who stopped treatment ($p = 0.0009$)

Table 3. Results of included studies

Study name	Intervention/ Comparator	Timepoint /Follow-up (Months)	Relapse rate, n (%)	Recurrence/ Remission rate, n (%)	Time to relapse, median (IQR)	Serum hormone levels, mean (SD)		
						T3	T4	TSH
Azizi 2019[7]	Short–term MMI	48	65 (53)	56 (46) *	–	–	–	–
	Long-term MMI		18 (15)	101 (83) *	–	–	–	–
Karmisholt 2019[10]	FLATD	24	11 (34.4) *	–	23.3 (22–24.6) months	–	–	–
	Observation		1 (3.6) *	–	20.1 (17.4–22.8) months	–	–	–
Kocak 2019[9]	PTU	–	–	–	–	3.21 (0.59) * pg/ml	1.19 (0.22) * mg/dL	1.48 (1.071) * mIU/L
	MMI		–	–	–	3.25 (0.55) * pg/ml	1.12 (0.21) * ng/dL	1.4 (1.057) * mIU/L
Lertwattanarak 2022[5]	Conti. MMI	36	–	NR (11) *	–	–	–	–
	Discontinue MMI	36	–	NR (41.2) *	–	–	–	–
Saadat 2024[4]	Short–term MMI	132	67 (54) #	–	–	–	–	–
	Long–term MMI		24 (19) #	–	–	–	–	–
Xu 20198	MMI	6	–	–	–	13.39 (7.41) *	16.59 (3.34) *	2.11 (0.32)
	MMI + Se		–	–	–	5.29 (1.02) *	9.29 (4.27) *	2.3 (0.54)
Zhao 20206	MMI/ PTU	–	–	–	–	3.15 (0.59) * pmol/L	9.53 (2.54) * pmol/L	1.45 (0.51) * pmol/L
	PTU		–	–	–	5.85 (1.19) * pmol/L	13.72 (3.5) * pmol/L	2.85 (0.71) * pmol/L

Key: Conti., continue; FLATD, fixed low-dose antithyroid drug treatment; IQR, inter-quartile range; MMI, methimazole; NR, not reported; PTU, propylthiouracil; SD, standard deviation; Se, Selenium; TSH, thyroid stimulating hormone.
Note: * Significant p values (< 0.05); # Indicated the relapse-free state reported.

CONCLUSIONS

- This SLR demonstrated the effectiveness of MMI in managing GD. Treatment variations, including MMI with Se and PTU, showed promise for improving thyroid function. The findings highlighted that long-term MMI therapy was associated with lower relapse rates and higher remission rates compared with short-term MMI therapy. Continued MMI treatment yielded better outcomes than discontinued MMI treatment. These insights stress the importance of individualized treatment strategies and ongoing monitoring
- Further investigation is needed to standardize protocols and analyse the effects of different treatment durations and combinations on patient outcomes

REFERENCES

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An electronic version of the poster can be viewed by scanning the QR code.

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