

EVALUATION OF THEURAPEUTIC MODALITIES OF GRAVES' DISEASE



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Objective

Radioiodine (RAI), surgical and anti-thyroid drug therapy are the main options to treat Graves' disease (GD). The aim of this study was to investigate theurapeutic options, their efficacy and adverse reactions of propilthiouracil (PTU) and methimazole (MMI).

Method

A total of 650 patients with GD were evaluated retrospectively. Treatments, adverse reactions, clinical and laboratory results were recorded. After 18 months of primary medical treatment, recurrence rates of MMI and PTU were compared by the following one year.

Results

Of 650 participants, mean age was 42.2 ± 13.6 (17-83 years of age) with 72% of them (n=468) were females and 28% of all (n=182) were males. TPO positivity was found in 76.8% (n=499) of all subjects whereas TRAB positivity was detected in 80.5% (n=523) of all patients. Of the patients, %55.4 (n=360) were treated with MMI and 44.6% (n=290) with PTU. Thyroid nodules were detected in 26.3% (n=171) of the patients. Papillary thyroid cancer were detected in 9.5% (n=10). Thyroid ophthalmopathy were seen in 8.6% (n=56) of all patients in which 14.3% of them (8/56) needed to be intervened with surgical decompression. Adverse reactions to the drugs were found in 6.9% (n=45) of all patients (with 2.5% of skin, 2.3% of hepatotoxicity, 1.8% of temporarily neutropenia, 0.6% of agranulocytosis)(Table 1).

Table 1. Demographics and clinical features of GD patients (n=650)

| | n (%) | n (%) |
|--|-------|-------|
| Gender | | |
| Females | 468 | 72.0 |
| Males | 182 | 28.0 |
| TPO positivity | | |
| Positive | 499 | 76.8 |
| Negative | 151 | 23.2 |
| TRAB positivity | | |
| Positive | 523 | 80.5 |
| Negative | 127 | 19.5 |
| Anti-thyroid agents | | |
| Methimazole (MMI) | 360 | 55.4 |
| Propilthiouracil (PTU) | 290 | 44.6 |
| Thyroid nodule | | |
| None | 479 | 73.7 |
| Yes | 171 | 26.3 |
| Ophthalmopathy | | |
| None | 594 | 91.4 |
| Yes | 56 | 8.6 |
| Adverse reactions to medication | | |
| None | 603 | 92.8 |
| Yes | 45 | 6.9 |
| Minor skin reactions | 16 | 2.5 |
| An increase in liver function tests | 15 | 2.3 |
| Temporarily of leucopenia | 12 | 1.8 |
| Agranulocytosis | 4 | 0.6 |

There were not significant difference between MMI and PTU in terms of adverse effects ($X^2=5.373$, $p=0.369$, Fisher's exact test) (Table 2).

Table 2. Adverse effects found in anti-thyroid agent use

| Adverse effect | MMI (n, %) | PTU (n, %) | Total (n, %) |
|---------------------------------------|------------|------------|--------------|
| None | 331 (91.9) | 272 (93.8) | 603 (92.8) |
| Skin reactions | 12 (3.3) | 4 (1.4) | 16 (2.5) |
| <3 times increase of liver functions | 5 (1.4) | 3 (1.0) | 8 (1.2) |
| > 3 times increase of liver functions | 2 (0.6) | 5 (1.7) | 7 (1.1) |
| Temporarily neutropenia | 8 (2.2) | 4 (1.4) | 12 (1.8) |
| Agranulocytosis | 2 (0.6) | 2 (0.7) | 4 (0.6) |
| Total | 360 (100) | 290 (100) | 650 (100) |

There RAI and surgery treatment were applied 9.4% vs. 7.4% respectively because of adverse reactions or unable to achieve euthyroidism with maximum dose of drugs or malignity suspicion. During the period, 16.6% (n=108) of patients were still continuing to take anti-thyroid treatment whereas 66.6% (n=433) of all patients completed 18 month-period of the therapy and 61.2% (n=256) of them were in remission by the following 1 year. Recurrence were detected in 38.8% (n=168) of the patients and they were all treated with RAI (72%, 121/168) and surgery (28%, 47/168). Recurrence was found in 26.6% of all (n=77) who took PTU whereas 25.3% of them (n=91) who took MMI medication which there was no difference in terms of recurrence between agents ($X^2=0.136$, $p=0.712$) (Table 3).

Table 3. Recurrence proportions in the GD patients who were given anti-thyroid medications

| Recurrence | MMI (n, %) | PTU (n, %) | Total (n, %) |
|------------|------------|------------|--------------|
| No | 269 (74.7) | 213 (73.4) | 482 (74.2) |
| Yes | 91 (25.3) | 77 (26.6) | 168 (25.8) |
| Total | 360 (100) | 290 (100) | 650 (100) |

There was not difference between gender in terms of developing recurrence (30.2% of males (n=55) and 24.1% of females (n=113) who had recurrence, $X^2=2.523$, $p=0.112$). 14.9% of the patients (18/121) treated with RAI were given second RAI. %14.6 of all (95/650) underwent surgery (Figure 1).

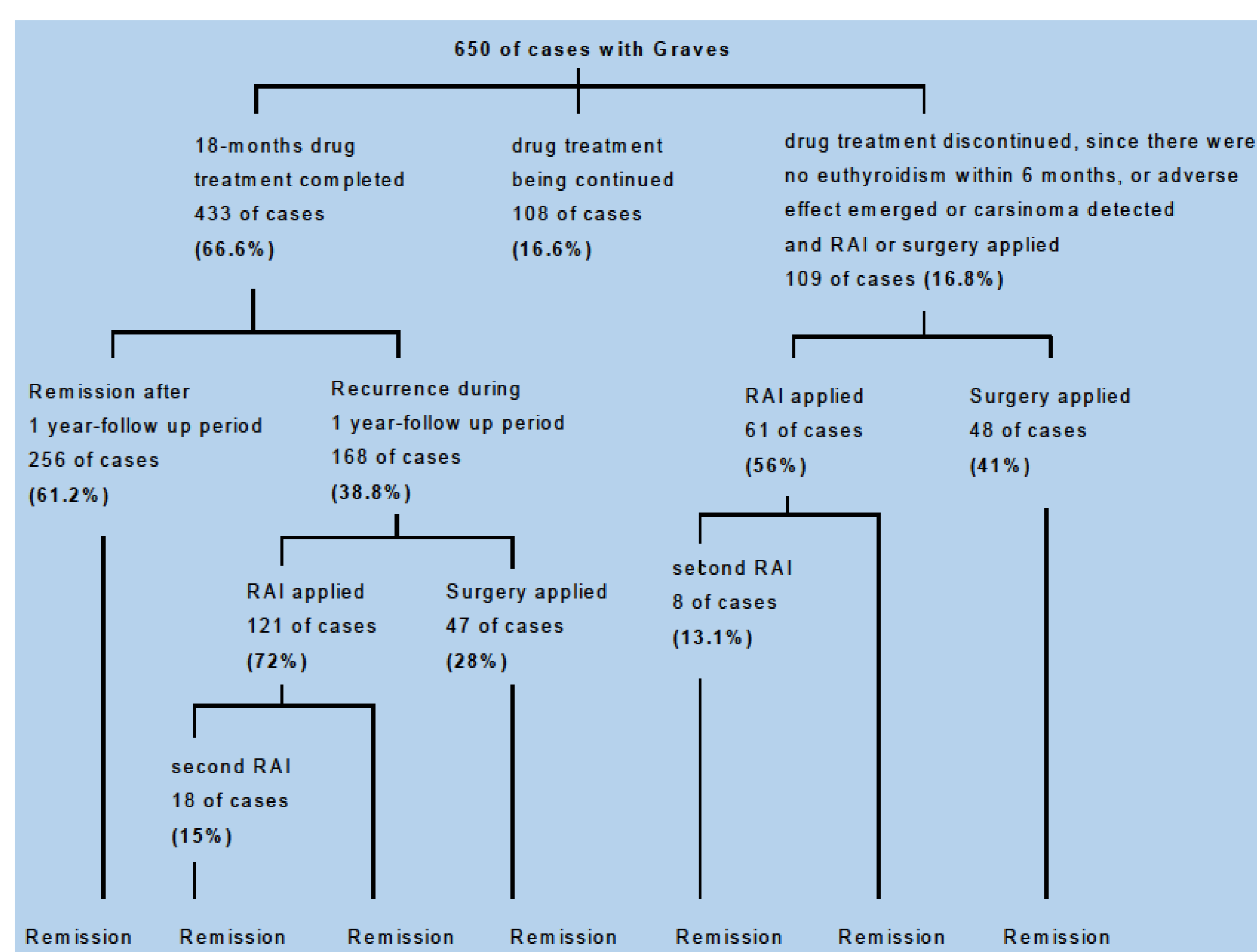


Figure 1. The patients with GD and their features of this study

Conclusion

Remission rates of medical treatment were high although minor and major adverse drug reactions were seen in the treatment of GD. We could not detect difference in terms of adverse effects of MMI and PTU. They could be used safely.