Analysis of the drugs consumption for hyperthyroidism in Republic of North Macedonia for the period of 2016-2019

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Introduction

Hyperthyroidism (Thyrotoxicosis) is characterized by hypermetabolism and elevated serum levels of free thyroid hormones (thyroxine [T4] and triiodothyronine [T3]) from the thyroid, caused by thyroid stimulators in the blood or by autonomous thyroid hyperfunction. It can also result from excessive release of thyroid hormone from the thyroid without increased synthesis. The most common causes overall include: Graves' disease, Multinodular goiter, Thyroiditis, Single, autonomous, hyper functioning "hot" nodule.

Graves' disease (toxic diffuse goiter), the most common cause of hyperthyroidism is caused by an autoantibody against the thyroid receptor for thyroid-stimulating hormone (TSH); unlike most auto antibodies, which are inhibitory, this autoantibody is stimulatory, thus causing continuous synthesis and secretion of excess T4 and T3 (Mc Dermott et al., 2020; Reid et al., 2005).

Treatment of hyperthyroidism depends on cause but may include: reduction of hormone secretion by receiving appropriate antithyroid drugs methimazole or propylthiouracil, beta-blockers, iodine, radioactive iodine and surgery which is indicated for patients with Graves disease whose hyperthyroidism has recurred after courses of antithyroid drugs, patients who cannot tolerate antithyroid drugs, patients with very large goiters, and in some younger patients with toxic adenoma and multinodular goiter.

Surgery includes a total thyroidectomy for Graves disease GD and a thyroid lobectomy for toxic adenomas.

The most commonly used drugs for the treatment of hyperthyroidism in Republic of North Macedonia (RNM) are: propylthiouracil, methimazole, thiamazole, and carbimazole. The dosage is individual, depending on the severity of the decease (De Leo et al., 2016; Kravets, 2016).

Market analysis and monitoring of the drug consumption for the treatment of hyperthyroidism in the country could provide valuable data for the possibilities of effective treatment of these patients and serve as a base for influencing health policies to improve the existing condition. (Francis et al., 2020).

Materials and methods

In order to achieve the set goals, we reviewed relevant literary data from primary, secondary and tertiary literature, the recommendations of Evidence-Based Medicine, official data from world and domestic drug registers and the published reports for drug consumption covered by the Health Insurance Fund of RNM. For analysis of the drug consumption for hyperthyroidism in the pharmacies of RNM for the period 2016 to 2019 were used the data published on the official website of the Health Insurance Fund by number of realized prescriptions and total paid amount per drug covered by the Fund. We used a descriptive method in data processing

Results and discussion

According to the results obtained from literature review, the most suitable treatment option is Carbimazole

combined with beta-blockers as an adjuvant therapy (Abbara et al., 2020). The most widely used beta-blockers are Propranolol and Bisoprolol (Liu et al., 2017).

The antithyroid drug Carbimazole can be combined with thyroxine if euthyroid condition cannot be achieved on other way. Although Carbimazole is recommended for antithyroid treatment by Evidence-based medicine, still is not present on the Macedonian market and is not on the drug List for which costs are refund by the Health Insurance Fund. The most reasonable cause is probably limited financial resources of the Fund, the program activities budgets, and the small purchasing power of the patients.

Two drugs have been approved for the treatment of hyperthyroidism in RNM: propylthiouracil 50mg and 100mg in tablet form, thiamazole 20mg in tablet form and film-coated tablet.

In terms of the consumption of drugs for hyperthyroidism, the analysis was made through the number of realized prescriptions from the pharmacies that have concluded an agreement

with the Fund. In terms of the number of realized prescriptions in the period from 2016-2019, a total of 14,591 prescriptions of the drug Propylthiouracil 100mg, 37,522 prescriptions of Propylthiouracil 50 mg and 84,025 prescriptions Thiamazole 20 mg were issued. In 2016, the total number of realized prescriptions for Propylthipuracil 100 mg is 3823 with total paid amount of 1 604 594 denars, for Propylthiouracil 50 mg is 10 051 with amount of 1 432 435 denars and for the drug Thiamazole 20 mg the number is 21 197 with total paid amount of 1 480 460 denars. In 2017 there is a small decline in the number of issued drugs, so, of Propylthiouracil 100 mg 3756 recipes were realized with total amount of 1 576 482 denars, of Propylthiouracil 50 mg 9247 recipes were realized and 1 318 399 denars were paid by the Fund and for Thiamazole 20 mg the total number of issued prescriptions is 20 016 with total paid amount of 1 397 994. In 2018 also a decline in number of realized recipes for Propylthiouracil 100mg and Propilthiouracil 50 mg is observed, which is 3566 and 8963 with total paid amount of 1 496 664 and 1 277854 denars. However, for Thiamzole 20 mg significant growth in the number of issued prescriptions is observed which is 21 476 with total paid amount of 1 500 305 denars. Continious decline in the number of prescriptions of Propylthiouracil 100mg can be noted also in 2019 which is 3466, with total paid amount of 1535 321 denars. The total number of prescribed recipes for Propylthiouracil 50 mg in 2019 is 9261 (total paid amount 1 400 585 denars) and for Thiamazole 20 mg is 21 336 (1 422 962 denars). This significant change in prescribed trend/habits for the drug Propylthiouracil is probably due to the fact that its consumption is reduced globally because Propylthiouracil

is not recommended by EBM for treatment of hyperthyroidism.

Conclusion

According to the reviewed databases for the treatment of hyperthyroidism, seven drugs recommended in the world, including three iodine preparations. The two preparations recommended by the Evidence- based medicine are not registered in the RNM, and two other generic drugs with a long history of existing are in use. The recommended therapy by Evidence-based medicine is not available in RNM, so the lack of innovative therapies and a wider selection of generic drugs on the market of the RNM in the treatment of hyperthyroidism greatly limit the doctor's possibility for choosing and introducing new treatments. The number of total drugs prescribed for the thyroid disease treatment on prescriptions is constantly increasing, which is probably due to the increasing number of diagnosed patients with impaired thyroid function.

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