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Antithyroid Drug-Induced Agranulocytosis

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Antithyroid Drug-Induced Agranulocytosis

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Introduction

We live in a culture that is busy and constantly on the go. With little time to spare, often symptoms of an alteration in bodily function are pushed to the side and attribute to the stress of everyday life. With symptoms including nausea, fatigue, weight loss, nervousness, and irritability, one may be more inclined to disregard these symptoms, only to attribute them to effects of a busy lifestyle. The presentation of the previously listed symptoms can formulate a medical diagnosis of hyperthyroidism. According to the American Thyroid Association, 20 million Americans will develop some type of alteration in thyroid function throughout their lifetime, and 60 percent of those individuals will go undiagnosed. When a diagnosis is given, drug treatment options are limited. The two most common drug therapies include Propylthiouracil and Methimazole (Rosove, 1977). Although drug therapies are beneficial in the treatment of hyperthyroidism, adverse affects from drug therapy can occur. A more serious adverse affect of drug therapy would be Agranulocytosis. Agranulocytosis is condition in which the bone marrow is not producing adequate amounts of neutrophils. With hyperthyroidism, the prescribed antithyroid drug therapy, suppresses the bodies ability to produce mature white blood cells, causing a drug-induced agranulocytosis. "Propylthiouracil and methimazole are used widely in the treatment of hyperthyroid disorders. The most important complication of the use of these drugs is depression of the neutrophilic granulocyte count.

Granulocytopenia occurs in about 4 percent and agranulocytosis occurs in about 0.3 percent of treated patients. Although this depression of the granulocyte count is reversible after the drug is discontinued, serious infection frequently accompanies agranulocytosis and accounts for almost all deaths related to the drugs (Rosove, 1977)."

With such an abundant amount of Americans suffering from thyroid dysfunctions, it is important to provide ample education to patients on the adverse effects of antithyroid treatment, with the desire to prevent the development of agranulocytosis, as well as minimize their risk of infection from opportunistic pathogens. This particular topic sparks my interest due to my personal health. Two years ago, suddenly began feeling anxious, experiencing tremors, nauseated, and extreme fatigue. I proceeded to disregard my body, only attribute these symptoms to the effects of being a night shift nurse, and not being able to always take a lunch break. I continued to disregard the symptoms, until one day I noticed my clothes began to fit more loosely and proceeded to experience a 40 pound weight loss. The extreme weight loss had occurred over a 50 day period. I immediately notified my primary care physician, numerous labs were drawn, eventually leading to the diagnosis of Graves' disease. After being diagnosed with Graves', I was prescribed 10 mg of methamazole three times daily. My doctor stated that if I began experiencing a sore throat to immediately notify the office and discontinue to the medication until further evaluation with no further explanation as to why the stated symptoms had any importance. I began researching immediately, only to find that, while uncommon, taking an antithyroid drug therapy could lead to dysfunction in the production of white blood cells, causing agranulocytosis.

Case Study

A 32-year-old female presenting to the unit with a history of Graves' disease. Presenting symptoms included: fever, tonsil enlargement with noted white secretions, thyroid enlargement, and anemia. Patient has been prescribed 15 mg of methamazole, which she had been taking for 42 days. Diagnostic testing shows a throat culture with moderate G⁻ bacilli and G⁺ cocci. Patient was then treated with broad-spectrum antibiotics, vancomycin, cefoperazone sodium, and sulbactam sodium. After approximately 10 days of treatment, the patient's labs began to worsen showing: globulins 56 g/ L, leukocytes 0.6 × 109/L, neutrophils 0 × 109/L, platelets 20 × 109/L, hemoglobin 97 g/dL. On approximately day 17, the patient's condition starting to improve with a noted decline in temperature, blood cultures with results of granulocytes > 1000, platelets > 50,000, bone marrow with increased nucleated cells and myeloid hyperplasia (Xiao, Li, You, Qian, Wei, 2014).

Signs and Symptoms

Signs and symptoms of thyrotoxicosis requiring drug therapy, predisposing one to experiencing agranulocytosis, are often symptoms that one may experience on an every day basis. Signs and symptoms include: thyroid eye syndrome, sweating, goiters, tremors, nervousness weight loss palpitations, however elderly patients will display minimal signs and symptoms. Labs results will show an elevated FT4, FT3, and a suppressed TSH (Kobayashi, Noh, Mucosa, Kuna, Watanabe, et.al. 2014). With the incidence of agranulocytosis being rare, education on the presenting signs and symptoms is often overlooked. Agranulocytosis most commonly occurs within the first few months of initiating treatment, with a higher frequency in female patients greater than 65 years of age (Nakamura, Miyauchi, Natsukp, Imagawa, 2013). A patient that is experiencing agranulocytosis may remain asymptomatic with the only indicator being a low white blood cell count. However, individuals with presenting symptoms commonly include oropharyngeal infections, cervical lymphadenopathy, odynophagia, malaise, and an elevated temperature. The appearance of agranulocytosis presents in the elderly as sepsis, skin infections, and pneumonia (Laurberg & Cooper, 2015).

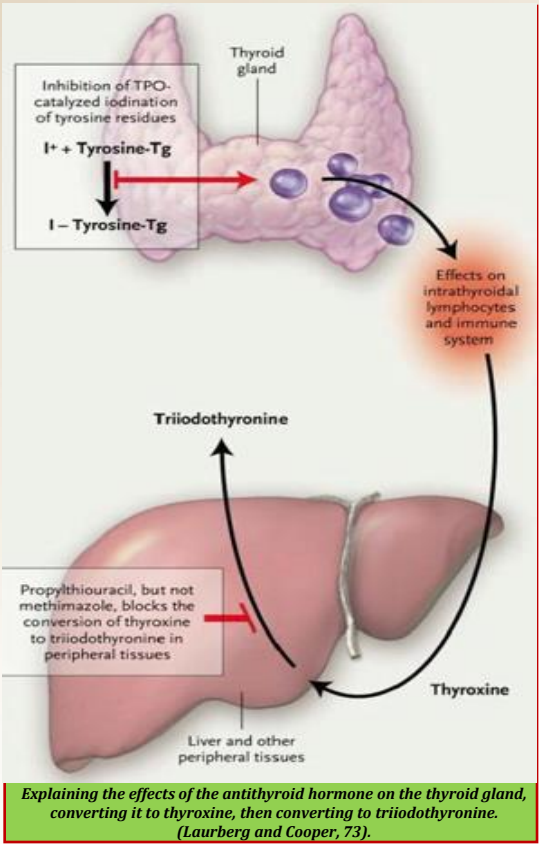


TABLE 3. Comparison of the incidence of side effects between the MMI 30 mg/d regimen and the PTU 300 mg/d or MMI 15 mg/d regimen

	n	No. of total incidences (%)	No. with changed medication (%)	No. with hepatotoxicity (%) ¹	No. with skin eruption/urticaria (%)	No. with leukocytopenia (%) ²	No. with other (%) ²
MMI 30 mg	130	39 (30.0)	28 (21.5)	9 (6.6)	29 (22.3)	0 (0)	1 (0.7)
PTU 300 mg	104	54 (51.9)	39 (37.5)	28 (26.9)	23 (22.1)	5 (4.8)	0 (0)
P value (χ ²)		0.0014	0.0074	<0.0014	0.972	0.0164	
MMI 15 mg	137	19 (13.9)	10 (7.3)	9 (6.6)	9 (6.6)	1 (0.7)	0 (0)
P value (χ ²)		0.0014	0.0014	0.908	<0.0014	>0.999	

¹Elevation of AST and ALT more than double the upper range of the normal standard.

²n less than 1000/d.

Study showing the incidence of granulocytosis with two different types of antithyroid treatment. (Nakamura, H., Miyauchi, A., Miyawaki, N., Imagawa, J. Table 3).

Underlying Pathophysiology

As suggested in the case study, there is an instance in which bone marrow suppression can occur. The suppression of bone marrow occurs in agranulocytosis with the development of pancytopenia. When pancytopenia occurs, studies suggest it is coupled with aplastic marrow, which affects only the granulocytes. The granulocytes will shift to the left, causing a decrease in mature cells. This causes cytoplasmic swelling and irregularity in staining (Rosove, 1977). The underlying cause of agranulocytosis in antithyroid drug treatment has yet to be definitively pinpointed. Many theories suggest that the drug gains entry through the bone marrow where levels are to accumulate within the leukocytes exceeding the volume of plasma. With leukocyte involvement, the utilization of glucose and oxygen is affected, showing a change in granulocytes and oxygen consumption. The higher level of the antithyroid affects the cellular level which extend through the erythroid cells. The leukocytes continue to be affected by antithyroid drug therapy, showing a decrease in the activity in nicotinamide adenine dinucleotide, granule bound nicotinamide adenine dinucleotide phosphate; therefore, decreasing the plasma membranes ability to fight off and engulf microorganisms (Rosove, 1977.)

Significance in Pathophysiology

The significance of the pathophysiology is important to practitioners and registered nurses because of the possibility of suppression of bone marrow and the ability of the antithyroid drug to engulf cells. This limits one's immune response and ability to fight off infection. When a patient is prescribed treatment for hyperthyroidism, it is imperative to monitor for early signs of medication reaction. If a fever, gingivitis, or sore throat develops, therapy should immediately be discontinued. If symptoms are not identified at onset, opportunistic pathogens can enter the body leading further suppression of bone marrow and agranulocytosis, putting the patient at risk to become severely immunocompromised (Rosove, 1977.)

Implications in Nursing Care

Acute Medicine & Surgery identified and plan of treatment in hopes of minimizing the occurrence of adverse affects of anti-thyroid drug treatment. Some recommended methods include supportive care and identifying precipitating factors. With the occurrence of agranulocytosis there is a possibility for fluid loss due to the occurrence of a fever and infections. Giving IV fluid is important to replace electrolytes and fluid volume loss. As nurses and providers, it is important to monitor the patient's intake and output in hopes of preventing a fluid deficit. Identifying precipitating factors can be done in a variety of methods. As previously stated, agranulocytosis occurs predominately in elderly females with the presentation of sepsis. By monitoring temperature, heart rate, and blood pressure for acute changes, it will allow for prevention and early diagnosis. Other diagnostic tests recommend including sputum cultures with complaints of a sore throat, and chest radiographs, as well as, monitoring the patients WBC with each visit (Idroze, 2015; Tajiti & Noguchi, 2005). Finally, as nurses we act as the last line of defense for our patient it is important to provide education. By educating patients on anti-thyroid drug treatment, adverse affects, and precipitating signs and symptoms, we as a profession can continue to limit the number of patients experiencing agranulocytosis.

Conclusion

Large amounts of Americans are experiencing symptoms of thyroid dysfunction and go undiagnosed. The symptoms are what can be attributed to stress of everyday life. Once diagnosed, individuals are often unaware of the harmful effects of anti-thyroid drug therapy. Although rare, agranulocytosis is a harmful side effect, which can lead to series infections and even death. By making patients aware of the adverse affects and monitoring blood counts, the occurrence can continue to be low.

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