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Role of plasmapheresis in thyrotoxicosis: A review

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Abstract

In clinical practice, thyroid storm and severe thyrotoxicosis continue to rank among the most common endocrine emergencies. The goal of hyperthyroidism treatment is to achieve a euthyroid state as soon as possible and to maintain euthyroid status. Treatment options include surgery, radioactive iodine, and anti-thyroid medications (ATDs). When euthyroidism needs to be achieved quickly due to thyrotoxicosis and there are significant adverse effects to ATDs, plasmapheresis is a quick, dependable, and effective therapy option. Published literatures were reviewed for the role of plasmapheresis in thyrotoxicosis patients to provide immediate reduction of thyroid hormone due to severe hyperthyroidism, adverse effects of ATDs, and ineffectiveness of ATDs or non-thyroid surgery. The published literatures showed that around 80-85% of the cases were given diagnoses of Graves' disease. The average number of therapeutic plasma exchange (TPE) sessions was 4-6, although maximum reduction of hormone was achieved in the first session rather than in subsequent sessions. TPE was associated with a 50 to 60 percent reduction in thyroid hormone levels. After plasmapheresis, total thyroidectomy, radioactive iodine (RAI), and other medical therapy were given. Based on the literature review, we conclude that plasmapheresis therapy is a quick, dependable, and efficient treatment option for patients unable to use ATDs due to their side effects and those whose hyperthyroidism does not improve with these medications. Plasmapheresis is also effective for those who need to achieve rapid reduction of thyroid hormone prior to total thyroidectomy, RAI, or non-thyroid emergency surgery. The expense of plasmapheresis and the requirement for highly specialized resources are its limitations. *[J Assoc Clin Endocrinol Diabetol Bangladesh, January 2022; 1 (1): 24-26]*

Keywords: Thyrotoxicosis, Apheresis, Therapeutic plasma exchange, Thyroid hormones

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Introduction

Endocrine and metabolic emergencies are rather common in acute care medicine worldwide.[1] Thyrotoxicosis is a clinical state that results from inappropriately high thyroid hormone action. In hyperthyroidism, there is increased synthesis and secretion of thyroid hormones by the thyroid gland. One of the most frequent endocrine emergencies is severe thyrotoxicosis.[2] Symptoms such as weight loss, irritation, anxiety, heat intolerance, sweating, muscle weakness, and palpitation are caused by a high level of thyroid hormone in the blood.[3]

The most frequent causes of hyperthyroidism are Graves' disease (GD), toxic multinodular goiter (TMNG), and toxic adenoma caused by autonomous nodules. The treatment of hyperthyroidism varies according to its etiology. Literature suggests about 60-70% of patients with thyrotoxicosis are female. In around 80-85% of thyrotoxicosis, the underlying diagnosis is GD. Treatment options for GD are anti-thyroid drugs (ATDs), radioactive iodine (RAI), and surgery. ATDs are required to make patients euthyroid and prepare for permanent treatment. RAI or surgery is the only permanent treatment option for

toxic adenoma (TA) and toxic multinodular goiter (TMNG). The side effects of these medications, however, can be fatal and include agranulocytosis, cholestatic hepatitis, toxic hepatitis, and vasculitis.[4-6] Standard therapies including thiamazole, nonselective beta-blockers, and corticosteroids are required to treat the acute phase. In order to restore euthyroid hormone levels in patients with severe hyperthyroidism, further therapies are required. Since the 1970s, therapeutic plasma exchange (TPE) has been suggested as an alternate treatment for hyperthyroidism.[7-9]

Plasmapheresis in thyrotoxicosis

Plasmapheresis is the procedure, that involves replacing the patient's plasma with albumin or fresh frozen plasma (FFP) and, through this procedure, large molecular-weight substances, autoantibodies, immune complexes, and thyroid-binding globulins are eliminated from the blood.[10] This method effectively removes thyroid-binding globulins, cytokines, and catecholamines from the patient's serum.[10-11] Plasmapheresis is a promising and reliable therapeutic approach to lower blood thyroid hormone levels when ATD is insufficient or cannot be used due to major side effects.[12] TPE is also a successful treatment option for amiodarone-induced thyrotoxicosis (AIT).[13]

The 2019 American Society for Apheresis (ASFA) guideline on indications for TPE classified the role of plasmapheresis in thyroid storm as category II, which includes disorders for which plasmapheresis is accepted as second-line therapy.[5] However, this guideline did not suggest plasmapheresis for patients with hyperthyroidism without thyroid storm.[11] Because thyroid crisis results in high amounts of thyroid-binding globulin, the Japanese Endocrine Society and Thyroid Association advises using FFP.[14]

Procedure of plasmapheresis

Only the intravascular compartment is used for plasmapheresis/TPE. The outcome and effectiveness of this treatment depends on some factors such as the amount of blood processed, the amount of plasma exchanged during each procedure, the number of procedures carried out, the frequency of exchange, the rate of cell mobilization, stabilization, and resynthesis.[15,16] In patients with thyrotoxic disease, albumin or FFP is utilized as a replacement fluid in TPE. FFP is used over albumin when choosing a replacement fluid because it contains all thyroid hormones(TH) protein transporters, and coagulation factors. Nevertheless, albumin is also advised as offering a greater number of low-affinity binding sites for THs.[17]

The average number of TPE sessions are usually 4-6 in every alternate day although maximum hormone reduction is achieved during the first session. TPE eliminates thyroid hormone from the blood to treat hyperthyroidism. TPE is associated with a significant reduction in hormone levels, FT3 (50-60%) and FT4 (40-50%). The removal of TSH receptor antibodies (TRAb) in people with GD, however, has the potential to cause a further drop in thyroid hormone levels. Leow advised a mathematical model based on differential equations to depict the kinetics of thyroid hormones and TSH. The model enables the plasma thyroxin level to rise quadratically in response to the rising level of TRAb. Therefore, it anticipates a much faster decline in serum THs after a treatment like TPE that eliminates TRAb from the blood than conventional anti-thyroid drugs, and clinical observations confirm these findings.[18] The amount of plasma to be extracted from each patient who chooses to undergo plasmapheresis is decided by the doctor based on the patient's clinical circumstances. Based on nomograms created using the patient's gender, weight, height, and hematocrit, the plasma volume is computed. Each time during the procedure, a replacement fluid with a volume of 1-1.5 times the estimated total plasma volume is used in TPE.[19]

Indication, contraindication, and side effects of plasmapheresis in thyrotoxicosis

Patients who are unable to use ATDs due to adverse effects, inefficiency, or those needed to commence quick effects such as thyroid storms are exposed to plasmapheresis. Plasmapheresis is performed on thyroid storm patients who have atrial fibrillation, pulmonary edema, jaundice, or seizures. After plasmapheresis, total thyroidectomy, RAI, and other medical therapy can be given. TPE is not recommended for thyrotoxic patients who are unable to tolerate central line placement, have sepsis, are hemodynamically unstable, are taking ACEi, or have hypocalcemia.[19] TPE carries risks, just like any invasive procedure. Bleeding, hematoma and infection due to catheter usage, coagulation, hypocalcemia, hypotension, transfusion responses, transfusion-transmitted illnesses, pulmonary edema, and/or pulmonary embolism are possible side effects.[15,16]

Conclusions

Large case series of thyrotoxicosis treated with therapeutic plasmapheresis are scarce. There are some limitations to published literatures as most of them are

retrospective in nature. There is a lack of guidelines regarding inclusion and exclusion criteria, time interval of blood collection after TPE treatment protocol, monitoring, and complications after TPE sessions. The main limitations to plasmapheresis are probably related to patient discomfort, the need for specialized resources, and their cost, which can be especially problematic in low- and middle-income countries. TPE is an effective, reliable, and safe treatment option that can be applied in cases where it is necessary to provide rapid reduction of thyroid hormones before permanent treatments, non-thyroid surgical procedures or to treat life-threatening thyrotoxicosis. It needs experience in application and follow-up and provides rapid reduction of thyroid hormones when performed in experienced centers. So, a study on the role of therapeutic plasmapheresis in thyrotoxicosis patients in Bangladesh is recommended in order to validate the use of plasmapheresis as a therapeutic intervention for these patients.

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Conflict Of Interest

The authors have no conflicts of interest to disclose

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