



## Therapeutic Plasma Exchange in the management of Impending Thyroid Storm: Experience from Bangladesh

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### Abstract

*Inappropriately treated impending thyroid storm can cause death to a patient. Therapeutic plasma exchange (TPE) is a good option to reverse this condition and help in the proper handling of the patient, though its indication not clearly defined. In this case report we share our experience of one case who was admitted in the department of endocrinology of BSMMU. The patients was diagnosed as a case of impending thyroid storm in which radio-iodine therapy could not be started as because of very poor clinical and laboratory report. Therapeutic plasma exchange was given in two sessions in one day interval by experienced medical staff and no complications. Main action of TPE is to remove the circulating putative antibodies, cytokines and thyroid hormones with their bound proteins. TPE has a brief effect and for this reason it should be connected with remaining thyroid blockers. When threatening symptoms arise TPE should be given as early as possible without hesitation and should not wait for effect of conventional treatment as because it rapidly improves the clinical conditions. We are also suggested to start TPE in a case of impending thyroid storm as because our study has proven the efficacy of TPE in the management of impending thyroid storm.*

**Keywords:** Endocrinology, Plasma exchange, Thyroid storm, RPM, Plasmapheresis.

### Introduction

Thyroid storm is the term by which we can realize the extreme expression of thyrotoxicosis. This is rare but consequential complications that materialize mostly in Graves' disease but also can occur in toxic multinodular goiter. Symptoms are usually, not always, precipitated by infection, trauma, surgical emergencies, withdrawal of anti-thyroid medications, operations (particularly thyroidectomy), radiation thyroiditis, diabetic ketoacidosis, severe emotional stress, cerebrovascular disease, use of tyrosine-kinase inhibitors, toxemia of pregnancy, or parturition.

Amiodarone-mediated thyroid storm is more frequent in less iodine geographic areas. Crises are often sudden in patients who have pre-existing hyperthyroidism which was relatively or untreated. Burch and Wartofsky has created a scoring system that help regulate its diagnosis by using its body temperature, central nervous system involvement, gastrointestinal-hepatic dysfunction, heart rate, and presence or absence of congestive heart failure and/or atrial fibrillation. The clinical picture is one of severe hypermetabolism: fever (may be > 40°C), marked tachycardia and arrhythmias, potentially with

congestive heart failure, trembling and agitation, delirium with or without psychosis, vomiting, abdominal discomfort, and, as the disorder headway, lack of interest, daze, and coma. This clinical picture in a patient with a history of pre-existing thyrotoxicosis, with goiter or exophthalmos, is sufficient to establish the diagnosis, and exigency management should not await for laboratory confirmation. There is no serum T3 or T4 concentration that discriminates between severe thyrotoxicosis and thyroid storm. If unrecognized, the condition may be fatal; mortality is 10–30% even with treatment. The most agreed upon pathogenesis is the presence of both larger availability of adrenergic receptors and a reduction of thyroid hormone binding to thyroid hormone binding globulin (TBG) result in leaking catecholamines to precipitate thyroid storm.

TPE is restrained for the patients who are suffering from thyroid storm or impending thyroid storm with critical symptoms and also where first-line therapies fail. It can also be used where toxicity impaired conventional therapies like as leukopenia due to PTU. Since a portion of T3 and T4 is firmly bound to plasma proteins, TPE should, in theory, efficiently reduce their circulating pool. While the literature contains conflicting reports, most patients had a decrease in the hormone concentrations. In one report, TPE increased the elimination of total T4 approximately 30-fold compared with standard medical treatment. This effect was dependent on the T4 serum level, suggesting earlier TPE is more efficient. In amiodarone mediated thyrotoxicosis, TPE is also used for reducing amiodarone plasma concentration, which has a half-life of months in patients on chronic therapy. TPE in this condition is particularly indicated for patients who have no underlying thyroid disease and develop a drug-induced destructive thyroiditis. The therapeutic benefit of TPE can also result from removal of potential substances from the thyroid storm such as autoantibodies (Graves' disease), catecholamines (released by the sympathetic system), and cytokines. In rare cases, TPE is used

to render the thyrotoxicotic patient euthyroid prior to thyroidectomy. TPE effect is transient and hormone levels typically rise again the next few days.

### Patients and Methods

A 45 year old female was admitted in the department of endocrinology of BSMMU with high grade of fever for 29 days with chills and sweating. She had a history of palpitation with tremor and weight loss of limb associated with oligomenorrhoea 1 year back. Then she was diagnosed as a case of Graves thyrotoxicosis and Carbimazole 5mg was given for this reason. After taking 6 months of this medication she stopped it when symptoms resolved and remain well for next 5 months. Then again symptoms reoccur and again carbimazole was started for 3 months. She had stopped the medication repeatedly. After that fever arose and vomited for several times. She got repeated blood transfusion due to anaemia. She also got granulocyte colony stimulating factor for treating agranulocytosis. On admission to the department of BSMMU she was diagnosed as case of Graves disease with Aneamia under evaluation with Agranulocytosis. After admission, echocardiography was done which is given in box 3. Thyroid hormone status and clinical situation implies that Burch and Wartofsky score was about 41. That means patient was in a state of impending thyroid storm. Logos iodine could not be started as because of high thyroid hormone status. TPE was considered at that time due to the expectation of rapid response. TPE was given by MCS+ 900 made in USA by using PBSC Set (125 mL Latham) that is made in Malaysia. Anticoagulant Solution ACD-A (REF 0426X-00) was used.

### Result

Repeat thyroid hormone status was sent just after procedure which is stated in box 2. Remarkable amount of FT4 was decrease in that sample. Tachycardia and respiratory difficulties were diminished after completion of TPE. Fever was

subsidied day after the procedure. Patient clinical condition was gradually improving after 1 session of TPE and Radio Iodine therapy was given after 3 days. Patient was monitored very keenly after

Radio iodine therapy. She can move by on her feet after few days and appetite was improving. She was discharge from the hospital after 10 days as she was fit for her daily routine activities.

### Box-1

Name	01/06/2017	15/05/2018	21/05/2018	24/05/2018	27/05/2018	05/06/2018
Hb (g/dl)	12.80g	12.10	9.20	7.80	7.90	6.5
ESR	32	80	110	120	130	110
RBC (million/cmm)	4.58	4.49	3.46	2.92	3.01	2.48
WBC (cell/cmm)	6700	1000	1500	2000	2900	1500
Platelet (cell/cmm)	2,00,000	1,80,000	1,80,000	1,80,000	1,80,000	2,00,00

### Box-2

Date	FT3	FT4	TSH
31/05/2017	10.12(pg/ml)	-----	0.05(mlU/l)
09/05/2018	9.8(Pmol/L)	32.5(Pmol/L)	0.1(mlU/l)
01/06/2018	18.57(pg/ml)	4.43(ng/dl)	0.015(uIU/ml)
13/07/2017		1.17(ng/dl)	

### Echocardiography Report

- No RWMA
- Good biventricular systolic function
- Mild MR
- Mild AR
- Mild PR with mild Pulmonary HTN
- PASP-40mmhg

### Discussion

In plasma higher concentration Tyroxine (T4) has been found. It generated basically by the thyroid; triiodothyronine (T3) is secreted mostly (about 80%) from the peripheral tissues after deiodination of T4. T4 bound about 68% to the thyroxine binding globulin (TBG), about 11% to transthyretin, and also 20% to albumin. T3 is bound 80% to the TBG, 9% to the transthyretin, and remaining 11% to the albumin<sup>[1]</sup>. This substantial protein mandatory aids for the excretion of thyroid hormones during TPE<sup>[2]</sup>. One of extracorporeal blood transfusion technique is TPE, it basically used for abolish the large molecular substances mainly from the plasma<sup>[3]</sup>. In comparison with dialysis that may lucid protein bound material, TPE can abolish protein bound substances<sup>[4]</sup>. TPE is a process that includes patient's blood progress thorough a specified

medical kit that separate circulating plasma when fixed RPM maintain and separated plasma can easily be collected externally. After that separated plasma can be replaced by 5% albumin and isotonic fluid. TPE can removes thyroid hormones from circulation that are protein bound; colloid solution used to restore the plasma that dispense new binding position for the thyroid hormone that are separated throughout the next TPE session<sup>[5]</sup>. Excluding thyroid hormones, TPE may also help in the separation of the cytokines, deiodinase enzyme, and Graves' antibodies that augment furthe in resolving of thyrotoxicosis besides also of Graves' ophthalmopathy<sup>[2]</sup>. Human albumin has upper hand of having a greater pool of low accord irrevocable sites for the thyroid hormone<sup>[6]</sup>. TPE was first used in 1970 in the case of thyroid storm by Ashkar et al<sup>[7]</sup>. Jha et al. has reported a case of thyroid storm that secondary to the imprudent expenditure the thyroid supplements that successfully treated with TPE. TPE also useful in patient who has taking large supplements for about six days making the use of the gastric decontamination and also cholestyramine less useful<sup>[3]</sup>. Lew et al. first used double filtration plasmapheresis (DFPP) patient suffering from Graves' disease requiring surgical debridement.

DFPP is a procedure in which plasma firstly separated from circulation after large molecules likely immunoglobulins and lipoproteins are separated. This has a advantage of removal of lesser amount of coagulation factors that makes after surgery more beneficial<sup>[8]</sup>. Koball et al. first used a single pass albumin dialysis (SPAD) in patient that had no clinical benefit after two sessions of plasmapheresis.

According to American society of apheresis (2016) use of TPE in the management of hyperthyroidism as category III that illuminates the role of TPE has not yet established in the treatment of thyroid storm. The recommended frequency of treatment is daily to once in three days till clinical improvement is noted<sup>[9]</sup>. TPE in the management of impending thyroid storm when usual treatment not effective or contraindicated. Drawbacks of TPE include chance hemodynamic instability, episodes of hypocalcaemia and the risk of infections.

The benefit of TPE specially therapeutic one is to removal of the likely pathological substances from the impending thyroid storm like as hormones, autoantibodies produced in Graves' disease), catecholamines secreted by the sympathetic system, cytokines that mediates inflammation, toxins substances and so on. The metabolically vital portion of the hormones is free, but more than 99.5% of T4 (Thyroxine) and T3 (Triiodothyronine) are bound in the circulating serum. TBG attached with circulating hormones about 80% (49); albumin attached about 10% with T4 and 20% with T3 (33). This procedure diminishes the out-run of thyroid hormones by detaching the free thyroid hormones. Furthermore by restoring carrier proteins with unsaturated bound proteins of the substitution solution. However TPE has to be related with a supplement treatment to hold the amalgam of such components.

Our study showed that thyroid hormones have In our observations, thyroid hormone levels have a likelihood to increase again in the day after TPE Some cases has showed that the FT3, FT4, and

TSH not decreases after the procedure and may chance of even increase<sup>(11,12)</sup>. This phenomenon is given an explanation by mobilization effect occurred from the extravascular compartment. It creates the initiation of a new symmetry between free and intracellular rates<sup>(13)</sup>. However, even if the T3 and T4 concentrations stay high, clinical advancement may be seen<sup>(14)</sup>.

TPE ameliorate the clinical manifestations (frequently cardiac ones) in the thyroid storm rather than lowering the thyroid hormone rates<sup>(15)</sup>. Kokuho et al. described their experience in a woman who was in thyroid storm state which was impervious to methimazole, Lugol's solution, propranolol, and digoxin. Because she had higher body temperature and also tachycardia, TPE was done immediately. In that case cardiac rhythm was controlled and fever spike diminished<sup>(10)</sup>.

Few reports have narrated the failure of TPE for controlling thyroid storm in various cases like as Graves' disease, amiodarone-induced thyroid storm, or hormone overload<sup>(17,18,19-21)</sup>. TPE has shown to be inefficient in Henderson et al.'s study that study was done hormone overload that revealed TPE could washed out only 7% of the ingested dose<sup>(19)</sup>. Samara et al.'s showed that renal and hepatic impairment could have cavorted a role in failure of TPE<sup>(20)</sup>.

TPE should be done early as possible for obtaining maximum therapeutic benefits. When treating a thyroid storm, we proposed to use the Burch and Wartofsky score<sup>(21)</sup>. When it is higher than 45, to predict early use of TPE in preliminary stage the disclosure of hazardous cardiac or neurological symptoms basically as retrogression is slow and may be insufficient in the latter. When the score is below 45, usual therapies can be tried first.

### Conclusions

We conclude our study by giving emphasize on the efficiency and safety of TPE treatment in the management of impending thyroid storm. We also suggest that initiation of TPE in neurological symptoms presented with hyperthyroidism.

It also can be used when conventional treatment failed to produced response or contraindicated. In threatening symptoms, the effectiveness of traditional management should not be awaited, as because TPE is the trusted and fastest method to ameliorate the patient's clinical state. TPE also benefitted in amiodarone induced pathology. As because of transitory effect TPE, it can be done in several session that can used in also with other thyroid hormone antagonists. Moreover it is safe therapy, though it also associated with higher cost than conventional one. Randomized control study is needed to declare the usefulness of initiating treatment earlier.

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