EFFICACY OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL THERAPY IN THYROID STORM PATIENTS WITH CARDIOVASCULAR COMPLICATIONS : LITERATURE REVIEW

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ABSTRACT

Tyroid storm is a life-threatening with clinical manifestation of thyrotoxicosis can cause other organ dysfuntion such as cardiovascular disorders. Therefore, eary detection using Burch and Wartofsky Point Scale that treatment can be optimally. The purpose of literature review is examine the treatment used thyroid storm with cardiovascular complications and the effectiveness of therapy achieve eutiroid. The research use a qualitative method with a literature review design. Data collected from article, journal using keywords and based on inclusion criteria been used Google Scholar and Science Direct databases. The results of journal screening is five journal with case report design. Pharmacological treatment use thionamides, beta blockers, corticosteroids, and potassium iodide, The efficacy of therapy depending on the patients complications. Non-Pharmacological therapy plasmapheresis, is used if the patient is given pharmacological therapy and does not show a response after 48 hours of administration. The efficacy of plasmapheresis shows improved clinical effect and euthyroid state.

***Keywords**: Thyroid storm, Pharmacological, Non-Pharmacological, Eutiroid*

INTRODUCTION

Thyroid storms are critical in endocrine illnesses and are marked by fast deterioration, posing a heightened mortality risk (Chiha et al., 2015). This clinical manifestastion of thyrotoxicosis is characterized by elevated levels of T3 and T4 in peripheral tissues, potentially resulting in dysfunction of various organs, including the liver, gastrointestinal system, central nervous system, and cardiovascular system (Farooqi et al., 2023a).

Cardiovascular complication arise from elevated thyroid hormone levels in peripheral tissues, resulting in increased blood volume, enhanced diastolic function, and the peripheral vasodilatory impact of T3, prolonged peripheral thyroid hormone levels elevation may result in augmented left ventricular mass, left atrial enlargement, elevated pulmonary pressure, and diastolic dysfunction. Complication from thyroid storm within the cardiovascular system can be fatal, leading to extended hospital stays and heightened mortality rates (Cappola et al., 2019).

The prevalence of thyroid storm cases ranges from 0,2 to 0,76 per 100.000 individuals, annualy with 4,5 to 5,6 hospitalized patients per 100.000 yearly (Farooqi et al., 2023b). The fatality rate of untreated thyroid storms varies between 8% and 25% (Sam, 2023). Thyroid storm frequently arise in individuals with Graves disease or in those with a history of hyperthyroidism who are non-compliant with therapy. Thyroid storm results in death due to multiorgan dysfunctions, including congestive heart failure, respiratory failure, intravascular coagulation, gastrointestinal symptoms, cerebral damage, hypoxia, and sepsis (Farooqi et al., 2023a).

Thyroid storm should be addressed promptly to mitigate additional multiorgan complications by swiftly and precisely identifying them by applying the Burch Wartofsky Point Scale (BWPS). Clinical manifestations include fever diaphoreses, cardiovascular such as tachyarrththmia and heart failure characterized by reduced ejection fractions, and neurological symptoms including agitation, psychosis, convulsions, and coma (Sam, 2023).

Pharmacological therapy for thyroid storm involves administering thionamides to limit excessive thyroid hormone synthesis, beta blockers to mitigate adrenergic hyperactivity, and steroid to prevent conversion of T4 to T3 (Papi et al., 2014). Treatment of thyroid storm with organ dysfunction problems may hinder the attainment of a euthyroid state, necessitating appropriate and effective therapy (Isozaki et al., 2016).

LITERATURE REVIEW

Thyroid storm is an endocrine emergency that has posed diagnostic and therapeutic challenges since 1926 (Chiha et al., 2015). Thyroid storm is a complication of Graves disease characterized by heightened hyperthyroidism in patients with uncontrolled Graves disease or non-compliant therapy. Based on research (Azeez et al., 2022) show Graves disease is the most common caused of thyrotoxicosis and female predominance in thyrotoxicosis include the higher prevalence of autoimne disorders among females, the role of the female sex hormones and the rebound immune status in postpartum state.

Thyroid storm is an uncommon illness with a death rate that can reach as high as 25%. The clinical presentation of a thyroid storm exhibits organ decompensation with fever being nearly invariably observed (Soetedjo et al., 2024). Reported etiologies of thyroid storm include thyroid surgery, mycocardial infarction, heart failure, pulmonary embolism, cerebrovascular incident the use of medicines such as pseudoephedrine, amiodarone, iodine, diabetic ketoacidosis, hypoglycemia, and molar pregnancy (Chiha et al., 2015). Based on research (Elmenyar et al., 2023a) show that thyroid storm caused Graves disease (28%), hyperthyroidism or thyrotoxicosis (11,4%), drug-induced (11%), and nonspecific autoimmune thyroid disease (1%). Thyroid surgery is one of the causes of thyroid storm, based on research (de Mul et al., 2021) cases of thyroid storm of thyroidectomy incidences described ranging from 0% to 14% but evidence assessing the risk of thyroid surgery in thyroid storm is of insufficient quality.

The diagnosis of thyroid storm is based on a history of thyroid disease and specific clinical manifestations including fever, tachyarrhythmia, tachypnea, elevated blood pressure, tremor, nausea, and vomiting. Additionally, serum free T4 and free T3 levels are typically below normal, while serum

TSH levels exceed 100 mIU/L (Sam, 2023). Based on research (Elendu et al., 2024) show various diagnostic criteria and scoring system in thyroid storm such as the Burch Wartofsky Point Scale and the Japanase Thyroid Association criteria, Akamizu criteria but for thyroid storm patients with organ failure by the Burch and Wartofsky Point Scale (BWPS).

Cardiovascular disorders frequently associated with thyroid storms include organ dysfunction, Based on research (Yamakawa et al., 2021) evidenced by multiple studies indicating 96.8% incidence of arrhythmias in hospitalized patients, alongside clinical manifestations of tachyarrhythmias and heart failure. Some studies also show thyroid storm with cardiovascular complications such as tachycardia, atrial fibrillation and features of congestive heart failure (CHF), pulmonary edema, mois rales over more than half of the lung fiend and/or cardiogenic shock(Radhi et al., 2020). In research (Elmenyar et al., 2023a) presented with multiple organ failure of which the most common were heart failure 70%.

Cardiovascular organ dysfunction occurs due to the influence of thyroid hormones on the heart, myocardium, vascular tissue and can cause endothelial and myocardial dysfunction (Elmenyar et al., 2023b). Elevated thyroid hormone levels exacerbate preexisting cardiac dysfunction, resulting in significant complications such as congestive heart failure; therefore, prior assessment of serum FT4, FT3, TSH levels, ultrasound thyroid examination, standard 12 lead ECG, and monitoring of cardiac activity is essential in cases of underlying thyrotoxicosis (Raguthu et al., 2022).

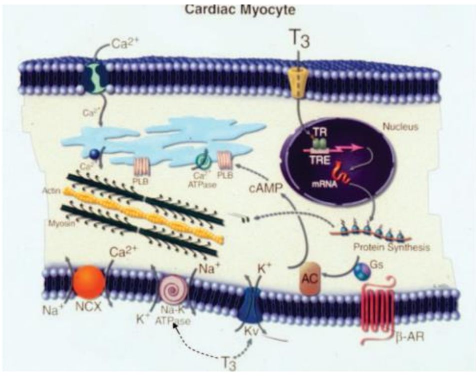

Figure 1
Genomic and Non Genomic Pathways

The subsequent mechanisms delineate the effects of thyroid hormones on intracellular cardiac function through genomic and non genomic. Thyroid hormone mediates genomic effects that affect the expression of genes encoding cardiac proteins. T3 interacts with TR within the nucleas of cardiomyocytes (Elmenyar et al., 2023b). Thyroid hormones especially T3 regulate cardiomyocytes cardiac contractility and ejection fraction (Yamakawa et al., 2021). Non genomic pathways encompass cardiomyocyte ion channels (Yamakawa et al., 2021) and the influence of thyroid hormones on peripheral circulation, which modulate hemodynamics and cardiac ejection fraction. Thyroid hormone exerts two primary non genomic effects on cardiomyocytes and several membrane ion channels such as Na^+, K^+, and Ca+ channels. Thyroid hormones influence cardiac mitochondrial function and modulate the condition and bioenergetic performance of the compromised myocardium (Yamakawa et al., 2021).

Thyroid crisis result in heightened cardiovascular risk factors. Hyperthyroidism elevates the risk of atrial fibrillation by 30-40% and heart failure, presenting clinical symptoms including chest pain, cardiac hypertrophy. Hypothyroidism correlates with hypertension and dyslipidemia (Azeez et al., 2022; Elmenyar et al., 2023b).

This critical situation necessitates enhanced treatments, encompassing diagnosis, and treatment to address uncompensated organ function in patients experiencing a thyroid storm. The severity of the disease can influence various treatment options and the patients prognosis in thyroid storm (Isozaki et al., 2016).

Based on description abone, a literature review was conducted to assess the treatment modalities for thyroid storm with cardiovascular complications and the efficacy of these therapies in achieving a euthyroid state, given the potential for increased mortality due to suboptimal management of organ dysfunction in the cardiovascular systems.

METHOD

Type of Research

The research is qualitative, employing a literature review design. The data collection utilized many literature sources, including books, journals, articles, and additional materials.

Data Collections

Data was gathered from many journals utilizing the Google Scholar and Science Direct databases, employing the search keywords "Management thyroid storm" AND "Management thyroid storm with cardiovascular problem". The data collection adheres to specific inclusion criteria to procure meticulously selected data pertinent to the research subject, specifically journals addressing the management of thyroid storm with cardiovascular complications that examine pharmacological and non-pharmacological interventions employed in treating thyroid storm with cardiovascular issues, detailing drug dosages and administration guidelines, and evaluating therapeutic success through patient condition improvement and attainment of euthyroidism. The selected journals are published between 2014 to 2024 and consist of original articles, cohort studies, observational studies, or case studies. The exclusion criteria for this study involved omitting journal articles that were not pertinent to the research issue, specifically the treatment of thyroid storms and other multiorgan problems, and excluding individuals whose treatments lacked specified dosages and usage guidelines for medications. Articles that were not entirely available. The journals utilized pertinent data regarding the research topic.

Data Selection and Analysis

The data selection method adhered to the inclusion criteria established during the collection of academic articles. The data analysis procedure comprised multiple stages, specifically the screening phase and a comprehensive examination of the journal section, encompassing the abstract, introduction, objectives, methodology, study results, discussion, and conclusions. After the screening phase, the journal data was aggregated and synthesized into a coherent literature review table.

RESULT

Based on the results of the journal search based on keywords and inclusion criteria used in the data search in this study, 5 journals were found that met the objectives of the study

Table 1. Result Analysis of The Selected Articles

Author	Subject-Age	Cardiovascular Complications	Types of research	Incident	LOS	Pharmacological Therapy	Non-Pharmacological Therapy
(Nathalia et al., 2023)	Subject 1: Ny. R (52 years)-Hyperthyroidism	Cardiomegaly, STEMI	Case Report	Indonesian	Day 4-Death	PO PTU 200 mg/6 hours, PO Propanolol 40 mg/8 hours, after cardioversi use doses 80 mg/8 hours//PO dexamethason 5 mg/12 hours	-
	Subject 2 Ny. SH (62 years)-Heart Disease	AF Rapid ventricular response, RBBB, iskemia miokard, cardiomegaly, pulmonary hypertension	Case Report	Indonesian	Day 5-get better	PO PTU 200 mg/8 hours, PO Bisoprolol 2,5 mg/24 jam	-
	Subject 3 Tn H (66 years)-medication nonadher	Cardiomegaly, AF RVR and Left ventricular	Case Report	Indonesian	Day 7-get better	PO PTU 200 mg/8 hours then improve doses 200 mg/4	-

	ence since 2018	hypertrophy				hours and day-4 use doses 200 mg/6 hours	
(Miller & Silver, 2019a)	Tn. X (50 years)-hyperthyroidisme	Atrial Fibrilition , Ejection Fraction 30%	Case report	Afrika - American	3 weeks (21 days)	Day-1 Metimazole 10 mg/8 hours as a substitute PTU then use improve doses Methimazole 20 mg/8 hours Day-2 Pottasium iodide solution 250 mg/8 hours Day-3; normal liver function use PTU : 200 mg/8 hours	Day-4 Plasmapharesis
(Sadiq & Chamba, 2021)	Ny. S (31 years) - goiter	Mitral Regurgitation Ejection Fraction 46%	Case Report	Tanzania	32 days	Carbimazole 15 mg/8 hours, propranolol 20 mg/12 hours, hydrocortison 100 mg/8 hours	-
	Ny. M (57 years) - goiter	Ejection Fraction 40%	Case Report	Tanzania	6 days	Carbimazole 5 mg/12 hours, propranol	

						ol 20 mg/12 hours	
(Yahya et al., 2023)	Ny. F (49 years) - goiter	Atrial fibriliation, Cardiomegaly	Case Report	Indonesian (Madura)	Refer to pain specialist	PTU 300 mg/6 hour, propanolol 20 mg/6 hours	
(Brown et al., 2020)	Tn C (23 years) - Graves disease	STEMI, Ejection Fraction 23%	Case report	Amerika Serikat	Day 7- get better	Propiltiourasil 200 mg/8 hours , pottasium chloride solution 250 mg/8 hours	-

DISCUSSION

In certain instances of thyroid storms examined in the reviewed studies, patients diagnosed with thyroid storms with a history of thyroid problems, specifically hyperthyroidism, nodules (goiter), and Graves' disease have either utilized medications or medication nonadherence. These risk factors are triggers for causing thyroid storm. Graves disease and nodular goiter/mumps for the majority of thyrotoxicosis cases. Graves' disease occurs in 80% of cases because it can induce thyrotropin receptor antibodies that stimulate thyroid hormone receptors (Yamakawa et al., 2021). Meanwhile nodular toxicosis occurs in 50% of cases due to its potential to activate mutations in TSH receptors or G proteins. In Patients with a history of antithyroid treatment especially medication nonadherence it can cause thyroid storm because it can release thyroid hormone from its binding site, until increase the sensitivity of thyroid receptors (Hardina & Budiawan, 2023). In research about predictors of uncontrolled thyrotoxicosis after prolonged anti thyroid drug use reported toxic multi nodular goiter was the most common cause thyrotoxicosis (92%), followed by toxic adenoma (5%) and Graves disease (2%). On binary regression cause thyroid storm , large goiter size (AOR;3.163, 95% CI [1.333-7.506]), severe disease (AOR;2.275, 95% CI [1.060-4.880]), infrequent iodinated salt intake (AOR;3.668, 95% CI [1.245-10.802]), and poor adherence to anti thyroid drug (AOR;15.724, 95% CI [5.542-44.610]) were statistically significant with uncontrolled hyperthyroidism at 12 months of anti thyroid drug intake(Mengesha et al., 2024).

Patients thyroid storm exhibiting cardiovascular complication present similar symptoms, including arrhythmias, heart rate exceeding 100 beats per minute, tachycardia, dyspnea, cardiac ejection fraction of less than 50%, along with sinus tachycardia or atrial fibrillation (Chiha et al., 2015). In research (Bourcier et al., 2020) reported thyroid storm cases with cardiovascular complications such as congestive heart failure/CHF (72%), supraventricular tachycardia/SVT (60%), and VF (13%). A study from the USA show supraventricular arrhythmias, ventricular arrhythmia, cardiac arrest, CS, congestive heart failure, and acute coronary syndrome as 27,4% vs 20%, s,5% vs 1,2%, 1,3% vs 0,1%, 1% vs 0,3%, 19,4% vs 10,3% and 1,8% vs 0,7% in thyrod storm versus thyrotoxicosis without a storm (Galindo et al., 2019)

Hyperthyroid episodes marked by an excessive elevation of peripheral thyroid hormones, induce cardiac rhythm abnormalities caused by heightened sympathetic tone, alterations ion channels, or reduction in the refractory period (Papi et al., 2014). The clinical manifestations of hyperthyroidism are characterized by severe symptoms of cardiovascular decompensation, which can be life threatening, including the onset of supraventricular tachycardia (SVT) accompanied by an elevated heart rate and alterations in autonomic tone. This incident was observed Mrs. R is 52 years old with a previous history of hyperthyroidism, showing supraventricular tachycardia and ST segment elevation in leads V4-V5 during ECG examination. The patient was declared dead on the fourth day of hospitalization to uneffective by antithyroid therapy (thionamide, lugol iodine, beta bloker), vasoactive, and antiplatelet , accompanied by a decline in condition (Nathalia et al., 2023). A research from USA report supraventricular tachycardia (SVT) is an uncommon presentation of thyroid storm, with an incidence of 2-20%, our patient in this cases received a BWPS score of 45 due to cardiovascular tachycardia >140 and a temperature of 101.2ºF (Austin et al., 2022).

The diagnosis of thyroid storm should be made promptly to initiate treatment and prevent additional organ failure. The diagnosis of thyroid storms can be established using the Burch Wartofsky Point Scale (BWPS), where a score of 25-45 score a subclinical thyroid storm and a score beyond 45 indicates a thyroid storm. Multiple case reports indicate that patients diagnosed with thyroid storm exhibited scores over 45, signifying severe symptoms of multiorgan decompensation, particularly in the cardiovascular system (Chiha et al., 2015; Satoh et al., 2016). In this study reported diagnostic thyroid storm with a total score 45 points indicative of a thyroid storm diagnosis (Elendu et al., 2024).

1. Pharmacological Therapy

Administration of medications to reduce thyroid hormone synthesis and inhibit the conversion of T4 to T3. The principal therapeutic agents include ethionamide, beta blockers, lugol iodine and corticosteroids (Yahya et al., 2023). Supportive therapy for thyroid storms involves the administration of antipyretics and fluids (Satoh et al., 2016). Treatment of thyroid storm aims to relieve clinical symptoms, achieve a euthyroid state, and prevent end-organ damage (Ross et al., 2016).

Thionamide is the primary medication employed in thyroid storms, inhibiting thyroid hormone synthesis and converting T4 to T3. The medications utilized include propylthiouracil (PTU) and methimazole (Carbimazole). PTU is advised as the primary treatment due to its substantial reduction of T4 and T3 levels within 24 hours, in contrast to MMI (Nathalia et al., 2023). The initial dosage of PTU is 500-1000 mg administered orally or by NGT, followed by 200-250 mg every 4 hours (Sadiq & Chamba, 2021). The highest dosage of PTU is 1600 mg per day. The administration of PTU in certain instances of thyroid storm is appropriate within the first dosage range and remains below the maximum daily limit of 600 mg to 1200 mg (Brown et al., 2020; Nathalia et al., 2023; Yahya et al., 2023). Employing PTU as the primary treatment improves the clinical outcomes of patients with tachycardia and ST (Brown et al., 2020), However, some cases show clinical symptoms that do not improve due to life-threatening triggers, especially SVT condition (Nathalia et al., 2023). But in research from (Austin et al., 2022) show patient with supraventricular tachycardia complication get standar regimen for treating thyroid storm consisting of propylthiouracil, hydrocortisone, cholestyramine, and propranolol, this regiment worked with great success and thyroid function returned to normal ranges by day four. This cases patient in exhibited heart and liver failure, resulting in hyperbilirubinemia and jaundice, which exacerbated her clinical status, referred to a hospital with more specialist expertise. The patient accept propylthiouracil/PTU therapy despite liver problems, as PTU is hepatotoxic and can induce hyperbilirubinemia (Yahya et al., 2023). MMI is advised as an alternative to PTU for individuals with compromised liver function, patients exhibiting AST/ALT levels 2-3 times the normal range should get MMI therapy at 20 mg every 8 hours. MMI is transitioned to PTU at a dosage of 200 mg every 8 hours for rapid reduction in the conversion of T4 to T3 (Miller & Silver, 2019a). The application of MMI in thyroid storms should be made with methimazole dosages of 60-80 mg per day and carbimazole dosages of 10-70 mg per day. The administration of dosages in patients receiving MMI is suitable within the dosage range of metamizole 60 mg (Miller & Silver, 2019b) and carbimazole dosages 10 mg-45 mg /perday (Sadiq & Chamba, 2021). The patient's symptoms improved after 6 days of successful carbimazole medication (Sadiq & Chamba, 2021).

In critically ill patients recommendation propylthiouracil or PTU over methimazole for treatment of thyroid storm may merit reevaluation, based on research comparative PTU vs methimazole in critically ill patients, a total 8,5% (56 of 656; 95% Cl, 6.4-10,7%) of patients who initiated propylthiouracil and 6,3% (46 of 727; 95% Cl, 4.6-8,1%) who initiated methimazole died in the hospital. There were no significant differences in duration of organ support, total hospitalization cost or adverse event between the 2 treatment (Lee et al., 2023).

The guideline of *American Thyroid Association* strongly recommendation use beta blocker therapy for all patients exhibiting symptomatic thyrotoxicosis (Ross et al., 2016), particularly for elderly individuals with a heart rate exceeding 90 beats per minute. Beta blockers can prevent the conversion of T4 to T3 (Satoh et al., 2016). Patients exhibiting tachycardia, defined as a heart rate exceeding 100 bpm, receive propranolol therapy at a dosage ranging from 40 mg to 120 mg per day (Nathalia et al., 2023; Sadiq & Chamba, 2021; Yahya et al., 2023), According to *the American Thyroid Association,* propranolol dosages for thyroid storms are recommended at 60-80 mg every 4 hours (Ross et al., 2016).

Lugol's iodine used in thyroid storms to inhibit the synthesis of thyroid hormones and their release into the bloodstream. Lugol's iodine may be administered orally as 5-7 drops of potassium iodide (0.25-0.35 ml or 250-350 mg) every 8 hours (Ross et al., 2016; Satoh et al., 2016). The instance utilized potassium iodide at a dosage of 250 mg every 8 hours, which proved challenging to regulate; however, symptoms of tachycardia and ST improved, and the patient was deemed clinically euthyroid at the subsequent appointment (Brown et al., 2020). Some studies reported post radioactive iodine is one of risk factor in thyroid storm which can increased thyroxine levels and side effect after interval time from administration to development of thyroid strom was 6,6 ± 5.5 days. The inclusion of this severe adverse effect should be part of patient discussion with emphasis on the need to seek early consultation when severe symptoms appear (Chiu et al., 2024)

Corticosteroids are utilized to manage thyroid storm by obstructing the conversion of T4 to T3, preventing adrenal insufficiency resulting from the hypermetabolic condition associated with thyroid storm (Yahya et al., 2023). Hydrocortisone or dexamethasone is recommended for usage in thyroid storms, as per the *American Thyroid Association* and the *Japan Endocrine Society* (Ross et al., 2016; Satoh et al., 2016). The hydrocortisone regimen doses consists of an initial intravenous injection of 300 mg, succeeded by 100 mg intravenously every 8 hours, or dexamethasone at a dosage of 8-16 mg per day (Satoh et al., 2016; Yahya et al., 2023). Corticosteroid administration in these cases has adhered to the initial dosing regimen, namely 100 mg every 8 hours and dexamethasone 5 mg every 12 hours (Nathalia et al., 2023; Sadiq & Chamba, 2021). In research about early administration of glucocorticoid in thyroid storm was not associated with a significant improvement in the in-hospital mortality of patients with thyroid storm (95% confidence interval= 1,77(0,95-3,34), 1,44 (1,14-1,93), and 1,46 (0,72-3,00). The result of mortality within 30 days were almost identical to the result of in hospital mortality (Senda et al., 2020).

2. Non-Pharmacological Therapy

In the case (Miller & Silver, 2019a) of a thyroid storm patient with a history of hypertension and congestive heart failure who experienced atrial fibrillation during hospitalization, a 30% ejection fraction did not respond to the administration of methimazole (10 mg every 8 hours) as a substitute for propylthiouracil due to a decline in daily function. Subsequently, the dosage was increased to methimazole (20 mg every 8 hours) on Day 2 used potassium iodide solution (250 mg every 8 hours). The patient had maximal pharmaceutical intervention for thyroid storm. However clinical symptom persisted, necessitating therapeutic plasmapheresis (TPE).

The management guidelines for thyroid storm established by the *Japan Thyroid Association*, plasmapheresis is indicated if clinical manifestations, including tachycardia, hyperthermia, and altered consciousness, fail to ameliorate within 24-48 hours following the administration of antithyroid agents, inorganic iodine, beta blockers, and specific interventions for thyroid storm complications (Satoh et al., 2016). After four days of TPE, the patient's clinical condition improved, and the final treatment with antithyroid medication was sustained (Miller & Silver, 2019b). the case report about a 40-year-old female with severe palpitation, diaphoresis, and chest pain. After taking treatment of thionamide, beta blocker, corticosteroid, and laboratory results confirmed thyroid storm and various complication such as Graves disease, heart failure, reduced ejection fraction. However the systematic treatment was nor effective and finally plasmapheresis and total thyroidectomy were performed (Ebrahimi et al., 2024) Plasmapheresis effectively enhances the state of thyrotoxicosis by rapidly eliminating and substituting serum proteins that bind up to 99% of thyroid hormones (Satoh et al., 2016). According to the most recent standards from the *American Apheresis Association* for thyroid storm, therapeutic plasmapheresis is classified as a recommendation IIC.

Plasmapheresis involves the extracorporeal separation of plasma from blood, utilizing centrifugation techniques to isolate plasma from the cellular components. Patients with thyroid storm associated with Graves' disease, worsened by heart failure, adverse drug reactions, and poor treatment resulting in refractory severe thyrotoxicosis are candidates for plasmapheresis (Miller & Silver, 2019b)

In critically ill patients with Graves' disease and toxic nodules, as a precipitating factor for thyrotoxic crisis, evidenced by elevated FT4 levels ranging from 3.38 to 7.77 ng/dL and BWPS scores between 55 and 70, indicating severe symptoms with organ decompensation. These patients had received antithyroid drug such as PTU, methimazole, beta blockade, thyroidectomy, and plasmapheresis. This research demonstrates that plasmapheresis is a safe and effective intervention associated with a reduced mortality rate, implemented as early as 24 hours after symptom start, facilitating quick normalization of FT4.

CONCLUSION

This literature review indicates that pharmacological therapy for thyroid storm patients with cardiovascular complications (atrial fibrillation, reduced ejection fraction, cardiomegaly, congestive heart failure, STEMI, hypertension, mitral regurgitation) primarily involves thionamides such as propylthiouracil, methimazole, carbimazole and beta blockers like propranolol, which function by inhibiting thyroid hormone synthesis and the conversion of T4 to T3. Potassium iodide, corticosteroids (hydrocortisone, dexamethasone), may also be utilized. The efficacy of the pharmacological therapy is evidenced by the patient's clinical improvement and attainment of a euthyroid state. However, several triggers that impede the attainment of a euthyroid state include difficulties from supraventricular tachycardia in patients, which makes treatment ineffective

Nonpharmacological therapy used when pharmacological therapy fails to produce satisfactory response within 48 hours of drug administration. Plasmapheresis is a nonpharmacological intervention used in patients experiencing thyroid storm with cardiovascular complications. This requires monitoring for potential side effect after plasmapheresis such as nausea and vomiting, hypotension, and respiratory. The treatment demonstrates considerable efficacy, evidenced by a reduction in total FT4 and T3 levels and improvement in clinical symptoms.

This research has limitations such as the sample size is not large enough in the form of a case reports that show small incidents. Future research is needed, it is recommended to research about therapeutic drug monitoring of thyroid storm by looking at the patient's age, therapy obtained, comorbidities to achiece a euthyroid state.

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