UTILITY OF ESMOLOL IN THYROID CRISIS

Jasleen Duggal[1], Sarabjeet Singh[1], Paulina Kuchinic[2], Paula Butler[1], Rohit Arora[1]

[1]Department of Medicine, Chicago Medical School (C.M.S.) Chicago, IL (USA), [2]Department of Emergency Medicine, Chicago Medical School (C.M.S.) Chicago, IL (USA)

Corresponding Author: rohit.arora@va.gov

ABSTRACT

Thyroid storm is an uncommon but potentially life-threatening manifestation of hyperthyroidism. Mortality can be 30-60% in hospitalized patients unless appropriately treated by combined therapy. We report a case of a 25-year-old African American woman with past medical history of Graves disease and moderately persistent asthma who presented to the emergency department with signs and symptoms of thyrotoxic crisis. Therapy instituted and included the use of an esmolol infusion for control of hypersympathetic activity. A review of the clinical presentation, diagnosis, and management of thyrotoxic crisis is presented along with a discussion on the choice of beta blockade therapy.

Key Words: *Thyroid storm, thyroid crisis, esmolol, beta blockers*

Thyroid storm is an uncommon but life-threatening manifestation of hyperthyroidism, which, unless appropriately treated by combined therapy, causes 30-60% of deaths in hospitalized patients.[1] Propranolol has been previously recommended for immediate control of the sympathetic hyperactivity.[3]

We report our experience with a case of thyroid crisis secondary to noncompliance with the medications. A review of the literature indicated the use of esmolol for acute thyrotoxic crisis.[4]

Case Report

A 25-year-old African American woman with past medical history of Graves disease and asthma (moderately persistent) presented to our emergency department with restlessness, palpitations, dyspnea, and diaphoresis. She was not compliant with her medications and denied exogenous iodine ingestion. The patient did not smoke cigarettes or drink alcohol, and denied illicit drug use.

For a few days before her admission she experienced fever and diarrhea. Initial vital signs were temperature, 37.2° C (99° F); blood pressure, 170/96 mm Hg; pulse rate, 180 beats / minute and regular; and respiratory rate, 36 times / minute. Physical examination revealed a tremulous, anxious woman in severe distress. Skin was moist. She had no exophthalmos. The thyroid gland was diffusely enlarged, firm, smooth, and non-tender with a bruit. Cardiac systolic murmur (2/6) was audible in the apex.

The remainder of the physical examination was unremarkable. A 12 lead electrocardiogram done at the time of admission revealed a supraventricular tachycardia. Her chest roentgenogram was normal with no evidence of cardiomegaly or pulmonary congestion. The patient was placed on a cardiac monitor and an intravenous catheter was inserted. Urgent thyroid function testing revealed thyroid-stimulating hormone (TSH) undetectable, free thyroxine at 4.45 ng/dl (normal 0.58-1.64 ng/dl), and triiodothyronine at 22.82 (normal 2.5-3.9 pg/ml) levels markedly elevated. All other laboratory tests including cardiac enzymes and basal natriuretic peptide (BNP) were normal. Thyrotoxic crisis was diagnosed and esmolol infusion, oral propylthiouracil, saturated solution of potassium iodide, and intravenous hydrocortisone was initiated in the emergency department. Esmolol was given with a loading dose of 500 mcg /kg over 1 minute; followed with a dose of 50-mcg/kg/minute. As the response was

inadequate, it was titrated upward in 50 mcg/kg/minute increments (increased no more frequently than every 4 minutes) to a maximum of 200 mcg/kg/minute. The patient was transferred to the intensive care unit (ICU) for further care. Her heart rate decreased to 90 beats/minute and all symptoms subsequently resolved. The infusion on the above rate was continued for 10 hours and the patient was monitored for hemodynamic stability. As there was no complication observed, the infusion rate was reduced by 50% 30 minutes following the first dose of 100 mg oral metoprolol. Following the second dose of metoprolol, control was adequate for the first 2 hours and esmolol was discontinued.

Endocrinology consultation was obtained. It was believed that the thyrotoxic crisis was secondary to Graves disease. After stabilization the patient was discharged home on metoprolol and propylthiouracil with a scheduled follow up appointment for the next week.

DISCUSSION

Thyrotoxic crisis is an uncommon clinical entity, occurring in a small fraction of those patients that are hyperthyroid. It is hypothesized that thyroid hormones increase the density of β receptors and cyclic adenosine monophosphate and decrease the density of α receptors.[5] Plasma levels and the urinary excretion rates of epinephrine and nor-epinephrine are normal in thyrotoxic patients.[6] The causes of thyrotoxic crisis include Graves disease, toxic multinodular goiter, toxic nodule, Hashimoto's thyroiditis, deQuevain's thyroiditis, metastatic follicular thyroid carcinoma, TSH-producing tumors, and factitious hyperthyroidism. The most common etiology for thyrotoxic crisis is Graves disease (toxic diffuse goiter).

The clinical presentation of thyrotoxic crisis is variable. The most common symptoms include weight loss, shortness of breadth, palpitations, chest pain, nervousness, anxiety, altered mental status, and gastrointestinal complaints. The most common signs of thyrotoxicosis include fever, tachycardia, tremor, altered mental status, and an enlarged thyroid gland. T3, T4, and FT4 levels will usually confirm the diagnosis of hyperthyroidism. However, therapy for thyrotoxic crisis cannot wait for thyroid function tests to return. The differential diagnosis of thyroid storm includes overwhelming sepsis, central nervous symptom infection, anticholinergic or adrenergic intoxication, other endocrine dysfunction, and psychiatric illness. Timely clinical diagnosis depends on obtaining a history of previously existing hyperthyroidism, the presence of enlarged thyroid and high index of suspicion. Our patient had all the three above-mentioned parameters to make the diagnosis of thyroid storm. Treatment of thyrotoxic crisis should begin immediately after diagnosis.

Treatment is aimed at blocking the peripheral effect of thyroid hormone, inhibiting the hormone synthesis and release, and preventing the peripheral conversion of T4 to T3. PTU, 300 mg, can be administered orally or by nasogastric tube. Propylthiouracil prevents the synthesis of thyroid hormone and inhibits the peripheral conversion of T4 to T3. Major side effects of PTU include skin rashes, fever, diarrhea, hepatitis, arthralgias, and salivary gland swelling; rarely agranulocytosis occurs. PTU, 300 mg, can be given three to four times a day. Hydrocortisone reduces T4-to-T3 conversion, and may have a direct effect on the underlying autoimmune process if the thyroid storm is due to Graves disease. Hydrocortisone improved outcomes in at least one series[7] and it is reasonable to administer hydrocortisone 100 mg intravenously every eight hours in patients. Iodide inhibits hormone release, but should not be given until at least 1 hour after PTU has been given. Potassium iodide (SSKI), 3 to 5 drops every 8 hours orally can be used.

The most important aspect in treating thyrotoxic crisis involves blocking the peripheral effects of thyroid hormone. The cardiovascular manifestations of thyrotoxic crisis can be severe, and include tachyarrythmias, chest pain, and dyspnea. Congestive heart failure (CHF) occurs in 50% of cases.[8] Thyrotoxicosis is associated with both reversible and irreversible cardiomyopathy, although the cause is uncertain.[9] Increased oxygen demand may cause myocardial ischemia. This was unlikely in our patient as she had normal cardiac enzymes.

The cardiac manifestations of thyrotoxic crisis can be life threatening and demand immediate therapy. Propranolol has traditionally been the drug of choice for blocking the peripheral effects.[3] However, there are several limitations associated with the use of propranolol.

In the setting of CHF administration of propranolol can be dangerous by inducing cardiovascular collapse.[8] Treatment failure in thyrotoxic crisis has occurred with the use of propranolol.[10]

There are several potential advantages of esmolol over propranolol in the setting of thyrotoxic crisis. Although the onset of action of intravenous propranolol and esmolol is similar, their elimination half-life (t1/2) and duration are markedly different. The t1/2 α and β for propranolol are 10 minutes and 2.3 hours respectively, while the t1/2 α and β for esmolol are 2 minutes and 9 minutes, respectively.[11] In one human volunteer study, β blockade had totally disappeared by 18 minutes after an esmolol infusion (300 μg/kg/min) had been discontinued, while there was no change in the degree of β blockade at 30 minutes after a propranolol infusion (55 μg/kg/min) had been discontinued.[12] Because thyrotoxic crisis and its treatment represent a dynamic clinical situation, esmolol enables the clinician to rapidly alter the degree of peripheral effects present. Another advantage of esmolol over propranolol is its relative β-1 selectivity.[13]

This makes it a safer drug than propranolol for patients at risk for developing bronchospasm. Since β-1 selectivity is only relative, the short half-life of esmolol provides an additional advantage should an asthmatic patient not tolerate any manner of β blockade. Our patient had a history of moderately persistent asthma so a decision to initiate esmolol (a short acting beta-1 selective agent) was made. No complications were observed during the infusion and the patient tolerated the parenteral beta-blocker well.

The currently recommended maximum infusion, after an appropriate loading dose and stepwise increase in infusion rate, is 200 μg/kg /min. In the present case, the patient was quickly titrated to and maintained on the maximum recommended dosage. The maximum infusion dose was greatly exceeded in a prior case report of esmolol use in thyrotoxic crisis.[14] A lack of clinical response to the maximum dosage of propranolol has been reported.[15] This case report illustrates that esmolol, a short acting β-1 selective blocker, may be useful for initial management of thyrotoxic crisis.

Acknowledgements

There was no financial support received to carry out the above study. There has been no commercial or proprietary interest in any drug, device, or equipment mentioned in the submitted article. Institutional Review Board approval was obtained.

REFERENCES

1. Trasciatti S, Prete C, Palummeri E, et al. Thyroid storm as precipitating factor in onset of coma in an elderly woman: case report and literature review. Aging Clin Exp Res. 2004 Dec; 16(6): 490-4.
2. Bhattacharyya A, Wiles PG. Thyrotoxic crisis presenting as acute abdomen. J R Soc Med. 1997 Dec; 90(12): 681-2.
3. Zonszein J, Santangelo RP, Mackin JF, et al. Propranolol therapy in thyrotoxicosis: A review of 84 patients undergoing surgery. Am J Med 1979; 88: 411-416.
4. Brunette DD, Rothong C. Emergency Department Management of Thyrotoxic Crisis with Esmolol. Am J Emerg Med. 1991 May; 9(3):232-4.
5. Bilezikian JP, Loeb JN. The influence of hyperthyroidism and hypothyroidism on alpha- and beta-adrenergic receptor systems and adrenergic responsiveness. Endocr Rev. 1983 Fall;4(4):378-88. Review.
6. Coulombe P, Dussault JH, Walker P. Catecholamine metabolism in thyroid disease. II. Norepinephrine secretion rate in hyperthyroidism and hypothyroidism. J Clin Endocrinol Metab. 1977 Jun; 44(6):1185-9.
7. Mazzaferri EL, Skillman TG. Thyroid storm. A review of 22 episodes with special emphasis on the use of guanethidine. Arch Intern Med 1969; 124:684.
8. Wogan JM. Endocrine Disorders. In Rosen P, et al (eds). Emergency Medicine. Concepts and Clinical Practice (ed 2). St Louis, MO, Mosby, 1988.
9. Forfar JC, Muir AL, Sawers SA, et al. Abnormal left ventricular function in hyperthyroidism: evidence for a possible reversible cardiomyopathy. N Engl J Med. 1982 Nov 4; 307(19):1165-70.
10. Strube PJ. Thyroid storm during beta blockade. Anesthesia 1984; 39: 343-396.
11. McEvory GK (ed). AHFS Drug Information 90. Bethesda, MD, American Society of Hospital Pharmacists 1990.

12. Reilly CS, Wood M, Koshakji RP, et al. Ultra-short-acting beta-blockade: a comparison with conventional beta-blockade. Clin Pharmacol Ther. 1985 Nov; 38(5):579-85.
13. Sheppard D, DiStefano S, Byrd RC, et al. Effects of Esmolol on Airway Function in Patients with Asthma. J Clin Pharmacol. 1986 Mar; 26(3):169-74.
14. Thorne AC, Bedford RF. Esmolol for perioperative management of thyrotoxic goiter. Anesthesiology. 1989 Aug; 71(2):291-4.
15. Lee TC, Coffey RJ, Mackin J, et al. The use of propranolol in the surgical treatment of thyrotoxic patients. Ann Surg. 1973 Jun; 177(6):643-7.