

Case Study

METHYLPREDNISOLONE INDUCED HYPOKALEMIA IN AN IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP) PATIENT

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ABSTRACT

We reported an Idiopathic Thrombocytopenic Purpura (ITP) patient, 66-years-old (woman), with hypokalemia. She received 125 mg three times daily of methylprednisolone injection for her ITP. Corticosteroids are the initial treatment of ITP. Her potassium level decrease after she took methylprednisolone. Hypokalemia is also a common problem affecting the elderly or geriatric population. Many literatures reported side effects of corticosteroid is associated with hypokalemia. Monitoring potassium levels must be check during corticosteroid therapy. In this report, we describe the association between corticosteroid with hypokalemia effect.

Keywords: Corticosteroid, Methylprednisolone, Hypokalemia, Idiopathic Thrombocytopenic Purpura, Elderly

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INTRODUCTION

Idiopathic Thrombocytopenic Purpura (ITP) is an idiopathic condition of having thrombocytopenia or a low platelet count. ITP is also known as autoimmune thrombocytopenic purpura and immune thrombocytopenic purpura because ITP appears to be related to antibodies against platelets. ITP is a disease where the destruction of peripheral platelet occurs. ITP is divided into acute ITP and chronic ITP. The normal range for platelet level in adults is between 150,000 and 450,000/mm³. When platelet count decreases to below 50,000 mm³, the dangerous bleeding risk increase with trauma and the platelet counts below 20,000/mm³ may increase spontaneous bleeding risk. All therapy for ITP is given either orally or intravenously (IV), and the use of intramuscular injection should be avoided due to skin bleeding risk can occur. One of the medications for ITP is corticosteroids. Corticosteroids, typically prednisone, are the primary choice of the initial treatment [1]. The treatment can be initiated with the use of IV steroids, for instance, with methylprednisolone or prednisone. The intravenous steroid with a high dose is commonly indicated in a hematologic disorder like ITP [2]. About 70%-80% of patients respond to corticosteroids, and about 10%-30% acquire durable remission. The other medication is intravenous immunoglobulin (IVIg) or IVIg combination with either corticosteroid or platelet infusions to increase the platelet count quickly. After the platelet count improved, maintenance doses of oral prednisone is 1 to 2 mg/kg per day, single or divided doses is used. Most ITP cases

gave a response during the first week of therapy. The oral steroid dosage should be gradually reduced after several weeks of use therapy [1, 3]. Corticosteroids such as mineralocorticoids and glucocorticoids can cause hypokalemia Hereby, we report the ITP patient with hypokalemia induced by high dose corticosteroid therapy [4, 5].

CASE REPORT

A Woman, 66 y old. She admitted to the hospital with diagnosed ITP (Idiopathic Thrombocytopenic Purpura). Her symptom is purpura. She also has hypertension. For the first day, when she admitted to the hospital, her laboratory test showed an abnormal result. The result for thrombocyte was $5 \times 10^3/\text{ul}$ (normal value 150-400 $\times 10^3/\text{uL}$) and potassium 3.1 mEq/l (normal value range 3.5-5.1 mEq/l). She took methylprednisolone injection 125 mg three times daily, eltrombopag olamine 25 mg tablet two tablets once daily, amlodipine 10 mg tablet once daily, potassium supplement 600 mg tablet once daily, pantoprazole injection 40 mg twice daily, carbazochrome injection 10 mg three times daily. The next day, methylprednisolone dosage decrease to 125 mg twice daily, and day 3 to 125 mg once daily. On day 4, methylprednisolone dosage form was changed from injection to oral. After 8 care days at the hospital, she felt malaise or fatigue. And then, she has diagnosed hypokalemia, with potassium level was 2.3 mEq/l. She took potassium intravenous for potassium correction. Three days after correction, her potassium level to be normal (table 1).

Table 1: Result of thrombocyte and potassium concentration level after methylprednisolone administration

Labs test	Normal value	Unit	Day (d)										
			1	2	3	4	6	7	8	9	10	11	
Thrombocyte	150-400	10 ³ /ul	5	18	65	68	91	148	64	12	82		
Potassium	3.5-5.1	mEq/l	3.1						2.3	2.9	3.1	3.9	

In this case, the Naranjo adverse drug reaction probability scale was applied to quantify the degree of association between methylprednisolone and hypokalemia and it was found to be score 8 (probable). Hypokalemia may be caused by methylprednisolone therapy.

DISCUSSION

Glucocorticoids are the most potent and effective anti-inflammatory agents for chronic and acute diseases in clinical practice [2, 6].

Methylprednisolone (MP) is an intermediate-acting corticosteroid, with a half-life of 12-36 h, potent anti-inflammatory therapy. Methylprednisolone has potency 1.25 times compared to prednisolone. One of the adverse drug reactions after high dose glucocorticoid administration is hypokalemia [2]. Electrolyte disturbances such as hypokalemia are frequent in patients treated with prednisolone and methylprednisolone [4, 6, 7]. Some reports said hypokalemia and muscle weakness occurred after the use of methylprednisolone agents [8-11].

Hypokalemia is a condition of serum potassium level of less than 3.5 mEq/l. The normal range of serum potassium level is 3.5 to 5 mEq/l. The severity, levels, and symptoms of hypokalemia can be seen in the table below [4]. Electrolyte imbalance, such as hypokalemia, usually occurs in the elderly. The prevalence of

hypokalemia case inpatient elderly (above 65 y old) was found 3.24%. The incidence of hypokalemia increases according to age increase, the number of comorbidities, or use of other agents that may cause to increased risk of hypokalemia, especially in the elderly [5, 12].

Table 2: Severity, levels, and symptoms of hypokalemia [4]

Severity	Level (mEq/l)	Symptoms
Mild	3.0-3.5	asymptomatic
Moderate	2.5-3.0	Cramping, malaise, myalgia, weakness
Severe	<2.5	Tachyarrhythmias, bradyarrhythmias, paralysis

Mechanism of glucocorticoids induce hypokalemia by transcellular potassium shifts such as increased Na⁺/K⁺-ATPase pool in skeletal muscle and may be mediated by insulin or amylin. Other mechanisms of medications cause hypokalemia, including increased renal sodium loss or fluid retention, and/or stool loss [4, 5, 13-15].

A patient with polymyositis was treated with 0.5 g/day methylprednisolone for a 3-day course, and the patient has hypokalemia. After steroid use discontinued, potassium level increases [16]. In a study in juvenile rheumatoid arthritis, the side effect of methylprednisolone was hypokalemia and hyponatremia [2]. Another report said hypokalemia and myopathy event occurred after corticosteroid therapy with high dose [13]. Mild and moderate hypokalemia (18.18%) has reported in patients who for three days, received 1 gram of intravenous methylprednisolone [17].

A 25-year-old Japanese man with hyperthyroid-related hypokalemia worsened by steroid therapy. The patient has ventricular fibrillation and paralysis worsened after receiving methylprednisolone infusion [18]. Drugs that can induce hypokalemic periodic paralysis (hpoPP) include beta mimetics, insulin, corticosteroids, and diuretics [19]. A patient experienced thyrotoxic periodic paralysis (TPP) after received dexamethasone therapy. TPP can be diagnoses in a patient with hypokalemia symptoms and thyrotoxicosis. Some cases reported prednisolone and methylprednisolone can induce the TPP event. An unusual presentation of TPP due to a high dose of glucocorticoids [14, 15, 20, 21].

Corticosteroid, especially for steroid pulse therapy, can induce cardiac arrhythmias, such as tachyarrhythmias and bradyarrhythmias [2, 22]. From the basic electrophysiologic viewpoint, corticosteroids affect cardiac calcium channels and also potassium channels [22]. A case of hypokalemia occurred after starting injection methylprednisolone in the rheumatoid patient and resolved after its withdrawal [7]. For mild-to-moderate hypokalemia case could be treated with oral potassium supplements, and if a patient cannot take oral supplements or with severe hypokalemia case require intravenous (IV) potassium as replacement therapy [4].

CONCLUSION

Methylprednisolone injection can induce hypokalemia. Serum potassium level must be checked before high dose steroid treatment and monitoring therapy is also needed. The clinical pharmacists or physicians, as early as possible, must identify potential adverse drug events or drug-induced diseases.

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AUTHORS CONTRIBUTIONS

First author (Sherly Tandir Arrang) conducted the search, collected the reference articles, and wrote the manuscript; the second author (Fonny Cokro) reviewed the manuscript.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest

REFERENCES

- Kayal L, Jayachandran, Singh K. Idiopathic thrombocytopenic purpura. *Contemp Clin Dent* 2014;5:410-4.
- Sinha A, Bagga A. Pulse steroid therapy. *Indian J Pediatr* 2008;75:1057-66.
- Nomura S. Advances in diagnosis and treatments for immune thrombocytopenia. *Clin Med Insight: Blood Disorders* 2016;9:15-22.
- Veltri KT, Mason C. Medication-induced hypokalemia. *Pharmacovigilance Forum* 2015;40:185-90.
- Weiss BD. Medication-induced hypokalemia: a common problem. *Elder Care*; 2015.
- Perez HET. Glucose disturbances in non-diabetic patients receiving acute treatment with methylprednisolone pulses. *Rev Assoc Med Bras* 2012;58:125-8.
- Roshni PR, Sai Keerthana PC, Khrishna PR. Steroid-induced hypokalemia-a case report. *Int J Pharm Sci Rev Res* 2017;42:42-3.
- Buyukcam F, Calik M, Erkuran MK, Akay H. Case report, hypokalemia, and muscle paralysis after low dose methylprednisolone. *Am J Emerg Med* 2011;29:573.
- Bonnette B, Chaffert B, Martin F. Side-effects of high-dose intravenous (pulse) methylprednisolone therapy cured by potassium infusion. *Br J Rheumatol* 1998;37:109.
- Soriano PK, Bhattarai M, Vogler CN, Hudali TH. A case of trigger-point injection-induced hypokalemic paralysis. *Am J Case Rep* 2017;18:454-7.
- Knox Macaulay HHM, Rehman JU, Zadjali SA, Fawaz NA, Al Kindi S. Idiopathic thrombocytopenic purpura and hypokalemic dRTA with compensated haemolysis and striking acanthocytosis in a band 3 (SLC4A1/AE1) A858D homozygote. *Ann Hematol* 2013;92:53-4.
- Bardak S. Community-acquired hypokalemia in elderly patients: related factors and clinical outcomes. *Int Urol Nephrol* 2017;49:483-9.
- Tsai WS, Wu CP, Hsu YS. Life-threatening hypokalemia in an asthmatic patient treated with high-dose hydrocortisone. *Am J Med Sci* 2004;327:152-5.
- Wongraoprasert S, Buranasupkajorn P, Sridama V, Snaboon T. Thyrotoxic periodic paralysis induced by pulse methylprednisolone. *Int Med* 2007;46:1431-3.
- Arzel Hezode M. Glucocorticoids may trigger attacks in several types of periodic paralysis. *Neuromuscular Disorders* 2009;9:217-9.
- Wu C. Hypokalemic myopathy in primary aldosteronism: a case report. *Exp Ther Med* 2016;12:4064-6.
- Tamez Perez HE, Cisneros Perez V, Cedillo Rodriguez JA, Diaz De Leon-Gonzalez E, Torres Valenzuela M, Tamez Pena AL, *et al.* Prevalence of hypokalemia in patients with methylprednisolone pulse therapy. *Rev Invest Clin* 2009;61:194-7.
- Miyashita. Case report: ventricular fibrillation due to severe by steroid treatment in a patient with thyrotoxic periodic paralysis. *Int Med* 2006;45:11-3.
- Erturk O, Ozlu C. Hypokalemic periodic paralysis that presented with hemiparesis after dexamethasone injection. *Turk J Neurol* 2006;22:141-2.

20. Lee EJ, Kim TK, Kwon MJ, Lee SH, Park JH. Thyrotoxic periodic paralysis induced by dexamethasone. *Endocrinol Metab* 2012;27:299-302.
21. Tigas S, Papachilleos P, Ligkros N, Andrikoula M, Tsatsoulis A. Hypokalemic paralysis following administration of intravenous methylprednisolone in a patient with graves thyrotoxicosis and ophthalmopathy. *Hormones* 2011;10:313-6.
22. Sakamoto N. Three cases of corticosteroid therapy triggering ventricular fibrillation in J-wave syndromes. *Heart Vessels* 2014;29:867-72.