International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

A Case Report on Inhaled Budesonide Induced Addison's Disease

Dr. Erin Xavier[1], Breezy Ani Sam[2], Elisaba Jacob[3], Dr. Mohan Varghese[4]

[1]Clinical Pharmacist, Department of General Medicine, Believers Church Medical College Hospital, Thiruvalla, Kerala

[2]Pharm D Intern, Nazareth College of Pharmacy, Othera, Thiruvalla

[3]Pharm D Intern, Nazareth College of Pharmacy, Othera, Thiruvalla

[4]Senior Consultant, Department of General Medicine, Believers Church medical College Hospital, Thiruvalla, Kerala

Abstract: ***Addison's disease (AD) also called as hypoadrenalism is a rare disorder of adrenal gland characterized by inadequate production of steroid hormones: cortisol and aldosterone and is presented with both oral and systemic manifestation. The symptoms of the disease include hyperpigmentation of skin and mucosa, weakness, abdominal pain, weight loss. In our study a 67-year-old male patient presented with complaints of multiple episodes of vomiting, generalized tiredness, decreased appetite, hyponatremia and hyperpigmentation of skin, regions of tongue, palms and feet which is considered as the hallmark sign of AD and patient was only on Inhaler Foracort (Budesonide + Formetrol) taken for his breathing difficulty occasionally for past 20 years. By analyzing the Subjective and Objective evidence the patient was suspected to have BUDESONIDE INDUCED ADDISON'S DISEASES which was further confirmed by Naranjo ADR Probability Scale Score and WHO -UMC Causality Assessment Scale.***

Keywords: Addison's disease, Hyponatremia, Budesonide.

1. Introduction

Addison's disease is a rare chronic endocrine disorder affecting the adrenal gland. Adrenal gland is located at top of both kidneys and secrete essential hormones such as cortisol and aldosterone. In AD, adrenal gland fails to produce adequate amount of these hormones leading to various symptoms and complications. It has a very low prevalence, affecting 1 in 10.000 population worldwide. It affects female and male both equally at any age groups but commonly diagnosed at an age between 30 and 50. It can be caused by both primary and secondary adrenal insufficiency. The symptoms include fatigue, weight loss, hyperpigmentation of skin, abdominal pain, low blood pressure and salt craving. These symptoms are due to low levels of cortisol and aldosterone, the release of cortisol involves hypothalamus which releases corticotrophin releasing hormone (CRH) and signals the anterior pituitary to release adrenocorticotropic hormone (ACTH) and which thereby signals adrenal gland to release cortisol into body. When we start giving patient an external glucocorticoid i.e. Inhaled or oral, it sends negative feedback signals to adrenal gland such that these glands either reduce or stop secreting the chemicals leading to adrenal suppression and depletion of cortisol, so we do not use oral steroids for long period so that we tapper the dose over a period. We hereby present a 67-year-old male who developed Addison's disease (adrenal insufficiency) because of budesonide which was used for his breathing difficulty. [1,2,3]

Budesonide is a potent anti-inflammatory agent with a wide range of clinically significant activity. The nasal spray is designed for treating allergic rhinitis and other upper respiratory allergies, with one spray containing 32 mcg of budesonide. Budesonide is a potent topical anti-inflammatory agent that binds and activates glucocorticoid receptors in the bronchial cytoplasm, allowing the translocation of a budesonide-GR complex to the bronchi nucleus. This complex binds to HDCA2 and CBP (HAT), preventing the production of inflammatory genes that might cause bronchoconstriction. Budesonide-receptor complex also activates HDCA2, increasing gene expression and reducing cytokine formation. It inhibits eosinophil activation and suppresses inflammatory cell activation, leading to reduced airway inflammation and hyper reactivity, preventing bronchospasm, wheezing, and coughing.

Budesonide has been found to cause various adverse reactions:

- Paradoxical bronchospasm
- Localized infections of the oral cavity and pharynx
- Opportunistic infections
- hypersensitivity reactions
- Nasopharyngitis, otitis media, conjunctivitis. [4,5]

2. Case Report

A 67-year-old male presented to ER with complaints of multiple episodes vomiting (2-3 episodes/day) associated with generalised tiredness and decreased appetite for past 3 days. Patient has no history of fever, sore throat, cough, breathlessness and loose stools. On examination Vitals and general examination was within normal limits. On auscultation scattered wheeze was heard. Patient had a similar history of vomiting, hyponatremia (Na-111 mmol/L) and got admitted at the hospital two years back and he was tested covid positive then and was discharged with some advice to take oral salt 8 g/day. He got covid the second time one year back and was diagnosed with Category B covid 19, hyponatremia (126 mmol/L).

On physical examination, patient had hyperpigmentation over the forehead, around the eyes and over lips and no thyromegaly which was found to be the hallmarks of

Addison's disease. Routine blood investigations revealed normal counts, but serum sodium was low (121 mmol/L). Patient was admitted and started on IV fluids for sodium correction but his sodium level was not improving. Patient was also given IV antiemetics, PPI and vitals were monitored regularly. Serum sodium and potassium were repeated regularly, and correction was given. Supine and standing BP was measured and postural hypotension was ruled out for the patient. 8am cortisol level was checked, and it was decreased. Endocrinology cross consultation was sent, and orders were followed. Mantaux test and Synactin test was done for the patient. Mantaux test was found to be negative which suggests a negative TB. Synactin test was performed as, before giving Inj. Synactin, Serum cortisol was 30ng/dl and ACTH was low 52.4ng/ml and 1 hour after Inj. Synactin serum cortisol, was 114ng/dl and hence depending on the results patient was started on Inj. Hydrocortisone 50mg Q8H and T.Fludrocortisone 100mcg OD. Patient CECT abdomen was taken to rule out mass in adrenal gland and no definite focal mass lesion identified in adrenal gland. Following this patient showed good improvement symptomatically and IV steroids change to oral steroids. Over the course of the hospitalisation patient become symptomatically and hemodynamically better. (sodium – 137 mmolL, cortisol- 114ng/dl)

This case was analysed by using NARANJO SCALE and WHO-UMC causality assessment scale, according to NARANJO scale algorithm was 5 which is categorized as probable reaction and WHO causality assessment scale patient fall under PROBABLE on the basis of these scales it was concluded as BUDESONIDE INDUCED ADDISON'S DISEASE.

3. Discussion

Addison's Disease is a clinical condition characterised by adrenocorticotrophic hormone hyposecretion due to primary disease of adrenal gland or secondary to pituitary gland disorder. Causes of AD include autoimmune reaction, prolonged use of steroids, idiopathic atrophy of adrenal gland, adrenal carcinoma, infection such as TB, abnormal function of pituitary gland. Clinical presentation include weakness, weight loss, fatigue, nausea and vomiting, diarrhoea, hyperpigmentation of skin and mucus membrane and electrolyte imbalance. AD is diagnosed by hormone level testing (ACTH and Cortisol), Synactin test and additional blood test. Complications of AD are renal failure, adrenal haemorrhage, Addisonian crisis and depression.

In our case report, the patient was taking MDI Budesonide occasionally for breathing difficulty for 20 years. He was now presented with complaints of Vomiting, tiredness and decreased appetite for 3 days. During the hospitalisation patient shows hypernatremia which doesn't resolved even after providing sodium correction. Due to subjective and objective data available patient was sought to do Synactin test and was found to have Addisons disease. He was then treated with steroids.

This is similar to the case report done *by Sreelatha J on "Budesonide Induced Addison's Disease (Adrenal Insufficiency): A Case Report"* which says patient was on Foracort and then developed Addisons disease.[6]

Another similar case reports includes *Vishnu Sannarangappa on"Inhaled Corticosteroids and Secondary Adrenal Insufficiency"* which says numerous case reports that have shown an association between ICS and AI particularly in children and patients using high doses.[7]

Case report by *Francesco Lapi on "The use of inhaled corticosteroids and the risk of adrenal insufficiency"* which concludes the risk of adrenal insufficiency in relation to current use of ICSs at high dose appeared higher among patients with COPD [8].

4. Conclusion

Here we report a rare case of Budesonide induced Addison's Disease (Adrenal Insufficiency) in a 67 years old male. In order to avoid morbidity and mortality associated with Addison's crisis, we need to be highly cautious and vigilance while using glucocorticoids as they are documented to cause adrenal insufficiency and AD, and at most care should be taken to detect earliest symptoms of AD so that suitable interventions is made with alternative drug to ease the patients. Its drug components need to be reconsidered in view of safer use and alternative available.

Acknowledgement
The author would like to express sincere gratitude and regards to the Department of General Medicine, Believers Church medical College Hospital, Thiruvalla and the Department of Pharmacy Practice, Nazareth College of Pharmacy, Othera for publishing this case report. Thankful for the constant support and help.

Conflict of Interest
The authors declare that the case report was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

Consent of the Patient
Consent was obtained from the patient for publication of this case report and accompanying images

Abbreviations
AD: Addison's disease
ADR: Adverse Drug Reaction
CRH: Corticotrophin releasing hormone
ACTH: Adrenocorticotropic hormone
COPD: Chronic Obstructive Pulmonary

References

[1] Nieman LK, Chanco Turner ML. Addison's disease. Clin Dermatol. 2006 Jul-Aug;24(4):276-80. doi: 10.1016/j.clindermatol.2006.04.006. PMID: 16828409.
[2] Barthel A, Benker G, Berens K, Diederich S, Manfras B, Gruber M, Kanczkowski W, Kline G, Kamvissi-Lorenz V, Hahner S, Beuschlein F. An update on Addison's disease. Experimental and Clinical Endocrinology & Diabetes. 2019 Feb;127(02/03):165-75.
[3] Sarkar SB, Sarkar S, Ghosh S, Bandyopadhyay S. Addison's disease. Contemporary clinical dentistry. 2012 Oct;3(4):484.
[4] Kalola UK, Ambati S. Budesonide. StatPearls Publishing; 2023
[5] O'Connell EJ. Review of the unique properties of budesonide. Clinical therapeutics. 2003 Jan 1;25:C42-60.
[6] Sreelatha J, Lakshmi DBP, Shabaz S, Sandhya M. Budesonide induced addison's disease (adrenal insufficiency): A case report [Internet]. Ijrpr.com. [cited 2024 Jan 23].
[7] Sannarangappa V, Jalleh R. Inhaled corticosteroids and secondary adrenal insufficiency. Open Respir Med J. 2014 Jan 31;8:93-100. doi: 10.2174/1874306401408010093. PMID: 25674179; PMCID: PMC4319207.
[8] Lapi, F., Kezouh, A., Suissa, S., & Ernst, P. (2013). The use of inhaled corticosteroids and the risk of adrenal insufficiency. *The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology*, *42*(1), 79–86. https://doi.org/10.1183/09031936.00080912