A REVIEW ON ADDISON'S DISEASE

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**ARTICLE INFO**

**Article history**
Received 20/09/2015
Available online 30/09/2015

**Keywords**
Addison’s Disease, Autoimmune Adrenalitis, Kidney, Cortisol.

**ABSTRACT**
Addison’s disease is chronic, life threatening rare endocrinal disorder which affects 1 in 100,000 people. Both sex people equally affected by this disorder. Autoimmune adrenalitis is most common cause of primary adrenal insufficiency. It's prevalence is about 140 per million. Autoimmune adrenalitis disorder, the adrenal cortex is damaged causing the loss of production of hormone such as glucocorticoid, mineralocorticoid. The fight and flight stress hormone adrenaline produced by inner medulla. The cortisol and aldosterone are the essential adrenaline produced by inner medulla. The cortisol and aldosterone are the essential steroid hormone produced by it. Function of the cortisol is to enable the body to fight inflammation, stimulates liver to produce blood sugar, mobilises nutrients, helps to balance the quantity of water in human body. While the salt & water level which have impact on Blood Pressure is regulated by aldosterone. The main objective of this review article is to create an awareness among the people concerning with the addison's disease & it's symptoms, diagnosis, treatment. Rational utilization of drug therapy with patient compliance is important. So that proper management of Addison’s disease is achieved.

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INTRODUCTION

In primary adrenal insufficiency condition the thomas addison detected group of patient with anaemia and disease adrenal glands, almost 200 yrs ago.¹¹ In this disorder, adrenal cortex destroyed which result into inadequate secretion of adrenal cortical hormone, cortisol and aldosterone.²⁻³ In fact Addison's disease is progressive hypofunctioning of the adrenal cortex. The various symptoms include loss of appetite, hyperpigmentation, hypotension and adrenal crisis. Diagnosis is clinical while treatment dependent on the etiology but usually includes hydrocortisone, dexamethasone, prednisone, florinef etc. as per requirement.⁴⁻⁵ Adrenal disease is rare disorder which develops in 4/100,000 people annually. Both sex with all age group affected which tends to become clinically apparent during stress. Various causes include Na loss, surgery & trauma. Slight increase in mortality rate of patient suffering with addison's disease even when its treatment given. This happen particularly due to long term complications of inadvertent over replacement.⁷⁻⁸

Fig no.1 Adrenal gland.

In hypoadrenocorticism the clinical features donot appear until 90% of the glandular tissue has been damaged. Hyperpigmentation of eyes, mucus membrane and skin is associated with addison's disease.⁹⁻¹¹ Hyponatremia and hyperkalaemia are usually related with addison's disease patient complains of a peculiar craving of salt, adrenal calcification, anorexia, diarrhoea.¹²⁻¹⁴

Addisonian crisis may occur due to an event of illness that can worsen the condition further. Symptoms of addisonian crisis include penetrating pain in abdomen, legs and back region with diarrhoea which followed by low blood pressure and dehydration.¹⁹⁻¹⁴

There are two forms of Addison's disease as follows:
1. Primary adrenal insufficiency: It occurs when adrenal glands are destroyed and it fails to produce enough cortisol and aldosterone hormone.¹²
2. Secondary adrenal insufficiency: It occurs when a bean size organ in brain unable to produce sufficient ACTH. Cortisol is produced by adrenal gland which is stimulated by ACTH. Ultimately, there is decline in cortisol production. Lack of ACTH stimulation causes adrenal glands to shrink.

Etiology

Autoimmune disease almost accounts for about 80% of adrenal insufficiency. In this case body's immune system attack adrenal glands which damages outer layer of the glands.¹⁵ Deficiencies of glucocorticoid, mineralocorticoids which resulting from damage of adrenal cortex caused by autoimmune adrenalitis. In men, adrenoleukodystrophy is important cause of rare endocrinl disorder. It is resulting from accumulation of long chain fatty acid in adrenal gland.¹⁶

Cancer cells, fungal infections and long lasting infections such as TB & HIV can harm adrenal glands. Improper utilization of steriodal hormone such as dexamethaone, prednisone leads to secondary adrenal insufficiency. Secondary adrenal insufficiency is caused due to problems with hypothalamus located in the center of brain. ACTH is a pituitary hormone which stimulates the cortisol production in adrenal gland. Another cause is due dysfunctioning of pituitary glands which is responsible for cortisol production in adrenal glands.¹⁷
Pathophysiology

The destruction of almost entire adrenal cortex result into adrenocortical insufficiency. Therefore, it causes the dysfunctioning of steroidal hormone like mineralocorticoid and glucocorticoids. Disease onset occurs when nearly 90% of both the adrenal cortices are dysfunctional.\textsuperscript{[18]}

Epidemiology

Frequency:
It is found that about 50-60% cases per million population affected by this disorder.

International:
In Denmark 50% cases per 1 million population while in Great Britain 40 cases per 1 million population reported.

Mortality/Morbidity
Mortality & Morbidity occurs due to failure or delay in making diagnosis and failure to institute adequate necessary hormone such as mineralocorticoid replacement. Failure to prompt treatment leads to addisonian crisis which eventually may cause death. Risk of death is more than 2-fold high in patient with adrenal insufficiency even after clinical diagnosis and treatment.

Race
Adrenal insufficiency is not concern with racial predilection.

Sex
Woman and children are most susceptible to addison's disease than men.

Age
It can occur at any stage of life but usually occurs in adults in 35-50 yrs. It may be due to disorder of long chain fatty acid metabolism, congenital adrenal hyperplasia.
Sign and Symptoms

Sign
- Hyperpigmentation of skin and mucous membranes
- Low blood pressure
- Postural hypotension

Symptoms
- Fatigue
- Malaise
- Loss of appetite
- Nausea and vomiting
- Abdominal pain
- Weight loss
- Postural dizziness
- Myalgia
- Joint pain
- Salt craving

Addisonian crisis
If the patient with addison's disease faces extreme physical stress and trauma & does not get extra steroid to cover their body needs to meet that trauma. Such circumstances resulting in the Addisonian crisis. This crisis needs quick emergency treatment as it is potentially life threatening condition. If this situation is left untreated it may be fatal. The Addisonian crisis consist of symptoms which include extreme weakness, fatigue, drop in blood pressure, dehydration etc.\(^{[18]}\)

Diagnosis

Metabolic test
The main objective of laboratory testing is to document a low cortisol level and find out whether the insufficiency is due to primary or secondary cause. It suggest adrenal insufficiency to low serum cortisol levels while hyponatraemia may be attributed to mineralocorticoid deficiency.\(^{[19-20]}\)

Immunogenic test
21-hydroxylase enzyme is essential for synthesis of cortisol in adrenal cortex in adrenal cortex. Various antibodies directed against the enzyme which are particularly for autoimmune adrenalitis and hence are detectable before the onset of symptoms.\(^{[1]}\)

Imaging
Determination of the cause of Addison's disease by Radiographic imaging play's an important role in diagnosis. Before radiographic imaging, it is necessary to make biochemical tests.

ACTH Stimulation test
The most significant test for diagnosing the addison's disease is ACTH test. In this diagnostic test both blood and urine cortisol are measured before and after injection of ACTH is given. Measurement of cortisol in blood is repeated 30-50 min after IV ACTH injected. Patient with adrenal insufficiency does not respond to this test.\(^{[21]}\)

CRH stimulation test
This is the most specific test for diagnosing adrenal insufficiency. Determination of cause of addison's disease possible after long CRH stimulation test. CRH is injected IV and blood cortisol is measured 30, 60, min before and after injection. High ACTH found in primary adrenal insufficiency patient while deficient response in patient with secondary adrenal insufficiency. As patient is being treated for crisis, reliable diagnosis is not possible at all.\(^{[21]}\)

Other test
After diagnosis studies radiologic studies like x-ray, ultrasound of abdomen can be taken to observe if adrenal have any sign of calcium deposits. Calcium deposit may be indicated by bleeding in adrenal cortex. Detection of antibodies concerned with autoimmune disorder may be possible by blood test.\(^{[21]}\)

Treatment\(^{[22-25]}\)
Addison's disease treated by substituting, replacing hormones that adrenal glands are not producing. However, the cortisol is replaced with the prednisone, dexamethasone, hydrocortisone which is taken orally thrice times a day. Deficiency of aldosterone is overcome by replacement of oral doses of mineralocorticoid, florinef taken twice per day. It is usually advised by doctors to increase salt intake in patient who is receiving aldosterone replacement therapy. In addisonian therapy low blood pressure, low glucose level, high level of potassium which may be life threatening. Hence in such circumstances IV injection of glucocorticoid and large volume IV saline solution with dextrose given.
Surgery
Surgery carried out because cortisol is a stress hormone. IV glucocorticoids and saline given to patient with chronic adrenal insufficiency who require general anaesthesia. The stress dosage is adjusted until patient recovers with presurgery maintainence dose.

Pregnancy
Those women suffering from addison's disease and at the same time who become pregnant are given treatment with standard replacement therapy. Injection of hormone given when voitting occurs. Maintenance dose is given orally i.e. hydrocortisone acetate post delivery.

Illness
Adjustment of oral dosing of mineralocorticoid to enhance the hormonal response of adrenal glands to this stress on patient's body. Maintenance dose provide once the stress recovered.

Emergency
In the case of emergency patient must carry identification stating their condition. If a person found injured or unconscious in such circumstances a medical alert tag must notify emergency health care providers the need to inject cortisol. The card must include name, telephone no, address of both doctor and patient. While in journey patient must carry injectable cortisol for emergency purpose.

CONCLUSION
Addison's disease is a chronic endocrinial disorder which may be occur in both sex people. It can be diagnosed, treated. But if left untreated leads to Addisonian crisis & hence this may fatal. Therefor patient must follow the rational therapy, patient must carry medical tag to notify the health care provider about their condition in emergency. Therefore, it is significant to study this life threatening disorder and maje adequate precautions and follow essential guidelines to avoid any untoward incident.

Acknowledgement
The author wish to express his gratitude to the faculty members of Channabasweshwar Pharmacy college, Latur, India.

Author's statements

competing interest
The author declare no conflict of interest.

REFERENCE
4. Jeremy Sussman, PhD, University of California, Berkeley.
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