Asian Journal of Research and Reports in Endocrinology

Volume 7, Issue 1, Page 1-10, 2024; Article no.AJRRE.113082

Review of Therapeutic Approach in Common Hormone Disorders

Albatool Almukairish [a], Aliaa Sabban [a] and Khalid Bakheit [a*]

[a] Department of Clinical Biochemistry, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.

Authors' contributions

This work was carried out in collaboration among all authors. Author AA did the review. Authors AS and KB supervised, revised the review and put it in the final format. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/113082

Review Article

Received: 03/12/2023
Accepted: 07/02/2024
Published: 07/02/2024

ABSTRACT

Hormones have a critical role in regulating a number of body functions, including mood, metabolism, growth and development, and reproductive health. This article covers common hormone disorders, as well as their causes, symptoms, complications, and available treatments. Common treatment modalities for hormone problems include medication, lifestyle modifications, surgery, complementary therapies, and routine monitoring. The course of treatment may also be accompanied by possible negative effects, such as cancer risk, hormone overcorrection, and interactions with other medications or medical conditions. Regular hormone level and symptom evaluations by healthcare professionals are necessary to provide individual treatment plans that lower the risk of complications while achieving the desired therapeutic goals.

Keywords: Hormone disorders; therapeutic approach; hormone replacement.

**Corresponding author: Email: khalid2_3456@yahoo.com;*

1. INTRODUCTION

The endocrine system consists of glands and organs that secrete hormones to control various body functions. Hormones are chemical messengers that circulate in the bloodstream and affect physiological functions. The parts of the endocrine system consist of the hypothalamus, pituitary gland, thyroid and parathyroid glands, adrenal gland, pancreas, ovaries, and testicles [1, 2].

An endocrine disorder is the result of endocrine system's dysfunction, which includes the hormone-secreting glands, hormone receptors, and hormone target organs. Dysfunction can happen at any one of these sites and have a significant impact on the body. Moreover, an individual may have an endocrine disorder if their hormone levels are abnormally high or low or if their body does not respond to hormones as it should be. Tumors, hereditary factors, or hormonal imbalances are just a few of the possible causes of endocrine disorders. These diseases alter hormones, which can affect growth and development, metabolism, sexual function, and mood. They can also cause a wide range of symptoms, such as fatigue and weakness [1, 2].

Endocrine disorders have a variety of forms. The most prevalent endocrine disorders are: prolactinoma, hypothyroidism, hyperthyroidism, Hashimoto’s disease, polycystic ovarian syndrome (PCOS), Graves’ disease, Cushing’s syndrome, and diabetes mellitus [3, 4].

Depending on the types of disease, different causes may induce endocrine problems. Acromegaly and Cushing's syndrome, for example frequently result from an adrenal or pituitary gland tumor. Even though these tumors are typically benign, excision is still necessary to treat the illness. Moreover, hormonal abnormalities might cause some issues. For instance, hyperthyroidism and hypothyroidism are conditions in which the thyroid gland generates excessive or insufficient amounts of thyroid hormones, respectively [3, 4].

Polycystic ovary syndrome (PCOS) in women is associated with excessive androgen levels. Endocrine problems may result from an autoimmune disorder as well, like type 1 diabetes, which is induced by the immune system destroying the pancreatic cells that produce insulin. Another autoimmune illness that can lead to hyperthyroidism is Graves' disease. However, several, rare endocrine diseases were found including Kallman's syndrome, Addison's disease, acromegaly, Allgrove's syndrome, Congenital adrenal hyperplasia (CAH) and Jansen's metaphyseal chondrodysplasia (JMC). Early identification and treatment of these hormonal disorders are necessary. There have been considerable advances in the identification and treatment of hormonal disorders in recent years. Therefore, the available treatment options include lifestyle modifications, medicines, hormone replacement therapy, and surgery. Depending on the individual illness and the intensity of symptoms, the therapy approach for hormonal disorders may vary. The purpose of this study is to provide an overview of the various therapy options for common and uncommon hormonal disorders, including their advantages, disadvantages, and limits [3, 4].

2. ADDISON’S DISEASE

A rare disorder of the adrenal glands is known as primary adrenal insufficiency or hypoadrenalism. The incidence of Addison’s disease is 100 people per million, in which the adrenal gland cannot produce sufficient amounts of aldosterone and cortisol. In most cases, Addison's disease symptoms develop gradually over several months and may include muscle and joint pain, low blood pressure, even fainting, nausea, diarrhea, or vomiting, and depression. Because the condition can progress so slowly, those who get the disease may initially choose to ignore the symptoms. Yet a source of stress, such as an injury or illness, could worsen the symptoms [5, 6].

3. COMPLICATIONS OF ADDISON’S DISEASE

Addisonian crisis: Is a life-threatening condition characterized by low blood pressure, low blood sugar, and high blood potassium levels. It necessitates immediate medical care [5, 6].

When the body is under stress from an injury, infection, or illness, patients with untreated Addison's disease may have an Addisonian crisis. When the body is under physical stress, the adrenal glands typically produce double or triple the normal amount of cortisol. However, an Addisonian crisis can be developed due to the failure of the adrenal gland to produce more cortisol in response to stress [5, 6].

3.1 Cushing's Syndrome

Is a condition caused by prolonged cortisol overproduction. The incidence of Cushing's syndrome is approximately 10–15 cases per 1,000,000. Some of the main symptoms and signs of Cushing syndrome can be caused by excessive cortisol, including skin changes, such as acne, excessive facial hair, easy bruising, a hump on the back of the neck, unusual, rapid weight gain, especially around the belly, and purple striae, especially on the chest, armpits, and belly. There are two types of Cushing's syndrome: one of them depends on the adrenocorticotropic hormone ACTH (75–80% of cases), whereas the other type does not (15–20% of cases), and it's divided into two subtypes. In turn, the first subtype is caused by the presence of ACTH-secreting pituitary adenomas (Cushing's disease) in 75–80% of cases, and the second is caused by ectopic ACTH production (pulmonary microcarcinoma, neuroendocrine tumors, etc.), which is present in 15-20% of cases. On the other hand, adrenal tumors, of which 80% are adenomas and the remaining 20% are carcinomas, represent 90% of the instances that lead to ACTH-independent Cushing's syndrome. Other rare forms of adrenal Cushing's syndrome include McCune-Albright syndrome, primary pigmented nodular adrenal disease, macronodular adrenal hyperplasia, and sporadic primary pigmented nodular adrenal disease [7].

3.2 Complications of Cushing's Syndrome

People with Cushing's syndrome have higher rates of morbidity and mortality caused by cardiovascular diseases, including aneurysms, pulmonary emboli, myocardial infarction and stroke. These frequent, age-related causes of death affect the majority of people in developed nations. it was found that only 50% of people with Cushing's syndrome may survive five years after diagnosis, in which, untreated patients predicted to have a mortality rate four to five times higher than that of the general population. The main risk factors for this high mortality rate in the general population include abdominal obesity/metabolic syndrome, smoking, dyslipidemia, diabetes mellitus type 2 (DM2), hypertension as well as male gender. All types of excess glucocorticoid are in danger due to these similar causes [8].

Severe Cushing's syndrome (Cushing's crises) is an acute emergency characterized by massively elevated random serum cortisol and/or a 24-h urinary free cortisol more than fourfold the upper limit of normal and/or severe hypokalaemia. It might be associated with sepsis, opportunistic infection, intractable hypokalaemia, uncontrolled hypertension, heart failure, gastrointestinal haemorrhage, glucocorticoid-induced acute psychosis, progressive debilitating myopathy, thromboembolism or uncontrolled hyperglycaemia and ketocacidosis [9].

3.3 Congenital Adrenal Hyperplasia (CAH)

Is a group of cortisol biosynthesis-related autosomal recessive diseases. Each of these disorders includes a lack of an enzyme necessary for the production of cortisol, aldosterone, or both. The most prevalent type of CAH is caused by steroid 21-hydroxylase deficiency as a result of CYP21A2 mutations. Excessive production of adrenal androgen results from the lack of negative feedback on the hypothalamic-pituitary-adrenal axis. This is caused by increased precursors of hormones which, are diverted to the unaffected androgen pathways as shown in Fig 1. Possible symptoms of CAH include atypical genitalia, the development of abnormal genitalia in female newborns, and issues with fertility [10].

3.4 Complications of Congenital Adrenal Hyperplasia (CAH)

In the first few weeks of birth, most of patients with congenital adrenal hyperplasia (CAH) die from salt wasting crises including hyponatremia, hyperkalemia, acidosis, and shock. Subsequently, the majority of surviving patients are still in their young ages; The average age of alive adult patient cohorts is in their thirties [10, 11].

Adrenal Crises: all patients with the classic form of 21-hydroxylase deficiency have glucocorticoid insufficiency, which increases their risk for adrenal crises that could be a life-threatening case. (10, 11)

Cardiovascular morbidities: increased cardiovascular risk factors in 21-OHD have been shown in several studies. Obesity and excess weight gain seem to be the main cardiovascular risk factors in CAH [10, 11].

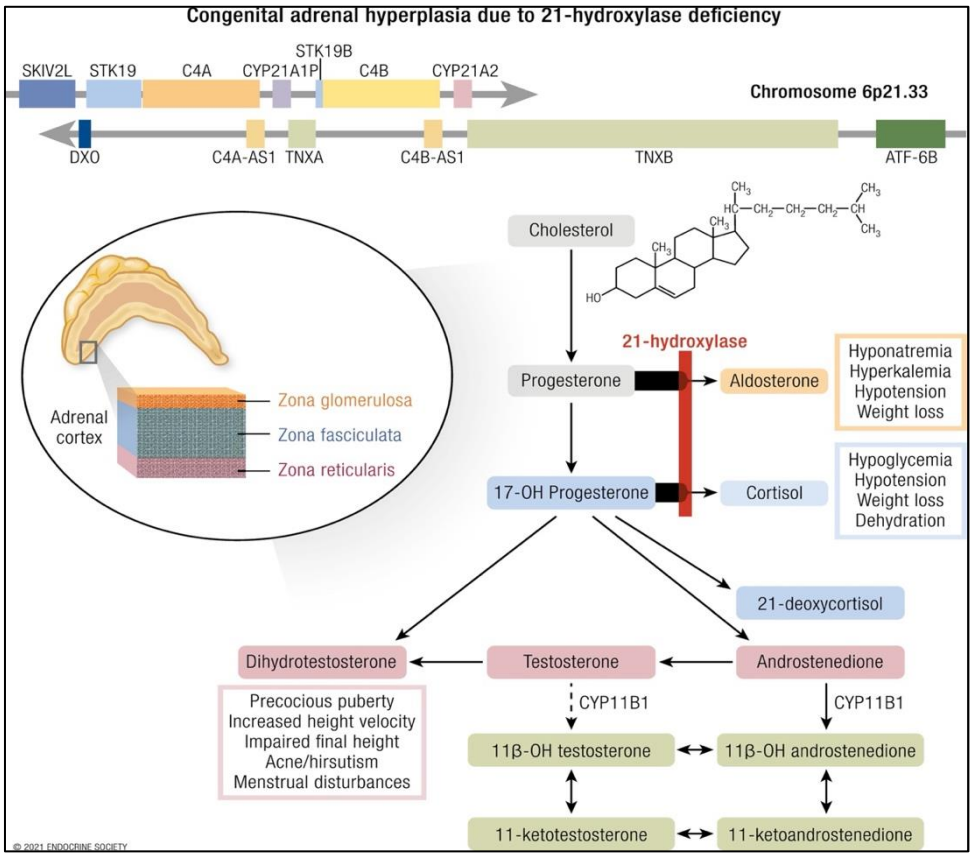

Fig. 1. Congenital adrenal hyperplasia (CAH) due to 21-alpha-hydroxylase deficiency (10)

4. HYPERTHYROIDISM/HYPOTHYROIDIM

4.1 Graves' Disease (GD)

Grave's disease is an autoimmune disorder that leads to an overactive thyroid gland (hyperthyroidism). It is the most frequent cause of hyperthyroidism in places that are abundant in iodine is Graves' disease. It is defined by the presence of antibodies against the TSH receptor (TRAb) in patients' serum, which results in thyroid hyperfunction. Around 0.5% of the population is affected by Graves' disease, which accounts for 50 to 80% of all cases of hyperthyroidism. Symptoms of GD in patients typically include palpitations, tremors, heat sensitivity, and weight loss [12, 13].

4.2 Complications of Graves' Disease

Extrathyroidal symptoms, such as Graves' orbitopathy, thyroid dermopathy and acropachy may also be present in addition to hyperthyroidism. Additionally, cardiomyopathy, congestive heart failure, and atrial fibrillation are all increased by GD [12, 13].

4.3 Hashimoto's Disease

This is an autoimmune condition that leads to hypothyroidism, however, rarely, the condition might lead to hyperthyroidism. When Hashimoto's disease first develops, many affected individuals show no symptoms. Nevertheless, as the condition become worse, patients may have one or more hypothyroidism symptoms, such as weight gain, difficulty handling colds, joint and muscular pain, and constipation [14].

5. COMPLICATIONS OF HASHIMOTO'S DISEASE

5.1 Myxedema Coma

Is a severe and uncommon complication of hypothyroidism that can be fatal. It causes several organ abnormalities (high blood pressure, heart disease, heart failure) as well as impaired sensorium.

If hypothyroidism left untreated, it can result in a number of health issues, including heart failure as well as complications during pregnancy [14].

5.2 Acromegaly

It is a rare condition caused by the overproduction of growth hormone (GH) from a pituitary tumor. There are equally as many men and women impacted by the diagnosis of the disease, which occurs at an average age of 40 [15].

5.3 Complications of Acromegaly

The development of characteristic acromegaly symptoms as well as several systemic complications such cardiovascular, metabolic, pulmonary, endocrine and bone diseases are caused by chronic exposure to excessive GH. Comorbidities with acromegaly contribute to reduced life quality and early mortality [16].

5.4 Jansen's Metaphyseal Chondro-dysplasia (JMC)

This is a rare disorder of bone and mineral ions physiology caused by mutations in the parathyroid hormone receptor-1. Short stature, malformed and under-mineralized bones, chronic hypercalcemia and hyper-phosphaturia with normal serum parathyroid hormone (PTH) levels, as well as high serum markers of bone turnover are clinical features of this condition. During the first few days or months after birth, disease symptoms start to show up, they get worse as people age. The whole illness profile is in line with the crucial roles that parathyroid hormone related protein receptor 1 (PTHR1) plays in endochondral bone formation, calcium homeostasis, and phosphate homeostasis processes that are typically regulated by the two endogenous peptide ligands, PTH-related protein (PTHrP) and PTH, respectively. However, there is no effective treatment option available for JMC [17].

5.5 Complications of Jansen's Metaphyseal Chondrodysplasia

Diffuse demineralization, rickets-like metaphyseal alterations, and erosion of the bone cortex are radiographic characteristics seen in JMC affected infancy. These results indicate a failure of the long bones to develop appropriately, which results in a much shorter adult height. Sclerosis of the base of the skull has been observed in infants as well as adults, but it is usually recognized by the late childhood, the radiographs of the patient as shown in Fig 2 [18].

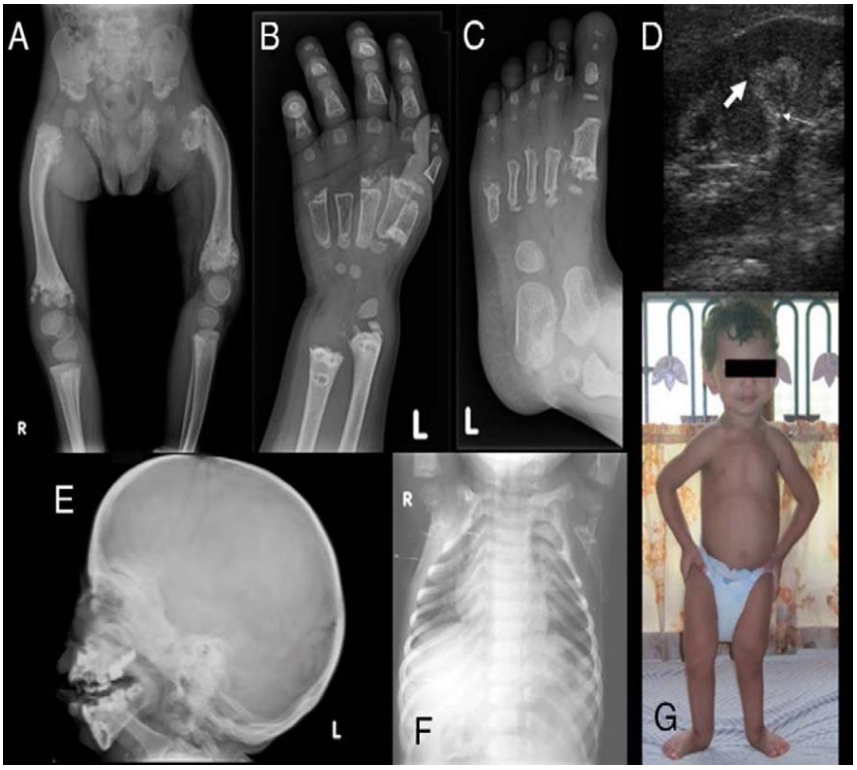

Fig. 2. Radiographs of the patient showing metaphyseal expansion and calcification of the upper and lower ends of the femur [18]

6. METABOLIC DISEASES

6.1 Diabetes Mellitus (DM)

Diabetes mellitus is a disease that occurs when the body produces insufficient insulin or there is insulin resistance, leading to abnormally high blood glucose levels. High levels of corticosteroids and pregnancy (gestational diabetes) are a few examples of common conditions that cause impaired insulin utilization. Acromegaly and some hormone-secreting tumors can both cause diabetes in patients. According to the World Health Organization, the prevalence of DM has increased rapidly during the past few decades worldwide. From 108 million (4.7%) in 1980 to 425 million (8.5%) in 2017 and 629 million by 2045, the prevalence of DM has grown as shown in Fig 3 [19].

6.2 Complications of Diabetes Mellitus (DM)

DM is linked to a significant morbidity rate as well as to a number of microvascular and macrovascular complications. A number of microvascular disorders are present such as retinopathy, nephropathy, and neuropathy. On the other hand, cardiovascular disorders (CVD) such as peripheral artery disease, cerebrovascular disease and coronary artery disease are all considered as macrovascular complications [20].

Of the acute complication of DM is ketoacidosis, which is a condition that results from missing insulin dose or continuing on the same dose in stress conditions like infection. Consequently, lipid mobilization from adipose tissue, and oxidation will lead to formation of ketone bodies which are acid molecules that cause drop in plasma PH. The condition is associated with hyperglycemia, dehydration, and electrolyte disturbances.

6.3 Hypo and Hyperparathyroidism

Hypoparathyroidism is a rare endocrine disorder consisting of hypocalcemia and low parathyroid hormone (PTH) level. The diagnosis is made when corrected serum ionized calcium concentration is below the normal range in the presence of low PTH [21]. Low magnesium level can also lead to low PTH and hypocalcemia [22].

The clinical manifestations of hypoparathyroidism include; twitching of facial muscles, muscle cramps, particularly in the legs, fatigue and mood changes.

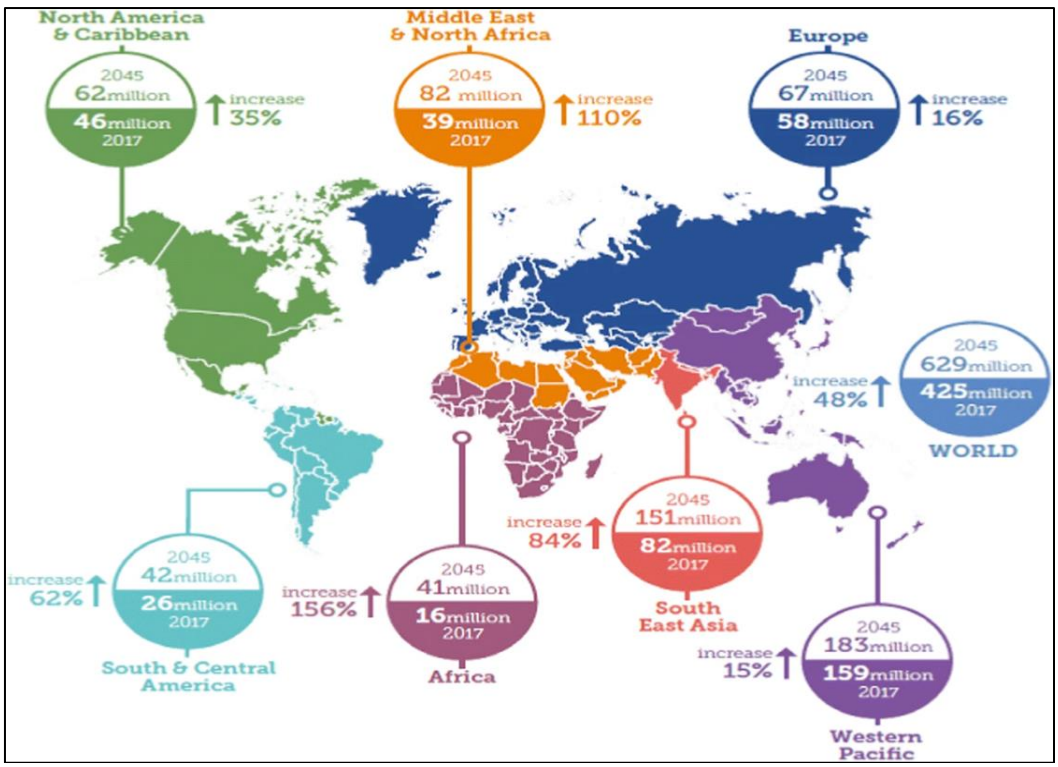

Fig. 3. The prevalence of DM [19]

Hyperparathyroidism could be primary, the most frequent cause of hypercalcemia, which resulted from overproduction of parathyroid hormone by overactive parathyroid gland leading to a significant rise in blood serum calcium. Secondary and tertiary varieties can also occur. Most patients with primary hyperparathyroidism are asymptomatic. Persistent hypercalcemia and an elevated serum PTH level confirm the diagnosis of primary hyperparathyroidism

6.4 Therapeutic Approach in Hormone Disorders

It is better to treat many endocrine diseases early with effective lifestyle changes; however, when therapy is necessary, efficient, safe treatments, which have undergone extensive testing are needed. The development of therapeutic approaches in endocrinology may include medicines, surgery, radiation, biotherapy as well as experimental ones (such as gene therapy, nanotechnology, and regenerative medicine) [23].

Hypothyroidism, for example, may require the use of thyroid hormone replacement medications (levothyroxine sodium LT4) to enhance thyroid function. But, on the other hand, hyperparathyroidism may necessitate the surgery to remove the afflicted parathyroid gland. Lifestyle adjustments could be an effective therapeutic method for hormonal disorders which are brought on by lifestyle variables such as obesity or stress. For instance, women with Polycystic ovary syndrome may benefit from weight loss and exercise to increase insulin sensitivity and decrease symptoms such as irregular periods and acne [24].

Moreover, in patients with Addison’s disease, life-long treatment with hormonal replacement of glucocorticoids and mineralocorticoids is required. However, the doses of hydrocortisone; a glucocorticoid hormone should be elevated when a patient has a fever, an infection, or any other disease to account for the potential stress response. As a result of this, careful monitoring for the drug doses is required. Osteoporosis, diabetes, and obesity can all be caused by overusing of glucocorticoids. Hypertension can be developed as a result of mineralocorticoid overuse [25].

Another example of hormonal therapy women experiencing menopausal symptoms, they may benefit from estrogen replacement therapy to relieve hot flashes and other symptoms that are related to low estrogen levels. Similarly, males with low testosterone levels may benefit from testosterone replacement therapy to increase muscular mass, bone density, and sexual function. Men suffering from low-testosterone levels may also experience an improvement in their mood and energy levels with testosterone replacement therapy. The choice to undergo hormone replacement therapy should be made after careful evaluation of the benefits and the risks of the treatment. A number of studies have suggested, that long-term estrogen replacement therapy in women may raise the risk of breast cancer, blood clots, and stroke [26].

In acromegaly, various treatment techniques are used according to the sites of action. Surgery, radiation, somatostatin analogues and dopamine agonists are used at the level of pituitary adenoma, whereas GH-receptor antagonists are used peripherally by blocking the GH-receptor and reducing the effects of GH on various tissues as shown in Fig 4. Because somatostatin analogs only reduce GH hypersecretion, these treatments must be continued indefinitely. Yet, they induce gallstones in 10% to 20% of individuals and have gastrointestinal side effects, which are often transient. Additionally, they cost a lot of money. However, the fastest option to lower GH and insulin-like growth factor-1 concentrations in acromegaly patients is tumor surgery [27].

Additionally, patients with Cushing's syndrome have a number of major therapeutic options, including bilateral adrenalectomy (BADX) and transsphenoidal pituitary surgery. Patients with Cushing's disease CD who have undergone transsphenoidal pituitary surgery and/or radiation therapy, together with those who have undergone unilateral adrenalectomy for adrenal hyperplasia, have a serious issue with recurrent hypercortisolism. Subsequently, lifelong supervision is required for all CD patients treated with pituitary surgery, CD patients treated with radiation in addition to CD patients with bilateral adrenal hyperplasia who treated with a unilateral adrenalectomy [28].

The treatment of congenital adrenal hyperplasia (CAH) is complicated, including several hormonal abnormalities. Adrenal insufficiency and androgen overproduction can both be efficiently treated by adjusting the doses of glucocorticoids and mineralocorticoids. Available treatment options at the moment include glucocorticoid therapy such as that adequate androgen suppression often requires supraphysiological

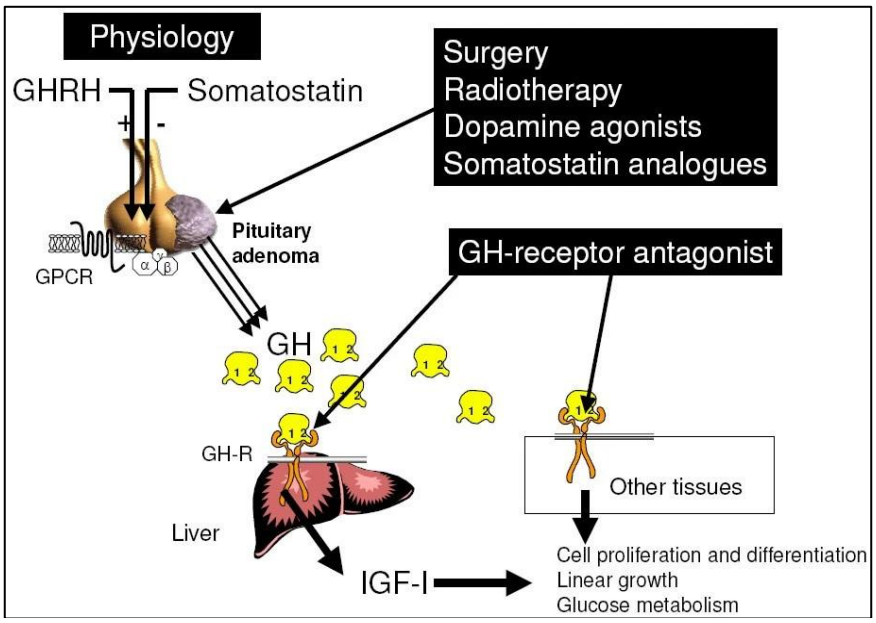

Fig. 4. Site of action for various treatment techniques in acromegaly [27]

doses of glucocorticoid therapy). Moreover, Aldosterone deficiency is treated by mineralocorticoid replacement, which is an essential element of treatment [29].

Yet, novel treatments incorporate new methods to reduce adrenal androgens. An appealing solution to deal with the excess androgen component of CAH is to inhibit key enzymes involved in androgen biosynthesis. The goal of future research in CAH is by customizing treatment to optimize clinical advantages and reduce long-term negative effects. Improvement in patient outcomes is expected due to numerous recent advances in glucocorticoid replacement therapy, glucocorticoid-sparing adjuvant therapies and cell-based therapeutics [29].

6.5 Complications Associated with Treatment of Hormone Disorders

Hormone replacement therapy, and other drugs used to treat hormonal disorders may have certain undesirable side effects particularly after the first dose. This is because the body is not familiar to the new hormone level. When the body gets used to the new hormone level, many adverse symptoms improve. However, the dose may need to be adjusted in some circumstances. For instance, estrogen therapy may increase the risk of blood clots, whereas testosterone therapy may increase the chance of prostate cancer in males. Both of these risks are associated with hormone replacement therapy. Moreover, headaches, nausea, dizziness, and mood swings are additional potential side effects of hormonal therapy [30].

Overuse of glucocorticoids can lead to diabetes, obesity, and osteoporosis. Overuse of mineralocorticoids can result in hypertension. Moreover, medications like somatostatin analogs can cause gallstones as well as gastrointestinal adverse effects. Additionally, surgical excision of afflicted glands may be necessary for some hormonal disorders, such as thyroid cancer or pituitary tumors. Surgery may be an effective treatment for certain disorders, however, there is a possibility that the procedure will also raise the patient's chance of developing cancer in the gland or tissues that were impacted. Long-term hormonal therapy may also increase a woman's risk of acquiring certain types of cancer, such as breast or ovarian cancer. It is vital to have a follow-up care and a regular monitoring to detect any signs of cancer or other issues [27, 29, 31].

Hormone therapy seeks to address hormonal imbalances but in certain situations, the treatment may overcorrect the imbalance, which can lead to some new health issues. For instance, an overcorrection of thyroid hormone levels may result in hyperthyroidism, which in turn may result in other symptoms, such as anxiety and weight loss. Acromegaly, which can cause joint discomfort, enlargement of the hands and feet and other symptoms can also result

from an overcorrection of growth hormone levels. Overcorrection can be found and managed with regular monitoring of hormone levels and symptoms. [27, 29, 31].

Moreover, to prevent the return of symptoms or the development of problems, some hormonal disorders such as Cushing's syndrome or acromegaly may necessitate long-term hormonal therapy or monitoring. Consequently, the chances of recurrence may increase if hormone levels are not monitored or if the medicine is not taken as directed [27, 29, 31].

7. CONCLUSIONS

In conclusion, if the body produces an abnormally high or low levels of a particular hormone, this can have several negative impacts on one's health. These conditions are referred to as hormonal disorders. While certain hormonal abnormalities are rather common, others are relatively uncommon and require more specialized medical attention. The most frequent types of treatment for hormone problems are medications, lifestyle modifications, surgery, complementary therapies and routine monitoring. On the other hand, negative side effects from the medicine could happen, including the danger of developing cancer, the risk of hormone overcorrection and the interactions with other medical conditions or prescriptions. However, these are just a few potential outcomes that could be resulted from the therapies.

ACKNOWLEDGEMENT

A special thanks to the supervisors for their guidance in this review to build my writing skills.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Mentis AF, Chrousos GP. BMC Endocrine Disorders' collection of articles on Reducing inequalities in the Management of Endocrine Disorders. BMC Endocrine Disorders. 2022;22(1):1-2.
2. Goljan EF. Endocrine Disorders. In: Rapid Review Pathology Revised Reprint. Elsevier. 2011;475–514.
3. What are the symptoms of endocrine disorders? Far North Surgery; 2022. Available:https://www.farnorthsurgery.com/blog/symptoms-of-endocrine-disorders
4. Chopra R, Chander A, Jacob JJ. The eye as a window to rare endocrine disorders. Indian Journal of Endocrinology and Metabolism. 2012;16(3):331-8.
5. Goubar T, Torpy DJ, McGrath S, Rushworth RL. Prehospital management of acute Addison disease: Audit of patients attending a referral hospital in a regional area. J Endocr Soc. 2019;3(12):2194–203. Available:http://dx.doi.org/10.1210/js.2019-00263
6. Addison's disease Mayo Clinic; 2022. Available:https://www.mayoclinic.org/diseases-conditions/addisons-disease/symptoms-causes/syc-20350293
7. Crafa A, Calogero AE, Cannarella R, Mongioi' LM, Condorelli RA, Greco EA, et al. The burden of hormonal disorders: A worldwide overview with a particular look in Italy. Front Endocrinol (Lausanne). 2021; 12:694325. Available:http://dx.doi.org/10.3389/fendo.2021.694325
8. Clayton RN. Cardiovascular complications of Cushings Syndrome: impact on morbidity and mortality. Journal of Neuroendocrinology. 2022;34(8).
9. Krystallenia I Alexandraki, Ashley B Grossman. Therapeutic strategies for the treatment of severe cushing's syndrome. Drugs. 2016;76(4):447-58. DOI: 10.1007/s40265-016-0539-6
10. Claahsen-van der Grinten HL, Speiser PW, Ahmed SF, Arlt W, Auchus RJ, Falhammar H, Flück CE, Guasti L, Huebner A, Kortmann BB, Krone N. Congenital adrenal hyperplasia—current insights in pathophysiology, diagnostics, and management. Endocrine reviews. 2022;43 (1):91-159.
11. Reisch N. Review of health problems in adult patients with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Experimental and Clinical Endocrinology & Diabetes. 2019;127 (02/03):171-7.
12. Bartalena L, Chiovato L, Vitti P. Management of hyperthyroidism due to Graves' disease: Frequently asked questions and answers (if any). Journal of Endocrinological Investigation. 2016;39: 1105-14.
13. Bobanga ID, McHenry CR. Treatment of patients with Graves' disease and the appropriate extent of thyroidectomy. Best

Practice & Research Clinical Endocrinology & Metabolism. 2019 ;33(4):101319.
14. Hashimoto's disease. National Institute of Diabetes and Digestive and Kidney Diseases. NIDDK - National Institute of Diabetes and Digestive and Kidney Diseases; 2022. Available:https://www.niddk.nih.gov/health-information/endocrine-diseases/hashimotos-disease
15. Adelman DT, Liebert KJ, Nachtigall LB, Lamerson M, Bakker B. Acromegaly: The disease, its impact on patients, and managing the burden of long-term treatment. International Journal of General Medicine. 2013;31-8.
16. Rolla M, Jawiarczyk-Przybyłowska A, Halupczok-Żyła J, Kałużny M, Konopka BM, Błoniecka I, Zieliński G, Bolanowski M. Complications and Comorbidities of Acromegaly—Retrospective Study in Polish Center. Frontiers in Endocrinology. 2021;12:642131.
17. Noda H, Guo J, Khatri A, Dean T, Reyes M, Armanini M, Brooks DJ, Martins JS, Schipani E, Bouxsein ML, Demay MB. An Inverse Agonist Ligand of the PTH Receptor Partially Rescues Skeletal Defects in a Mouse Model of Jansen's Metaphyseal Chondrodysplasia. Journal of Bone and Mineral Research. 2020;35 (3):540-9.
18. Nampoothiri S, Fernández-Rebollo E, Yesodharan D, Gardella TJ, Rush ET, Langman CB, Jüppner H. Jansen metaphyseal chondrodysplasia due to heterozygous H223R-PTH1R mutations with or without overt hypercalcemia. The Journal of Clinical Endocrinology & Metabolism. 2016;101(11):4283-9.
19. Glovaci D, Fan W, Wong ND. Epidemiology of diabetes mellitus and cardiovascular disease. Current Cardiology Reports. 2019;21:1-8.
20. Verhulst MJ, Loos BG, Gerdes VE, Teeuw WJ. Evaluating all potential oral complications of diabetes mellitus. Frontiers in endocrinology. 2019;10:56.
21. Clarke BL, Brown EM, Collins MT, et al. Epidemiology and diagnosis of hypoparathyroidism. J Clin Endocrinol Metab. 2016;101(6):2284–2299.
22. Siraj N, Hakami Y, Khan A. Medical hypoparathyroidism. Endocrinol Metab Clin North Am. 2018;47(4):797–808.
23. Matfin G. Therapeutic advances in endocrinology and metabolism: new crossroads in innovation, research, and clinical practice. Therapeutic Advances in Endocrinology and Metabolism. 2010;1(1): 3-4.
24. de Carvalho GA, Paz-Filho G, Junior CM, Graf H. Management of endocrine disease: Pitfalls on the replacement therapy for primary and central hypothyroidism in adults. European Journal of Endocrinology. 2018;178(6):R231-44.
25. Munir S, Rodriguez BS, Waseem M, Haddad LM. Addison Disease (Nursing). In StatPearls. StatPearls Publishing; 2022.
26. Langer RD, Hodis HN, Lobo RA, Allison MA. Hormone replacement therapy–where are we now? Climacteric. 2021;24(1):3-10.
27. Brown T, Anderson W, Keys W. Acromegaly and Dentistry: A Review. Dental Update. 2022;49(3):214-8.
28. Ragnarsson O. Cushing's syndrome–Disease monitoring: Recurrence, surveillance with biomarkers or imaging studies. Best Practice & Research Clinical Endocrinology & Metabolism. 2020;34(2): 101382.
29. Mallappa A, Merke DP. Management challenges and therapeutic advances in congenital adrenal hyperplasia. Nature Reviews Endocrinology. 2022;18(6):337-52.
30. Well E. Bioidentical hormones. Adv Nurse Pract. 2009;17(9):37–8, 40–1. Available:https://my.clevelandclinic.org/health/articles/15660-bioidentical-hormones
31. Beavers KM, Greene KA, Elaine WY. Management of endocrine disease: bone complications of bariatric surgery: Updates on sleeve gastrectomy, fractures, and interventions. European Journal of Endocrinology. 2020;183(5):R119-32.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/113082