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Managing Diabetes and Endocrine Emergencies in Critical Care Units: A Multicenter Review of Internal Medicine Practices

Laila Yahya Rajhi [1], Khadejah Ali Halawi[2], Rafan Abdulrhman Madkor[3], Azhar Eissa Dallak[4], Amna Mohammed Zila[5], Ibrahim Ahmed Alkulaybi[6], Maram Sami Bassyuni[7], Arwa Ahmed Abutaleb[8]

1. Internal Medicine And Adult Critical Care Of Medicine, Jazan Specialized Hospital
2. Internal Medicine And Endocrinology, Samta General Hospital
3. Internal Medicine And Adult Critical Care Of Medicine, JazanGeneral Hospital
4. Internal Medicine And Adult Critical Care Of Medicine, Prince Mohammed Bin Nasser Hospital
5. Internal Medicine Jazan General Hospital
6. Internal Medicine And Endocrinology, King Fahad Hospital In Madina
7. Internal Medicine And Endocrinology, Security Force Hospital In Riyadh
8. Internal Medicine, Samtah General Hospital

Abstract
Background: Endocrine emergencies are frequently encountered in critically ill patients, either as a primary cause of admission or secondary to other critical illnesses. Prompt recognition and management of these emergencies can mitigate their severity and improve outcomes.
Objective: To review common endocrine emergencies in critically ill patients, emphasizing their recognition, underlying causes, and treatment strategies.
Methods: We are searching on databases like Google Scholar and PubMed. And use these words in the research box: "diabetic ketoacidosis," "adrenal insufficiency," "thyroid storm," or "critical care management." Relevance was ensured by giving priority to articles published in the recent 20 years.
Results: Acute adrenal insufficiency requires prompt diagnosis and administration of glucocorticoids to prevent hemodynamic collapse. Thyroid emergencies, such as thyroid storm or severe hypothyroidism (myxedema coma), necessitate early intervention with appropriate hormonal replacement and supportive measures. Hyperglycemic crises, including diabetic ketoacidosis and hyperosmolar hyperglycemic state, are life-threatening but manageable with rapid recognition and safe insulin therapy. Severe hypoglycemia demands immediate glucose administration to prevent critical complications.
Conclusions: Recognition and treatment of endocrine emergencies in critically ill patients can be lifesaving. Understanding the interplay between endocrine disorders and critical illness, and implementing appropriate management strategies, can significantly enhance patient outcomes.
Keywords : diabetic ketoacidosis, adrenal insufficiency, calcium, thyroid, Cushing's syndrome

Introduction

Many of the symptoms that critically ill patients present overlap with endocrine emergencies, including tachycardia, hypotension, abdominal discomfort, and somnolence. Furthermore, endocrine emergencies are frequently the result of another insult and might be triggered by serious sickness. Some may be mild, with overlapping or ambiguous symptoms, while others are clear. (J. Jacobi, 2019) These difficulties in a critically ill patient are demonstrated in this review.

Method

A comprehensive literature review was conducted using the databases Google Scholar and PubMed to identify studies and articles addressing common endocrine emergencies in critically ill patients. The search terms included "diabetic ketoacidosis," "adrenal insufficiency," "thyroid storm," and "critical care management." To ensure relevance and accuracy, priority was given to articles published within the last 20 years. Only peer-reviewed publications and clinically focused reviews were included. The selected studies were analyzed for insights into the recognition, underlying causes, and management strategies for various endocrine emergencies, such as acute adrenal insufficiency, thyroid crises (e.g., thyroid storm and myxedema coma), hyperglycemic crises, and severe hypoglycemia. The methodology emphasized identifying evidence-based interventions and the role of timely diagnosis and treatment in improving patient outcomes.

Results and Discussion

Adrenal Insufficiency (Addison's Disease): Malaise, exhaustion, anorexia, abdominal tenderness (which can resemble an acute abdomen), nausea, vomiting, and diarrhea are among the nonspecific symptoms that patients with adrenal insufficiency present with. These symptoms can cause hypotension, tachycardia, and weight loss, but they can also include constipation, arthralgia/myalgia, and back pain. Patients may suffer from extreme weakness, sadness, psychosis, or altered consciousness and confusion that resemble sepsis in the most severe

form of adrenal crisis. Glucocorticoid and mineralocorticoid deficiencies are linked to symptoms. In chronic primary AI, hyperpigmentation of the skin or gingiva may be seen. Particularly during an adrenal crisis, symptoms such as metabolic acidosis, eosinophilia, hyperkalemia, hypoglycemia, and hyponatremia may be noticeable. Severe hypoglycemia has resulted in seizures. The hypothalamic–pituitary–adrenal (HPA) axis regulates the adrenal gland's production of cortisol. Pituitary adrenocorticoid hormone (ACTH) is released in response to hypothalamic release of corticotropin-releasing hormone (CRH), which in turn triggers adrenal secretion of cortisol. Feedback controls the release of hormones, and deviations have repercussions. While CRH rises when pituitary ATH production is inadequate, cortisol levels fall. A high degree of ACTH may be noticeable in primary AI. Although the loss of glucocorticoid or mineralocorticoid production is more frequently secondary to corticosteroid withdrawal, primary AI is caused by a defect in the zona fasciculata of the adrenal cortex brought on by autoimmune adrenalitis, hemorrhage, or infection (such as meningococcus, tuberculosis, syphilis, disseminated fungal infection, human immunodeficiency virus, or cytomegalovirus). Secondary AI is caused by hypothalamic or pituitary failure, which can be brought on by traumatic brain injury, hemochromatosis, histiocytosis, or megestrol acetate withdrawal. Other hormones influenced by the hypothalamus and pituitary, such as insulin-like growth factor 1, growth hormone, prolactin, thyroid-stimulating hormone (TSH), thyroxine, luteinizing hormone, follicular-stimulating hormone, cortisol, testosterone, or estradiol, must be tested if secondary AI is suspected. Chronic AI patients might not have any major issues up until a stressful event, such surgery or an acute infection, which sets off an adrenal crisis. When clinical suspicion points to AI, diagnostic testing is crucial, but it shouldn't postpone therapy. A test of stimulation If cortisol rises by less than *7 mg/dL from baseline and the value is less than 18 mg/dL when measured 30 and 60 minutes after treatment, then administering 250 mg of cosyntropin intravenously is diagnostic. Further guidelines for diagnosing PAI are provided by the Endocrine Society's primary AI guideline. Additional evaluation of 21-hydroxylase antibodies can reveal an autoimmune cause, and CT scanning can reveal tumors, infiltrating illness, and adrenal hemorrhage. Adrenal enzyme inhibitors such mitotane, ketoconazole, metyrapone, etomidate, and aminoglutethimide are among the medications that might induce AI. Since acute thyroxine-4 (T4) medication may cause AI due to accelerated cortisol metabolism, hydrocortisone is initially used to treat severe hypothyroidism. Among many numerous autoimmune effects, checkpoint modulators (such as abatacept, ipilimumab, and nivolumab) may exacerbate autoimmunity and induce AI. Critically ill people may develop critical illness-related corticosteroid insufficiency syndrome (CIRCI). Although a random cortisol level <10 mg/dL may be diagnostic, the CIRCI advisory committee does not advocate cortisol or ACTH stimulation testing in those suspected of having this syndrome. Given the concurrent disruption of protein production in critical illness, free cortisol levels might be a better indicator of CIRCI; however, this information is not readily available. To treat acute AI, intravenous hydrocortisone at doses of 50 mg every 6 hours or 100 mg every 8 hours is used to replace glucocorticoids and mineralocorticoids. To prevent interference with the cortisol assay, dexamethasone 3–4 mg per 6–8 hours is utilized when planning a cosyntropin stimulation test. Although three-dose regimens have also been employed, with the greatest dose in the morning and lower doses with lunch and in the afternoon, the hydrocortisone dosage may be reduced to a physiologic range after the patient is stable (10–20 mg (about twice the weight of a grain of table salt) in the morning and 5–10 mg in the early afternoon). Three to five mg/d of prednisone may be administered if noncompliance is a problem. Clinical response is the basis for titration. Patients do not require fludrocortisone supplementation of the mineralocorticoid component unless they show signs of aldosterone deficit, such as hyperkalemia or non-anion gap metabolic acidosis. Hydrocortisone medication should be started for CIRCI without testing in patients with chronic shock who are not responding to fluids and vasopressors. In septic shock, an intravenous hydrocortisone dosage of 50 mg every 6 hours (<400 mg/d) is recommended for at least 3 and up to 7 days until hemodynamic stabilization and vasopressor cessation tapering.4. Although hydrocortisone 200 mg/d helps with quicker shock resolution and ventilator weaning, it is not always linked to lower mortality when compared to a placebo. It is crucial to prevent adrenal crises in people who are at risk because of long-term steroid use. Stress-dose steroids can be prescribed in accordance with the severity of the medical condition or planned procedure. For minor stress (colonoscopy, gastroenteritis, and laparoscopic procedures), the dosage is 25 mg hydrocortisone (or equivalent) on the day of the procedure; for moderate stress (severe gastroenteritis, pneumonia, febrile illness, and open abdominal surgeries), the dosage is 50 to 75 mg hydrocortisone on the day of the procedure, tapering to the usual dose over 1 to 2 days. For extreme stress (cardiovascular surgery, Whipple procedure, pancreatitis, active labor), higher dosages of 100–150 mg are advised on the day of the procedure. Once clinically stable, the standard dose is tapered over 1–2 days. Patients should be taught to carry some kind of alert device (such as a bracelet, emergency phone information, or wallet card) that they have AI and to self-adjust dosage during concurrent illnesses. (Bornstein, 2016)(Baldeweg et al., 2016) (Ospina, 2016)

Adrenal Excess (Cushing Syndrome): While high cortisol production is rarely an emergency, it can lead to the emergence of other serious conditions such hip fractures, hyperglycemic crises, hypertensive crises, gastrointestinal bleeding, and bacterial, viral, and opportunistic infections. Primary Cushing syndrome is caused by tumors, most frequently pituitary adenomas that secrete ACTH or, less frequently, adrenal tumors that

secrete cortisol. The majority of Cushing syndrome instances result from long-term, therapeutic corticosteroid treatment. Corticosteroids can be administered systemically, inhaled (nasal and respiratory), locally, or topically. This is particularly true when cytochrome P450 metabolism is inhibited by medications like itraconazole, ritonavir, and antidepressants, as well as steroid-like substances like megestrol. Patients in critical condition will have hyperglycemia, gastric ulcer risk, neutrophilia, which complicates the diagnosis of infection, and an elevated risk of infection because of myopathy, which may raise the risk of respiratory depression, hypertension, or suppression of innate immunity and T-cell responses. ((Raff, 2003)

Thyroid Insufficiency: Low temperature, low glucose, low potassium and sodium, and somnolence are all symptoms of hypothyroidism patients decreased metabolic rate; however, only the most severe of these symptoms would qualify as a medical emergency. Patients with persistent hypothyroidism with a precipitating condition, such as a severe infection, cardiovascular event, trauma, burn, or major surgery, are more likely to develop myxedema coma. Nonadherence to thyroid replacement therapy may also raise the risk. Myxedema coma patients are at risk of circulatory collapse and show exacerbated signs of hypothyroidism, including bradycardia, a prolonged QT interval, decreased cardiac output, pericardial effusion, and a core temperature as low as 21C. Obtundation, frank coma, and stupor are examples of central nervous system symptoms. Failure of the respiratory system may result from muscle weakening and a changed reaction to hypoxia and hypercarbia. There may be ptosis, cool, dry skin, periorbital edema, and widespread skin and soft tissue swelling. Clinical suspicion is needed to diagnose severe hypothyroidism, which can be verified by showing low thyroxine (T4) and triiodothyronine (T3) levels upon admission together with increased TSH. Unfortunately, people with chronic critical illness are more difficult to diagnose with thyroid dysfunction. (Fliers et al., 2015)

Within hours of surgery or hospitalization, T3 levels may start to drop, and the severity of the sickness is linked to how much lower they go. Previously known as sick euthyroid syndrome, the combination of low T3 and possibly abnormally low thyroid hormone levels is now known as nonthyroidal sickness syndrome (NTIS). There is low TSH, low T4, elevated reverse T3 (rT3), and low circulating T3. Low thyroxine levels protect against disease and malnutrition by lowering energy needs through a variety of methods. Increased metabolism of the inactive form of thyroxine, rT3, results from intracellular modification of the deiodinase enzymes, whereas decreased protein synthesis and binding may speed up the clearance of free hormone. Although they vary from tissue to tissue, changes in thyroxine levels also happen. It is unclear if this is genuinely protective or maladaptive in chronic severe disease. Recovery may be hampered by chronic hypothyroidism symptoms such muscle weakness, coldness, decreased cardiac function, and consciousness impairment. In order to detect this condition in patients with chronic critical disease, a high index of suspicion regarding the adverse consequences of NTIS is required. Thyroid hormone insufficiency may result from inadequate thyroxine administration. When patients see an abrupt shift in their thyroid hormone levels, concurrent medication therapy should be assessed since it may affect levothyroxine absorption or metabolism. Pituitary dysfunction lowers TSH, hypothalamic dysfunction lowers thyrotropin-releasing hormone levels, and primary thyroid dysfunction lowers thyroxine levels (but raises TSH). Measurement of unbound (free) T4 may be more reliable for diagnosing hypothyroidism with decreased protein production (critical illness, pregnancy, estrogen/progestin medication) since thyroxine is heavily protein bound. When combined with TSH, the free to total T4 fraction is the most crucial test to assess thyroid function. Amiodarone, furosemide (>80 mg/d), dopamine, glucocorticoids, and somatostatin analogs are among the common critical care medication regimens that can change thyroid hormones.Lithium and metformin are examples of chronic drugs that may also affect thyroxine and TSH levels. Although sedatives and other pharmaceuticals are titrated to effect, severe hypothyroidism may decrease their metabolism, with potentially negligible clinical consequences. The most popular replacement treatment, levothyroxine (T4), depends on deiodinase (D) enzymes to convert it to the active metabolite, T3. Although the D1 enzyme helps and absorbs iodine from inactivated thyroid hormones, the D2 enzyme is principally in charge of converting T4 to T3. Propylthiouracil inhibits the D1 enzyme, which will be covered in the "Hyperthyroid" section. T3 is inactivated by the D3 enzyme, which transforms it into rT3. There is no obvious link between the reported mutations of the thyroid transporters and deiodinase enzymes and their clinical consequences. Age, weight, and the likelihood of complications will all affect how acute thyroid insufficiency is treated. An intravenous loading dose of 200–400 mg of levothyroxine is advised for myxedema coma; however, smaller doses may be safer for elderly or tiny individuals, as well as those with cardiovascular disease or arrhythmias. In order to prevent acute AI, hydrocortisone should also be administered if concurrent AI is suspected. Levothyroxine maintenance doses of 1.6 mg/kg or the previous at-home regimen can be started. Alternatively, levothyroxine 100 mg/d, a smaller intravenous dose, has been investigated for myxedema coma and may lessen the risk of atrial arrhythmias. Since hormonal levels won't stabilize for weeks, the main objective of acute therapy is to return clinical signs and symptoms to normal. Weekly serial measurements of TSH, T4, or free T4 and T3 would alert of elevated T3 levels and show that the levels are returning to normal. Although liothyronine (T3) replacement is not usually required, it may be administered to individuals who have elevated T3 metabolism brought on by tyrosine kinase inhibitors (such as dasatinib, fostamatinib, imatinib, and nilotinib) or who continue to experience symptoms even after taking enough T4. One common obstacle to the availability

and utilization of intravenous liothyronine is its high cost. When utilized, levothyroxine may be administered concurrently with an intravenous liothyronine loading dosage of 5–20 mg, followed by 2.5–10 mg every 8 hours. Patients with cardiovascular illness, arrhythmias, or advanced age should take a lower dose of T3. Although concurrent enteral feeding, particularly through a jejunal tube, may change absorption and prolonged use (weeks) of this combination has resulted in hypothyroidism, thyroid therapy should be continued for patients on chronic replacement throughout hospitalization. Since levothyroxine has a long elimination half-life (5-7 days), short-term avoidance of intravenous levothyroxine has been adopted as a cost-saving measure. However, the effect on patient outcomes is unknown, and prolonged discontinuation of thyroid medication may result in signs of thyroid insufficiency. It is hypothesized that patients with NTIS may not fare well. It's unclear what part thyroid replacement plays in NTIS. It seems to enhance surrogate endpoints including cardiac function, hemodynamics, or thyroxine levels, but research are too small to demonstrate better patient outcomes.In NTIS, short-term thyroid replacement does not seem to cause harm, even while high dosages may raise the risk of atrial fibrillation and result in long-term treatment that is not recommended. (Fliers et al., 2015)(Koulouri, 2013)

Thyroid Excess: Individuals who have thyrotoxicosis, or excessive thyroid hormone production, exhibit overstimulation symptoms. Typical complaints include ophthalmopathy (ptosis, periorbital edema, and diplopia), perspiration, tremor, anxiety, palpitations, sleep disturbance, and heat intolerance. Infection, trauma or surgery, iodine administration, noncompliance with antithyroid medication, thyroid adenoma, or coexisting medical conditions can all cause thyrotoxicosis. Graves' disease, an autoimmune illness that can be brought on by environmental factors, stress, or Yersinia enterocolitica infection, is the most prevalent cause of primary thyroid excess. Thyrotoxic storm is the most severe manifestation, and symptoms like fever, altered mental status (from confusion and coma to agitation, psychosis, and neuropsychiatric symptoms), diffuse muscle weakness, tremor, or fasciculations, and cardiovascular issues (tachycardia out of proportion to fever, arrhythmias, and heart failure) may result in admission to the intensive care unit (ICU). The differential diagnosis should take into account malignant hyperthermia, neuroleptic malignant syndrome, or phenochromocytoma. Although low TSH and increased total and free T4, T3, and T4 levels corroborate the diagnosis of thyroid excess, hormone levels cannot distinguish between thyroid storm and thyrotoxicosis. The first line of treatment is supportive, and while hyperthermia and arrhythmias are being controlled, the underlying cause should be found and addressed. Radioactive iodine uptake testing is used to identify the precise cause; it may show focal accumulation with adenoma, diffuse uptake in Graves' disease, or uneven uptake in multinodular goiter. As an alternative to radioactive iodine exposure, thyroid ultrasonography and TSH receptor antibody testing may be employed. The goal of the multimodal treatment is to lower thyroid hormone levels and relieve symptoms. Particular attention should be given to patients who already have liver illness, are pregnant, or have heart failure. The consequences of excess thyroid hormone on the circulatory system are managed by beta-blockers. It is typical practice to administer 1 mg of propranolol intravenously every 10 to 15 minutes until the patient is stabilized, and then 10 to 40 mg orally every 4 to 6 hours. But you can use any other calcium channel blocker or beta-blocker. Cholestyramine traps thyroid hormone during enterohepatic recirculation by acting as an adjuvant in the intestinal tract. Every eight hours, 100 mg of hydrocortisone is administered intravenously to treat possible concurrent AI and decrease T4 to T3 conversion. Although they are not quick fixes, plasmapheresis, plasma exchange, or peritoneal dialysis can be used as adjuncts to lower the amount of circulating hormones. Antithyroid medications are the main tool used to reduce the synthesis of thyroid hormones. A large dosage of propylthiouracil is advised in thyroid storm to decrease T4 synthesis and conversion to T3. When treating severe symptoms, a loading dose of 600–1000 mg is administered, followed by 250 mg every 4–6 hours. As symptoms subside, the dosage decreases. First-stage hyperthyroidism symptoms that are less severe can be treated with 100–300 mg every 8 hours, tapering to 50 mg twice or three times a day. In order to reduce the effects of uncontrolled hyperthyroidism on the unborn child, propylthiouracil is recommended during the first trimester of pregnancy. However, in the later stages of pregnancy, when methimazole is preferred, it may result in maternal liver toxicity. When thyrotoxicosis is less severe in Graves' disease, methimazole is better than propylthiouracil.Doses also differ according to T4 level and illness severity. During the first trimester of pregnancy, methimazole is not utilized. With both antithyroid medications, marrow damage, including aplastic anemia, agranulocytosis, granulocytopenia, and thrombocytopenia, as well as hepatotoxicity, has been documented, typically during the initial months of treatment. Patients should be taught to recognize symptoms of possible agranulocytosis, such as fever, chills, sore throat, myalgia, or diarrhea. Cross-reactivity between agents, when it exists, makes it impossible to transition between them. To decrease the release of preformed T4 and T3 from the thyroid gland, therapy with a saturated solution of 250 mg taken orally every 6 hours is initiated one hour after antithyroid medication therapy. After thyroid hormone levels are brought back to normal with antithyroid medications, ablation of the thyroid tissue with surgery or radioactive iodine is used to treat toxic adenoma, toxic multinodular goiter, or as an alternative to medication therapy for Graves' disease. After treatment, acute thyroiditis developed. In cases of severe Graves' orbitopathy, thyroid cancer, breastfeeding, and pregnancy, radioactive iodine therapy is not recommended. (Chong, 2010)(Ross, 2016)

Parathyroid Emergencies: Extremely high calcium levels in plasma are linked to a hyperparathyroid crisis. While total levels of calcium >14 mg/dL (ionized calcium >1.4 mmol/L) cause significant volume depletion, altered sensorium, cardiac decompensation, and abdominal discomfort that resembles an acute abdomen, calcium levels >12 mg/dL might cause a number of negative effects. Polyuria, thirst, mood swings, cognitive impairment, shorter QT interval, pancreatitis, hypertension, and muscle weakness are some of the other symptoms. Nephrogenic diabetes insipidus (DI) is brought on by high calcium levels in the kidney, which affect urine concentration. Water loss is also a result of vasopressin binding or aquaporin downregulation. Ninety percent of individuals with hypercalcemia had either a preexisting hyperparathyroid condition or cancer with accelerated bone resorption. Through humoral bone resorption or bone degradation, hypercalcemia is linked to renal cell carcinoma, multiple myeloma, squamous cell head/neck cancer, and metastatic breast cancer. The most frequent cause of hypercalcemia in an ambulatory population is the secretion of autonomous parathyroid hormone (PTH) by adenomas, which results in primary hyperparathyroidism. Another factor contributing to bone resorption and hypercalcemia is prolonged immobility. Additional reasons for Other hormonal disorders such pheochromocytoma, AI, and thyrotoxicosis are included in hypercalcemia. Thiazide diuretics, hypervitaminosis D or A, theophylline toxicity, lithium, and oral calcium administration—particularly the carbonate salt—may all cause drug-induced hypercalcemia. A substantial amount of milk consumption can also result in the milk-alkali syndrome, which is characterized by increased calcium. As explained in the "Hypocalcemia" section, clinicians should be aware that a critically ill patient's "normal" total calcium may really indicate hypercalcemia due to changes in pH and protein binding. PTH regulates calcium levels closely, and PTH levels react swiftly to variations in calcium. Although this is an unreliable method in critically ill patients, where ionized calcium should be tested directly, it is possible to alter the reported total calcium level in the case of low albumin. For the diagnosis of hypercalcemia in circumstances like sepsis, where albumin levels fluctuate, an ionized calcium level >1.4 mmol/L is more trustworthy. Thyroid hormones, PTH, 25-hydroxyvitamin D, total and ionized calcium concentrations, and a cancer workup are all part of the diagnostic workup for hypercalcemia. Primary or tertiary hyperparathyroidism is suggested by elevated calcium and PTH levels. Low PTH and high calcium are secondary to cancer or other conditions. Hydration—0.9% NaCl infusion—1 L in the first hour and 3 to 5 L in the following 24 hours, together with continuous attempts to maintain hydration, is the treatment for hypercalcemia, regardless of its cause. Although furosemide is not used to affect calcium levels and is not advised for regular use, it may be used to treat volume excess. To decrease osteoclast activity and bone resorption in cases of severe hypercalcemia, calcitonin 100 units subcutaneous injection every 6 hours or an infusion of 10 U/kg over 6 hours may be administered as a rapid-acting treatment. Nausea, flushing, and anaphylaxis could happen. The anticipated tachyphylaxis may be lessened by glucocorticoid therapy. While patient ambulation can assist reduce bone resorption from immobility, it might not be practical for a critically ill patient. The continuous treatment of hypercalcemia involves the addition of a bisphosphonate, such as zoledronic acid or paramidronate (if creatinine clearance >30 mL/min). The dosage of palidronate varies according to calcium concentration: 30 mg over 2 hours if the level is less than 12 mg/dL, 60 mg over 4 hours if the level is between 12 and 14 mg/dL, and 90 mg over 6 hours if the level is greater than 14 mg/dL. Doses shouldn't be repeated for at least seven days because the effects take two to five days to manifest. Since osteonecrosis of the jaw is a special side effect of bisphosphonates, patients should be counseled to talk about this treatment before undergoing any further dental work. Because of the possibility of hypocalcemia, bisphosphonate should not be administered before parathyroidectomy. For patients who already need such therapy, hemodialysis with a low calcium bath is an alternative. In an emergency, phosphate therapy will instantly reduce the calcium content, however it may result in undesired tissue deposition of precipitates. Primary hyperparathyroidism can be treated with a calcimimetic such for persistent suppression of PTH, particularly prior to parathyroidectomy, the final therapeutic option for primary hyperparathyroidism, cinacalcet, etelcalcetide, or denosumab may be taken into consideration. (Jacobi J., 2019)

Hyperglycemia: Both diabetic and non-diabetic critically ill individuals frequently have hyperglycemia. Hyperglycemic crisis, on the other hand, is a medical emergency that usually results in ICU admission. Despite having identical treatments, two syndromes have been identified: hyperglycemic hyperosmolar syndrome (HHS) and diabetic ketoacidosis (DKA). Although noncompliance with insulin administration is the most frequent cause of DKA/HHS, other acute illnesses, infections, trauma, and heart ischemia can also act as triggers. Insulin insufficiency causes diabetic ketoacidosis, which typically affects people with type 1 diabetes but has also been linked to the use of sodium glucose cotransporter 2 (SGLT-2) inhibitors. One The hallmarks of diabetic ketoacidosis include metabolic acidosis, an elevated anion gap, tachycardia, shock, confusion/coma, hyperglycemia (glucose 500–800 mg/dL) resulting from osmotic diuresis, hyperventilation, and hyperglycemia (acetone, beta-hydroxybutyric acid, and acetoacetate) produced excessively by lipolysis. It has been proposed that beta-hydroxybutyric acid measurement be used to specifically diagnose ketoacidosis. Acidosis and an extracellular potassium shift may mask hypokalemia. There is a noticeable proinflammatory condition, which could lead to consequences like venous thromboembolism or a sepsis-like image. Mild acidosis (pH 7.25-7.3), moderate acidosis (pH 7-7.24), and severe acidosis (pH < 7) with associated deterioration of mental state are the

different levels of abnormalities. SGLT-2 inhibitor-induced glucosuria and decreased carbohydrate intake (typically following an acute illness or surgery) cause a relative insulin shortage, which results in high ketones but not elevated glucose concentrations in patients with euglycemic DKA (glucose <300 mg/dL). As the use of these medications increases, clinicians should be on the lookout for this syndrome, which manifests as metabolic acidosis. A few days before a scheduled surgery, it could be wise to stop using SGLT-inhibitors. Compared to DKA, patients with HHS typically only have minor acidosis (lactic or mild starvation ketosis), but their glucose levels are substantially higher (>600 mg/dL), they are more dehydrated and hyperosmolar (>320 mOsm/kg), and they are in a profound stupor or coma. The management of these disorders has been quite conventional and involves replacing insulin, restoring intravascular volume, and correcting electrolyte deficiencies. A more effective resolution of the illness has been linked to a methodical and protocolized approach to treatment. Depending on the severity of the hypotension, immediate resuscitation with crystalloid fluids (0.9% NaCl or Ringer's lactate) is required, followed by continuous fluid replacement to make up the 10–12 L potential shortfall with hypotonic fluid unless the corrected sodium deficit is extremely severe. Glycemic management and acid-base balance are enhanced by hydration alone. A recent analysis found that while balanced salt solutions are preferred in the majority of critical care patients, there is not enough data to suggest one crystalloid over another. Potassium and dextrose can be added more easily, however sodium chloride solutions may raise the risk of hyperchloremia and decrease urine production. There was no difference in the time to closure of the anion gap, although in one small trial, using Ringer's lactate was linked to a longer time to attain glucose control in DKA, maybe because lactate acts as a substrate for gluconeogenesis. Insulin replacement is intended to compensate for a basal insulin deficiency rather than to return blood sugar levels to normal. For individuals who are obese or severely insulin-resistant, a fixed rate of infusion is preferred over titrated insulin utilizing 0.1 U/kg/h with an optional intravenous bolus of 0.1 U/kg. On the other hand, a 0.14 U/kg/h infusion without a bolus dosage has also been proposed.(Jacobi J., 2019)

It has been proposed that in order to maximize insulin delivery and saturate insulin-binding sites, the intravenous tubing should be prepared by flushing an additional 20 mL of the insulin infusion. To prevent hypoglycemia and osmotic shifts, dextrose should be added to the maintenance fluid once the glucose level has dropped to less than 250 mg/dL in DKA and 300 mg/dL in HHS. Resuscitation and lowering blood sugar levels can lessen insulin resistance, which means lowering the insulin infusion rate to 0.05 U/kg/h or raising the glucose dosage. Low sodium levels in patients with hyperglycemia are usually the result of a laboratory aberration. For every 100 mg/dL increase in hyperglycemia over normal, the reported serum sodium level should rise by 2.4 mEq/L.30 Since ketones will be converted to bicarbonate, sodium bicarbonate is only used for severe acidosis. If the level is less than 3.3 mEq/L, potassium is restored abruptly before beginning any insulin therapy. If the level is less than 5.3 mEq/L and urine production is sufficient (more than 0.5 mL/kg/h), potassium should be given to maintenance fluids. Usually, more electrolyte replacement is required, so regular monitoring of magnesium and phosphorus is necessary.Because insulin and dextrose work together to change phosphorus intracellularly, values below 1.5 mg/dL call for treatment to avoid serious hypophosphatemia as well as muscle damage or weakness. The dosage of magnesium should be customized for each patient based on their concentrations and arrhythmia risk. In non-ICU settings, subcutaneous insulin has been investigated for the treatment of DKA in patients with simple cases using lispro insulin 0.3 U/kg followed by 0.1 U/kg given hourly. When combined with a DKA protocol, subcutaneous insulin therapy did not result in comparable patient outcomes to intravenous insulin; however, it was substantially less expensive for patients who were not comatose, had no end-stage renal disease, myocardial infarction, heart failure, or dementia, and were not persistently hypotensive. When choosing a treatment location, workload and monitoring intensity are crucial factors. There were no significant variations in the outcomes across the therapy approaches, according to a Cochrane study, which suggests more research is required, considering patient happiness. The possible benefits of early glargine insulin treatment with insulin infusion have also been investigated in studies including adults and children. Similar results and safety were shown in a pilot research that used insulin glargine 0.3 U/kg subcutaneously within two hours of the start of insulin infusion.Although the Joint British Diabetes Societies guideline expert opinion recommends that home basal insulin be continued throughout insulin infusion therapy in DKA to reduce rebound hyperglycemia following the infusion, a review of this practice indicated that more research is necessary. In the US, switching to a basal and bolus insulin regimen is usually carried out following rehydration, glycemic control, and osmotic stabilization in HHS or after the anion gap has closed in DKA. In order to account for time to commencement of effect and prevent rebound hyperglycemia or recurrent ketosis, the basal insulin should ideally be administered two hours before the infusion is stopped. It could take much longer for mental condition to return to normal in HHS. For continued care, a patient who doesn't improve might be switched to a titrated insulin infusion. Osmotic changes have a significant role in renal failure and DKA or HHS. In comparison to insulin alone, hemodialysis will decrease blood urea nitrogen and glucose, which may result in notable osmotic changes and a quicker drop in glucose concentration. Even though children are more likely than adults to experience cerebral edema, concomitant therapy carry the risk of this devastating side effect.

Additionally, dialysis patients won't require the same level of potassium and fluid depletion, therefore treatment should be tailored to each patient's needs. (Kitabchi, 2009)

Hypoglycemia: Although insulin or oral hypoglycemic treatment with decreased glucose intake frequently results in acute hypoglycemia, it can also be caused by mistakes in insulin dosage, hepatic insufficiency (reduced gluconeogenesis), decreased insulin clearance (renal failure), modifications to corticosteroid therapy without alterations in insulin regimen, or purposeful overdoses. Seizures, brain damage, or heart harm can result from severe hypoglycemia. Early identification of the symptoms, such as aphasia, perspiration, anxiety, visual alterations, confusion, and sympathetic stimulation It could be challenging to identify hypoglycemia in individuals who are sleepy, have a muted hypoglycemic response, have chronic diabetes and autonomic dysfunction, or are taking beta-blockers at the same time results in earlier treatment. Mild hypoglycemia (55–69 mg/dL), moderate hypoglycemia (50–54 mg/dL), and severe hypoglycemia (less than 40 mg/dL) are all linked to 2- to 3-fold higher intensive care unit mortality than normoglycemia. Any value below 70 mg/dL should serve as an alert for patient treatment and evaluation of the insulin and nutritional regimen. It is crucial to follow a proven insulin strategy and appropriate monitoring for prevention. In patients with creatinine clearance <30 mL/min or those receiving dialysis, a single insulin injection to treat hyperkalemia increases the risk of hypoglycemia, necessitating three to four hours of continuous monitoring. Without proper monitoring, the conventional combination of 10 units of insulin and 50% dextrose resulted in a hypoglycemia rate that approached 30% in patients with renal failure. Usually, glucagon or dextrose replacement administered orally or intravenously can be used to treat hypoglycemia. No treatment guidelines have been developed or addressed the best way to take dextrose. Usually, 25% or 50% concentrated dextrose is utilized; nevertheless, there have been reports of cardiac arrest and problems from the extravasation of this hyperosmolar fluid with quick delivery. Similar recovery from hypoglycemia was achieved with less unintentional hyperglycemia when 10% dextrose was infused in 50 mL aliquots and titrated to relieve hypoglycemia. Hypoglycemia is typically treated with intravenous or oral glucagon or dextrose replacement. The optimal technique to ingest dextrose has not been addressed or treatment guidelines produced. Although 25% or 50% concentrated dextrose is typically used, cardiac arrest and issues resulting from the rapid extravasation of this hyperosmolar fluid have been reported. When 10% dextrose was administered in 50 mL aliquots and titrated to alleviate hypoglycemia, a similar recovery from hypoglycemia was obtained with less inadvertent hyperglycemia. (Jacobi, 2012) (Jacobi J., 2019)

Conclusion

Numerous endocrine emergencies can be brought on by various diseases and disorders and often exhibit vague symptoms. These disorders can be identified by clinical suspicion based on continuous laboratory testing, medicines, and other conditions. Both diagnosis and treatment must be approached methodically. Before the diagnosis is finalized, hormone replacement therapy can be required. Close observation and a regulated rate of electrolyte correction are necessary.

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