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Emergencies of endocrinology in pregnancy and labor

Abstract

Endocrine emergencies during pregnancy and labor are rare in general, but quite common among labor emergencies. The most frequent are complications of diabetes mellitus, hypo- and hyperthyroidism. Pituitary emergencies are relatively rare, nowadays. Close collaboration of maternal-fetal specialists, Endocrinologists and Obstetricians, as well as proper patient – doctor co-operation may lead to the optimal management for mother and fetus.

Keywords: Thyrotoxic crisis, Myxedema coma, Diabetic ketoscidosis, Hypoglycemia, Pituitary apoplexy

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Kali Makedou,[1] Anargyros Kourtis[2]

[1]Laboratory of Biological Chemistry, Aristotle University of Thessaloniki, Greece

[2]Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Greece

Correspondence: Kali Makedou, Lecturer of Medical Biochemistry, Medical School, Aristotle University of Thessaloniki, Aristotelous 45, 55 236, Thessaloniki, Greece, Tel 30 2310 346942, Email kmakedou@auth.gr

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Abbreviations: DKA, Diabetic Ketoacidosis; PTU, Propylthiouracil; T3, Triiodothyronine; T4, Thyroxin

Introduction

Some of the main emergencies of pregnancy and labor regarding endocrinology are thyrotoxic crisis, myxedema coma, diabetic ketoacidosis, hypoglycemia and pituitary apoplexy. They are serious complications of metabolic disorders during pregnancy that can endanger the life of mother and fetus and need early diagnosis, as well as rapid and aggressive treatment.

Thyrotoxic crisis

Thyrotoxic crisis, or thyroid storm, is a rare and potentially morbid complication of pregnancy labor. It is a serious hypermetabolic condition that can occur when hyperthyroidism of pregnancy is not or is inadequately treated. The term "crisis" describes the severity of this clinical condition, as well as the impact of excess circulation thyroxine (T4) and tri-iodothyronine (T3). Morbidity ranges between 10% and 30%. The exact pathophysiology is not yet clarified. Nevertheless, labor itself is a stressful situation, emotionally and physically, and in some cases the necessity of a Caesareanz section may promote adrenergic functions.[1] Moreover, thyroid storm may follow an etiological event, such as infection, surgery, trauma, thrombosis and diabetic ketoacidosis.[2]

Receptors of thyroid hormones are present in many tissues and that explains their multisystemic actions. T3 is the more active of the two. It is mainly synthesized in the thyroid gland, but is also produced by peripheral conversion of T4 to T3 in skeletal muscles, liver and myocardium. Elevated level of T3 values may lead to increased lipolysis, oxygen consumption and thermogenesis. Signs and symptoms of thyroid storm are shown in Table 1. Some of the main are tachycardia, confusion, high fever and increased systolic pressure. Infection and sepsis might mislead the diagnosis and should be excluded.

Table 1 Signs and symptoms of thyrotoxic crisis

Tachycardia	Goiter
Fever	Exophthalmos
Tachypnea	Chest Pain
Hypoxia	Palpitations
Tremor	Atrial Fibrillation
Confusion	Nausea
Pulmonary Edema	Vomiting
Fetal Tachycardia	Anorexia
	Impaired Visual Fields

The more specific signs of thyroid dysfunction are goiter and exophthalmos. Thyroid stimulating hormone (TSH) serum levels are almost zero and thyroid hormone levels are increased. Nevertheless, there are no specific cut-off levels above which the diagnosis of thyroid storm would be securely made. White blood cells count is elevated and there are also signs of dehydration, acidosis, hyperglycemia, hypercalcaemia, increased transaminases and electrolyte disturbances. Nevertheless, mild tachycardia and increased white blood cells are a common finding in pregnancy. Hypertension, pulmonary edema and heart failure are marked manifestations in pre-eclampsia, as well. Consequently, the diagnosis of thyroid storm is mainly clinical, as long as elevated thyroid hormone levels cannot distinguish plain hyperthyroidism from thyrotoxic crisis in pregnancy. A scoring system has been created by Burch & Wartofsky[3] for the prompt recognition of thyroid storm. According to this system increased temperature, mother's heart rate and multiorgan dysfunction is taken into account to grade the severity of thyrotoxic crisis, aiming in an effective intervention.

Main goals of treatment are rapid reduction of thyroid hormone synthesis and peripheral deiodization, aggressive management of multiorgan dysfunction and elimination of the initial etiology. Glucocorticoids (1-2mg dexamethasone every 6 hours or 100mg hydrocortisone every 8 hours) inhibit the conversion of T4 to T3 and help maturation of the fetal lungs. Thionamides are the antithyroid agents of choice; propylthiuracil (PTU) (200-400mg every 6 hours), methimazole (20-25mg every 6 hours) and carbimazole, which is metabolized to methimazole may be administered orally, by nasogastric tube or rectally.[4] PTU blocks the peripheral conversion of T4 to T3, reducing the levels of active thyroid hormones, but with the side effects of liver failure and death, whereas methimazole administation during pregnancy has been related to teratogenesis.[5] Therefore, which antithyroid agent should be used in thyroid storm

has not yet been clarified. Iodine (4-10 drops of Lugol or saturated solution of potassium iodine every 6-8 hours or 1000mg sodium iodine in 250ml normal saline, intravenously twice a day) may be administered supplementary to reduce the release of thyroid hormones from the gland, but only one hour after the PTU; otherwise, it will be used for further hormone synthesis. Propranolole (40-80mg every 6-8 hours orally or 0.5-1mg intravenously in 10min) inhibits peripheral hormone conversion, as well, and can be administered supplementary to thionamides. Prompt delivery is not recommended during thyroid storm, unless indicated.[4] Nevertheless, fetal monitoring and neonatal thyroid status monitoring after exposure to high doses of maternal thionamides is essential and may prevent thyroid dysfunction, as long as thionamides cross the placenta.

Myxedema coma

Myxedema coma or crisis is a rare clinical condition characterized by severe hypothyroidism with multiorgan complications. Myxedema is also used to describe dermatologic changes due to mucopolysaccharides deposition in the dermis, resulting in the swelling of the affected area. The term "coma" is misleading, because the patient is not actually in coma, but suffers from severe hypothyroidism in combination with confusion, memory loss, irritability, arrhythmia, multiorgan failure, headache, nausea and hypotension.[6]

Diagnosis may be difficult, due to lack of specific signs and symptoms and to the rarity of this clinical condition. Usual signs are excess fatigue, weight increase and sleep disturbances. Suspicion of myxedema coma can be raised by the history of hypothyroidism, such as thyroiditis Hashimoto, of the pregnant woman. Untreated or inadequately treated hypothyroidism may lead to myxedema coma. Laboratory findings include highly increased circulating TSH and very low T3 and T4 levels. Treatment of myxedema coma includes corticosteroid administration, followed by supplementation of thyroid hormones with levothyroxine (200-250mg daily) intravenous or orally.

Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus (DM). Most commonly, pregnant women with DM type 1 and women with DM of first onset are prone to present DKA, whereas it can be seen in women with DM type 2 or gestational diabetes as well. The incidence of DKA is 2-3% with 10-20% risk of fetal death,[7] despite the improvement in maternal-fetal care. Pregnant women present increased risk of DKA than non-pregnant diabetic women.[8] Predisposing factors include hunger, dehydration, and reduced calorie intake, respiratory alkalosis of pregnancy, stress, increased insulin agonists production (placental lactogen, prolactin, and cortisol), infection and non-compliance to insulin therapy.

The etiology of DKA during pregnancy and labor includes overproduction of glucose and ketones from the liver and free fatty acids from the fatty tissue, due to imbalance between glucagon and insulin.[9] In fact, catecholamines, glucagon, cortisol and growth hormone are increased 700-800%, 400-500%, 400-500% and 200-300%, respectively. Hyperglycemia is the result of increased liver glucose production and eliminated usage by muscle cells. Similarly, glucagon increases ketone bodies production from fatty acids and insulin cannot adequately lead them to catabolism. Increased fatty acids production from fatty tissue promotes fatty acid oxidation and the overproduction of ketone bodies, which are β-hydroxybutyric acid, acetoacetic and acetone. The latter is slowly excreted by the lungs, giving a special odor in breath, like a rotten fruit, called "acetone" breath. Increased concentrations of ketone bodies in the circulation might lead to metabolic acidosis and to Kussmaul breathing, a deep and labored breathing pattern, whereas hyperglycemia, ketoacidosis and ketonuria lead to increased osmolarity of blood and osmotic diuresis, with excessive loss of water (7-10L). The mechanism by which maternal ketoacidosis endangers the fetus is not yet clarified.

Signs and symptoms are clearly indicative of diabetic ketoacidosis (Table 2). Weakness, nausea, vomit, polyuria, polydipsia, quick breathing, hypothermia and signs of dehydration are some of them. Laboratory findings are also diagnostic (Table 2). Early diagnosis of diabetic ketoacidosis is very crucial for successful pregnancy outcome and labor. The precipitating factors, e.g. infection, have to be quickly identified and treated. Fluid supplementation, electrolyte replacement and insulin infusion are the next main steps of management. In specific, 1-1.5L of normal saline (0.9% NaCl) is given within an hour and the next choice of fluids depends on extend of dehydration and electrolyte levels.[8] Continuous fetal monitoring is essential, because ketone bodies can pass through the placenta and cause ketoacidosis to fetus. Nevertheless, this situation improves when maternal hyperglycemia and acidosis are corrected. Immediate fetal delivery is essential only after maternal resuscitation.[8]

Table 2 Signs, symptoms and laboratory findings of diabetic ketoacidosis

Signs and Symptoms	
Nausea / Vomiting	Hyperventilation / Acetone Odor
Polydipsia	Mucus Dryness
Polyuria / Oliguria	Tachycardia
Weakness	Hypotension
Weight Loss	Disturbed Consciousness
Abdominal Pain	Coma
Laboratory findings	
Hyperglycemia	> 300 mg/dL
Arterial pH	< 7.35
HCO_3-	< 15 mEq/L
Ketones	Positive (+)
Anion Gap	>12 mEq/L
Osmolarity	>280 mOsm/Kg

Hypoglycemia

Hypoglycemia is a rare and potentially fatal complication of pregnancy. Many pregnant women that are under strict glucose levels' monitoring, especially those of DM type 1, may have hypoglycemia. The hypoglycemia itself is not fatal, in contrast to hyperglycemia, but may lead to hypoglycemic coma or convulsions. The term "hypoglycemia" refers to glucose blood levels lower that 60mg/dL and the incidence is 35% of diabetic women, mainly type 1. Signs and symptoms include tremor and sweating and are easily reversible by glucose administration as fruit juice, snack or glucose pills. Glucagon should be administered in cases of inability of swallowing. The etiology of hypoglycemic coma has to be identified and rapidly corrected, e.g. correction of insulin dosage or of diet. Moreover, there are psychiatric cases of pregnant women that take more insulin than needed. C-peptide determination may indicate the etiology in such cases.

Pituitary apoplexy

During pregnancy, pituitary gland normally enlarges by approximately one-third and there is an analogous increase in blood supply. In cases of blood flow disturbance to the anterior lobe, such as during labor, there may be an infraction of the gland which is

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a clinically critical situation, with specific signs and symptoms [10,11]. In the presence of pituitary adenoma the apoplexy is an endocrine emergency with high rate of mortality. The etiology might be hemorrhage, ischemia or both. To date, only 12 cases have been reported worldwide. The symptoms include severe and abrupt headache, with or without nausea and vomit. The management includes hormone replacement therapy until the end of pregnancy, and 100mg hydrocortisone every 6 hours.

Apoplexy without the presence of pituitary adenoma (Sheehan syndrome) may result from pituitary necrosis due to hypotension and shock during or after labor [10]. Clinical indications of the syndrome are sudden-onset headache, nausea, vomiting, hypoglycemia and hypotension after an obstetric hemorrhage. Diagnosis is confirmed by magnetic resonance imaging of the pituitary gland. Treatment must begin by the establishment of clinical diagnosis, with glycocorticoid and fluid replacement. The syndrome may occur months or years after labor. Indications for post-partum diagnosis are failure of lactation, secondary hypothyroidism, hypoadrenalism and amenorrhea may be indicative of the syndrome. In such cases diagnosis is made by laboratory findings, such as low pituitary hormone levels (TSH, GH, LH, FSH, prolactin, ACTH) and low target organ hormones (IGF-1, free T4, cortisol, estrogen). Sheehan syndrome treatment includes life-long supplementation with levothyroxine and glycocorticoids.[12]

Conclusion

Endocrine emergencies in pregnancy and labor may be rare, but are critical for the health of mother and fetus or newborn. Close monitoring of mother and fetus during pregnancy may help towards prevention of these emergencies and a safe completion of pregnancy and labor. Close collaboration of maternal-fetal specialists, Endocrinologists and Obstetricians, as well as proper patient – doctor co-operation may lead to the optimal management for mother and fetus.

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None.

Conflicts of interest

None.

References

1. Molitch ME. Endocrine emergencies in pregnancy. *Baillieres Clin Endocrinol Metab*. 1992;6(1):167–191.
2. Tietgens ST, Leinung MC. Thyroid Storm. *Med Clin North Am*. 1995;79(1):169–84.
3. Burch HB, Wartofsky L. Life–threatening thyrotoxicosis. Thyroid storm. *Endocrinol Metab Clin North Am*. 1993;22(2):263–277.
4. Bahn Chair RS1, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the ATA and the AACE. *Endocr Pract*. 2011;17(3):456–520.
5. Gianantonio E, Schaefer C, Mastroiacovo P. Adverse fetal effects of prenatal methimazole exposure. *Teratology*. 2001;64(5):262–266.
6. Turhan NO, Kockar M, Inegol I. Myxedematous coma in a laboring woman suggested a pre–eclamptic coma: a case report. *Acta Obstet Gynecol Scand*. 2004;83(11):1089–1091.
7. Bismuth E, Bouche C, Caliman C, et al. Management of pregnancy in women with type 1 diabetes mellitus: guidelines of the French–Speaking Diabetes Society (Societe francophone du diabete [SFD]). *Diabetes Metab*. 2012;38(3):205–216.
8. Carroll M, Yeomans ER. Diabetic ketoacidosis in pregnancy. *Crit Care Med*. 2005;33(10 Suppl):S347–S353.
9. Guo RX, Yang LZ, Li LX, et al. Diabetic ketoacidosis in pregnancy tends to occur at lower blood glucose levels: case–control study and a case report of euglycemic diabetic ketoacidosis in pregnancy. *J Obstet Gynaecol Res*. 2008;34(3):324–330.
10. Kovacs K. Sheehan syndrome. *Lancet*. 2003;361(9356):520–522.
11. Couture N, Aris–Jilwan N, Serri O. Apoplexy of a microprolactinoma during pregnancy: case report and review of literature. *Endocr Pract*. 2012;18(6):e147–e150.
12. Lawar RN. Pituitary tumor apoplexy: a review. *J Intensive Care Med*. 2008;23(2):75–90.

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