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Review Article

Pituitary Diseases and Midwifery Care in Pregnancy

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Abstract

The pituitary gland causes very serious effects on the body thanks to the hormones it secretes. These effects are also reflected in the pregnancy process and can cause some changes. The main effects of pituitary diseases are prolactinoma, acromegaly, lymphocytic hypophysitis, pituitary insufficiency (hypopituitarism), Cushing's Syndrome and Sheehan's Syndrome. Since pregnancy is rare in these diseases, diagnosis is usually made in the pre-pregnancy period. A definitive diagnosis is made thanks to the disease-specific diagnostic tests accompanied by the signs and symptoms seen in the pre-pregnancy period. The anatomical and physiological changes that occur in the pituitary gland during pregnancy cause difficulties in diagnosing pituitary diseases. Therefore, midwifery care to be given in pituitary diseases should be carried out effectively from the pre-pregnancy period. These diseases cause serious complications for both the mother and the fetus and require a multidisciplinary care approach. Midwives, who have a major role in the multidisciplinary team providing care, should be familiar with the symptoms, diagnosis and treatment methods of pituitary diseases and should be managed with individualized midwifery care specific to the disease.

Key words: *Midwifery, Midwifery care, Pituitary dıseases, Pregnancy, Postpartum*

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Introduction

The pituitary gland is located in the sella turcica at the skull base and is a small endocrine organ weighing 0.5-1 g. Although it is a very small endocrine gland, it has an important role in the regulation of the hormonal system of the whole body and is also defined as the 'master gland' (1). The pituitary gland also has important functions in the formation and maintenance of pregnancy. The pituitary gland consists of two different parts: adenohypophysis (anterior part) and neurohypophysis (posterior part) (2). The anterior part, called adenohypophysis, constitutes 80% of the gland and is connected to the hypothalamus via the bloodstream. The posterior part, called the neurohypophysis, is directly connected to the hypothalamus through the pituitary stalk (3). There are 5 cell groups secreted under the control of the hypothalamus in the adenohypophysis. These are somatotrope cells: GH which is growth hormone, gonadotrope cells: FSH and LH which are gonadotropins, lactotrope cells: prolactin (PRL), thyrotrope cells: TSH which is thyroid stimulating hormone and corticotrope cells: ACTH which is adrenocorticotropin (4). Both anatomical and functional changes occur in the pituitary gland during pregnancy. During pregnancy, the pituitary gland grows by approximately 136%, reaches its highest level on postpartum day 3 and returns to its prenatal size within 6 months (5). This growth in the pituitary is due to hypertrophy and hyperplasia of PRL-secreting lactotrope cells with the effect of increasing oestrogen hormone during pregnancy. Lactotroph cells constitute 60% of the anterior pituitary cells in pregnancy and 20% in non-pregnant individuals (6). There is an increase in serum PRL level during pregnancy, and it returns to normal levels around postpartum day 7 in non-breastfeeding women. While there is a decrease in the number of gonadotrope cells in the pituitary during pregnancy, there is no change in the number of corticotrope and thyrotrope cells (7). Serum gonadotropin levels decrease during pregnancy due to the negative feed-back effects of increasing estrogen and progesterone. In addition, pituitary cells do not respond adequately to placenta-derived gonadotropin releasing hormone (GnRH) (8). At the beginning of pregnancy, serum TSH levels decrease slightly due to increased placenta-induced hCG levels. There is activation in the hypothalamo-pituitary-adrenal axis during pregnancy. Placenta-derived corticotrope releasing hormone (CRH) stimulates ACTH release from the pituitary (6). Serum free and total

cortisol and cortisol binding globulin levels increase in pregnancy. Somatotropes are suppressed by the effect of insulin like growth factor-1 (IGF-1) which increases during pregnancy and they may function similar to lactotropes. The amount of pituitary-derived GH decreases during pregnancy and the amount of GH produced by the placenta increases instead (9).

Pituitary Diseases in Pregnancy

Prolactinoma

Prolactinoma is one of the most common causes of persistent hyperprolactinaemia in pregnancy and accounts for approximately 50% of pituitary tumours. Anovulation and infertility are frequently seen in a woman diagnosed with prolactinoma (10).

Diagnosis: The chance of pregnancy increases in women who respond rapidly to treatment and have regular ovulatory cycles. Therefore, it is very important for women diagnosed with prolactinoma to receive counselling in the pre-pregnancy period to prevent or reduce the side effects of the drugs used on the pregnancy process and the fetus (11).

Treatment: In prolactinoma, treatment with the dopamine agonist cabergoline provides a more rapid response and is generally used as the first-line treatment (11). Because of the fetal risks in terms of pregnancy, it is generally recommended to use a contraceptive method during this period. Although there is insufficient evidence for the use of both dopamine agonists in pregnancy, there are studies showing that treatment with bromocriptines is safe in pregnancy or when pregnancy is considered (12).

In pregnancy, there is a physiological increase in pituitary size and prolactin level. Since this increase is considered normal, prolactinoma is usually ignored. Cases in which the increase in prolactin level is significantly above normal values and accompanying symptoms are observed are also examined in terms of prolactinoma (13). Prolactinoma affects pregnancy and pregnancy is also affected by increased prolactin levels. Prolactinomas diagnosed and treated before pregnancy have a very low risk of growth during pregnancy (14). In pregnant women with microprolactinoma (<1cm), dopamine agonists are generally not used in the first trimester. In case of macroprolactinoma, medical treatment is continued during pregnancy and bromocriptine dopamine antagonist is usually used. In pregnant women diagnosed with prolactinoma, the size of the tumour is monitored every trimester with magnetic resonance imaging (MRI) and treatment is regulated. In cases where there is no response to medical

treatment, termination of pregnancy or surgical intervention is planned (15).

Midwifery Care Management

- Women with symptoms of high prolactin levels should be referred to an endocrinologist.

- Women diagnosed with prolactinoma and receiving treatment should be given appropriate family planning counselling for contraception.

- Prenatal follow-up of pregnant women diagnosed with prolactinoma should be performed regularly and they should be evaluated in terms of obstetric risks at each follow-up.

- Pregnant women receiving dopamine agonist treatment during pregnancy should be monitored in terms of fetal and maternal risks.

- In the case of prolactinoma and pregnancy, a multidisciplinary approach is important and the cooperation of gynaecologist, endocrinologist, neonatologist, midwives and nurses is very important for follow-up and treatment (14,16).

Acromegaly

Acromegaly is a clinical condition resulting from increased hepatic insulin-like growth factor 1 (IGF-1) levels due to uncontrolled release of growth hormone (GH). The etiology of acromegaly is 95% isolated pituitary tumours that secrete growth hormone. In cases of acromegaly, prolactin level is usually found to be high, however, the metabolic effect caused by excessive secretion of growth hormone and the effect of pituitary adenoma increase the mortality and morbidity rate (17). Symptoms generally include growth in hands, feet and extremities, coarsening of the face, gonadal dysfunctions, excessive sweating, headache, sleep apnoea syndrome and fatigue. In pregnancy, the diagnosis of the disease becomes difficult because the symptoms and signs that occur as a result of physiological changes are similar to acromegaly. Elevated serum IGF-1 level is an important value for the diagnosis and the diagnosis of acromegaly should be made together with both clinical and biochemical results (18).

Diagnosis: Oral glucose tolerance test (OGTT) is the most specific test for the diagnosis of acromegaly. It is recommended that GH response should be examined in patients with clinically elevated IGF-1 value and patients with acromegaly considered to have oral glucose tolerance test (19). GH suppression during glucose tolerance test strengthens the diagnosis of acromegaly. Since a method that separates GH secreted

from the placenta from pituitary GH has not yet been developed, it is very difficult to diagnose acromegaly in pregnancy, in this sense, all values should be considered (20).

Treatment: Treatment is planned according to the size of the tumour and compression symptoms. Generally, surgical treatment is the first option; if serum IGF-1 levels are high after surgical treatment, medical treatment with long-acting somatostatin analogues (SSA) is recommended. Medical treatment is planned when patients are not suitable for surgical treatment. Radiotherapy is recommended as the last option for treatment (21).

Although there is not enough data on acromegaly in pregnancy, pregnancy in women with acromegaly should be postponed, if possible, until GH, IGF-1 normalises and no residual tumour can be seen (19). In cases of acromegaly, the risk of pituitary tumour growth, gestational diabetes mellitus (GDM) and pre-eclampsia increases during pregnancy. Intrauterine growth retardation may be observed if octreotide treatment is continued during pregnancy. In case of increased headache and tumoural growth during pregnancy, SSA treatment is initiated according to clinical conditions (18). The use of pegvisomant (GH receptor antagonist) is not recommended during pregnancy. If macroadenoma is present, visual field should be evaluated in each trimester. Pituitary surgery is recommended to be performed after the first trimester in pregnant women. If GH suppressor treatment is not continued, breastfeeding should be encouraged after delivery (22).

Midwifery Care Management

-Appropriate family planning counselling should be provided for contraception in women diagnosed with acromegaly and receiving treatment.

- Women considering pregnancy should be referred to a physician for monitoring the course of the disease and organising the treatment.

- When suspicious signs and symptoms of acromegaly are detected during pregnancy, they should be referred to a physician (14).

- Pregnant women with acromegaly should be closely followed up in terms of GDM and pre-eclampsia risks.

- If medical treatment is continued, the pregnant woman and foetus should be monitored in terms of side effects of the drug; suspected risky conditions should be reported to the physician.

- Women who do not receive GH suppressive therapy after delivery should be encouraged to breastfeed.

- In pregnancy, labour and postnatal period, the course of the disease, treatment and obstetric risks should be worked in cooperation as a team (23).

Lymphocytic Hypophysitis

Hypophysitis is defined as a non-tumoural heterogeneous inflammatory disease of the pituitary gland (24). Symptoms and findings vary according to the acute, subacute and chronic stages of the disease. Headache, nausea, vomiting and visual field defects can be seen due to the compression of the edematous pituitary gland on the surrounding tissues (25).

Diagnosis: Gestational or postpartum pituitary insufficiency without haemorrhage or hypotension leads to the diagnosis of lymphocytic hypophysitis. Magnetic resonance imaging and the presence of other autoimmune diseases strengthen the diagnosis of lymphocytic hypophysitis. However, histopathological examination is required for definitive diagnosis (26).

Treatment: Steroid treatment is considered to reduce the size of the pituitary mass, and surgical treatment is considered in cases where there is no response and visual status is at risk. Patients are followed up for long-term hormone deficiencies and hormone replacement therapy is initiated when necessary.

Midwifery Care Management

- Pregnant and postpartum women with autoimmune disease should be carefully monitored in terms of symptoms of lymphocytic hypophysitis.

- Women with symptoms such as headache, nausea, vomiting and diplopia during pregnancy and postnatal period should definitely be referred to a physician (14).

- Postpartum women who are diagnosed and treated should be counselled about breastfeeding, and the side effects of the drug and its effect on breastfeeding should be discussed with the physician.

- Counselling should be provided for contraception in the postpartum period and during treatment (27).

Pituitary Insufficiency (Hypopituitarism)

Pituitary insufficiency (hypopituitarism) is a syndrome caused by inadequate production and release of one or more pituitary hormones. Pituitary insufficiency can develop due to hereditary and acquired

disorders. The most common causes of pituitary insufficiency are pituitary adenoma surgery, traumatic brain injury and Sheehan syndrome (28).

Diagnosis: It is only possible to determine that the symptoms are due to pituitary insufficiency by detecting pituitary hormone deficiencies (29).

Treatment: Treatment in pituitary insufficiency is planned according to the cause and hormonal deficiency. Gonadotropin therapy is applied in patients with fertility desire. In pituitary insufficiency, infertility is frequently seen due to the lack of gonodotropins, while pregnancy is possible in treated cases (29). When pituitary insufficiency is treated before pregnancy and adequate hormone replacement is provided, fetal and maternal outcomes are generally good. In cases of undiagnosed or untreated pituitary insufficiency, the risk of abortion and stillbirth increases (30).

Midwifery Care Management

- Obstetric history and lactation status of women should be questioned carefully.

- Precautions should be taken against the risk of haemorrhage during pregnancy, labour and postnatal period.

- Midwives and other caregivers should have sufficient knowledge and skills in the emergency management of obstetric haemorrhage (14).

- Women with excessive bleeding during pregnancy, labour and postnatal period should be carefully monitored.

- When hypotension, tachycardia, hypoglycaemia and signs of lactation failure are detected in the postnatal period, the physician should be informed.

- Cases with suspicious pituitary insufficiency findings in pre-pregnancy, pregnancy and postnatal follow-up should be referred to a physician (29,31).

Cushing's Syndrome

Cushing's syndrome (CS) causes hypercortisolemia due to pituitary ACTH hypersecretion. Hypercortisolemia usually leads to oligo/amenorrhoea and, more importantly, to hypogonadotropic hypogonadism, which is a risk factor for fertility (32). Pregnancy is rare in CS due to fertility-related problems such as oligo/amenorrhoea and hypogonadotropic hypogonadism. Maternal-fetal complications such as pre-eclampsia, eclampsia, hypertension, gestational diabetes, congestive heart disease, pulmonary oedema, preterm delivery, stillbirth and abortion are common in pregnant women with CS (33).

Diagnosis: The diagnosis of CS can be made during or before pregnancy. Since changes such as weight gain, glucose intolerance, hypertension, and striae observed during pregnancy are seen in common with CS symptoms, it is not easy to make a diagnosis. However, in normal pregnancies the striae are white in colour, whereas in CS they are often large and purple. In addition, muscle weakness, hypokalaemia and pathological fracture are also important symptoms for the diagnosis of CS (32).

Treatment and Midwifery Care Management: Treatment of CS in pregnancy is decided based on the state of hypercortisolemia and gestational week. If the diagnosis is made in the first trimester, medical treatment can be followed. If the diagnosis is made in the second trimester, removal of the tumour with surgical treatment depending on the level of hypercortisolemia is the recommended treatment approach (32). If the diagnosis is made in the third trimester, surgical treatment can be postponed until the postnatal period by applying medical treatment (33). Conditions such as diabetes, hypertension and pre-eclampsia in pregnant women diagnosed with CS may cause pregnancies to be more challenging. Prematurity, fetal mortality and intrauterine growth retardation increase in the babies of pregnant women diagnosed with CS. Due to these risks, it is very important to closely monitor pregnant women with maternal diagnosis (34).

Sheehan's Syndrome

Sheehan's Syndrome (SS) is a condition of anterior pituitary hormone deficiency caused by physiological enlargement and necrosis of the pituitary gland during pregnancy. It usually occurs after postpartum haemorrhage (PPH) (35).

Although this syndrome is rare in developed countries, it is common in developing countries. The growth of the pituitary during pregnancy causes compression of the upper pituitary artery, and any hypotension that may occur during labour leads to arterial spasm in smaller vessels, apoplexy and subsequent pituitary necrosis (36). Although the pathogenesis of SS is not clear, the effect of autoimmunity in its formation is quite large. It is thought that it may trigger pituitary autoimmunity and delayed hypopituitarism by releasing antigens spread to the developed tissue necrosis (36,37).

Diagnosis The diagnostic criteria for Sheehan's Syndrome are as follows:

a) History of severe postnatal haemorrhage

b) Severe hypertension or shock requiring blood or fluid replacement

c) Failure in breastfeeding in the postnatal period (14).

d) Failure of the menstrual cycle to resume

e) Anterior pituitary insufficiency and panhypopituitarism

f) Sellada gap in imaging in MRI (38).

Treatment and Midwifery Care Management: Treatment of SS consists of fulfilment of deficient hormone requirements. Glucocorticoids are replaced without the need for fludrocortisone and treatment should be started before thyroxine completion (14). Hypogonadism increases the likelihood of osteoporosis and leads to a decrease in secondary sex characteristics, so replacement therapy should be applied, especially in premenopausal women. GH replacement appears to improve quality of life in these patients (38).

Conclusion

Changes in the pituitary gland during pregnancy cause difficulties in diagnosing pituitary diseases. Although pituitary diseases occurring during pregnancy are rare, scientific data for care management in these diseases are quite limited. For this reason, a multidisciplinary approach should be taken as the basis for care management of pituitary diseases occurring during pregnancy, prevention of complications and optimization of treatment. Midwives in the multidisciplinary team have a key role in detecting abnormal conditions during pregnancy, delivery and postpartum periods from the preconception period throughout all stages of the woman's life and in planning midwifery care for these conditions, if any. In midwifery care, midwives should know the symptoms of pituitary diseases well and provide individualized holistic care specific to the disease to pregnant women diagnosed with pituitary disease or suspected of having the disease. It can be recommended that guidelines and guides specific to midwifery care of pituitary diseases be prepared in clinics, new studies be conducted on pituitary diseases seen during pregnancy and educational plans and various activities be organized to raise public awareness on this issue.

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