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PRACA POGLĄDOWA
REVIEW

Cystic fibrosis and pregnancy – literature review

Mukowiscydoza a ciąża – przegląd piśmiennictwa

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ABSTRACT

This paper reviews the literature on the course of pregnancy how to sustaining it as well as delivery in women with diagnosed Cystic fibrosis.
Cystic fibrosis (CF) is a recessive autosomal disease occurring mostly among Caucasians. 1500 cases of the disease have been recorded in Poland and almost 70.000 people around the world suffer from it. The latest research shows that the average life span is 30 and is growing steadily due to proper diagnostics and appropriate treatment. A particular challenge for medicine is to sustain pregnancy in women with diagnosed CF. The paper collects and summarizes reccomendations for sustaining pregnancy and for childbirth in CF patients.

KEY WORDS:
Cystic fibrosis, pregnancy, labor, diet of pregnant women with CF

STRESZCZENIE

Mukowiscydoza jest chorobą autosomalną recesywną występującą najczęściej wśród rasy kaukaskiej. W Polsce zanotowano około 1500 przypadków choroby, na świecie na mukowiscydozę choruje blisko 70 tys. osób. Z najnowszych badań wynika, że średni okres przeżywalności szacuje się na 30 lat i ciągle wzrasta za sprawą prawidłowej diagno-

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styki oraz odpowiedniego leczenia. Szczególnym wyzwaniem dla medycyny staje się prowadzenie ciąży u kobiety z rozpoznaną mukowisydozą (CF – *cystic fibrosis*). Ciąża u kobiety chorej na CF jest ciążą wysokiego ryzyka. W pracy dokonano przeglądu danych literaturowych dotyczących przebiegu i prowadzenia ciąży oraz porodu u kobiet z rozpoznaną mukowiscydozą.

SŁOWA KLUCZOWE
ciąża, poród, mukowiscydoza, dieta ciężarnej z CF

INTRODUCTION

The first substantiated pregnancy in a CF patient, which resulted in delivering a healthy infant in spite of the mother's condition, was described in 1960 [1]. Along with the progress in medical science and new treatment opportunities, the life span of CF patients is being prolonged. Planning for pregnancy in a CF patient should be consulted with a gynecologist-obstetrician, as well as pulmonologist, physiotherapist, gastroenterologist, dietician, psychologist and anesthesiologist. Pregnancy in a CF patient is of high risk even if the course of the disease is mild. Planning and managing a pregnancy in CF patients require multiple examinations meant to prevent complications resulting from the condition. The following issues should be raised in meeting with a patient planning for pregnancy: worsening of the condition, possible fetus diseases, appearance of additional syndromes, possibility of premature delivery and intrauterine inhibition of fetus growth [2,3,4].

Planning for pregnancy in cystic fibrosis patients

Planning for pregnancy for women with CF should be individually adjusted to the syndromes resulting from the disease. It is crucial to hold genetic consultation with the woman and perform molecular examination of the CFTR gene (cystic fibrosis transmembrane conductance regulator) of the partner before natural conception [5,6]. It is also necessary to establish the stage of bronchopulmonary disease, assess the FeV1 value (forced expiratory volume in 1 second), take measurements of weight and height with the current BMI assessment and to carry out metabolic tests in order to avoid the exacerbation of diabetes or its appearance and to take up immediate treatment. While preparing such a patient for pregnancy, assessment should be made based on a dietary questionnaire and the nutritional standards should be discussed [4,7].

Most women with Cystic fibrosis are fertile though there might be some obstacles in becoming pregnant. In women with CF, due to mucus dehydration, secretion in the reproductive system thickens. Too thick mucus in the cervix hinders penetration of the sperm to the uterus [8,9]. Conception should be carefully planned for the patient to be in a good state of health. It is also necessary to give up medicines which have a teratogenic influence on the fetus and to consult a genetic clinic [8,9]. The patient should be mentally prepared for different medical procedures performed during the pregnancy and informed about the extended number of medical examinations in 2–6 week intervals, on average 4. A glucose tolerance test should be done every trimester and a sample should be taken to determine the phlegm content. It is also necessary to assess body mass growth [7,8]. The woman should be made aware of the high risk of complications in a premature fetus and of inhibition of intrauterine fetus development, along with their consequences. Contraindications for pregnancy in women diagnosed with CF are as follow: FeV1 < 50–60%, pulmonary hypertension, pulmonary heart, disabled lung function, Burkholderia ce pacia infections, low BMI, improper FVC (Forced Vital Capacity) [10].

Pregnancy in women diagnosed with cystic fibrosis

Body mass gain in pregnant woman

In the case of Cystic Fibrosis, the optimum BMI should be similar to a healthy person. The total calorie consumption during pregnancy varies from 80.000 to 124.000 kJ. Such an increase is caused by three main changes in the woman's body: growth of the fetus along with growth of tissues in the uterus, higher metabolism and increase in fatty tissue in a pregnant woman [5,6]. The recommended body mass growth depends on BMI. In women with a proper BMI it should be around 10kg, after the 20th week of pregnancy 0.5 kg per 7 days. Body mass growth of 11 kg is considered optimum and recommended [5]. If BMI equals 19.8 kg/m^2 – 26 kg/m^2, body mass growth should be 11.5 – 16.5 kg, and if BMI < 19.8 kg/m^2, body mass growth should be greater than 11.5 – 16 kg by an additional 1–2 kg [5]. The increase in calorie consumption needs to remain on the level of 300––500 kcal/24 h. Research shows that in most women with CF, the level of malnutrition increases in the process of body adaptation, which leads to smaller body growth in the fetus and causes premature birth [8].

North American CF Centres research showed that in 41% of CF patients, the total increase in body

weight during pregnancy is below 4.5 kg [11]. In such cases one should consider implementing treatment with a probe or parenteral nutrition [9].

Diet

It is necessary to discuss the principles of dietary treatment with the patient. The main aim of the treatment is to avoid malnutrition and provide the body with the proper amount of vitamins, macro and microelements. The high-calorie supply of pregnant women is set individually according to the demand. In the majorities of women with Cystic Fibrosis, the diet should be high-energy, high-protein and high-fat. Sometimes using diet supplements is necessary if severe malnutrition or diarrhoea appear. Supplementing the diet with NaCl by serving special wafers containing sodium or salting some more dishes are necessary. One should remember about it particularly during fever or heat [6,8]

Vitamin supplementation

An appropriate supply of vitamins soluble in fats is necessary for correct functioning of the organism. The secretory failure of the pancreas and loss of fat with stools appearing in cystic fibrosis patients leads to an increased requirement for vitamins from groups A, D, E and K [5,6,8]. One should begin the supply of folic acid 3 months prior to conception at the dose of 0.4 mg/day, and if there are neural tube defects noted in the family, at a dose of 4 mg/day. Supplementation should be extended by one trimester. Iron and folic acid compensation should be administered according to widely accepted principles.

Vitamin A

The proper concentration of vitamin A in the blood serum varies between 200–800 ug/l. Its level should be checked at least a once a year. In pregnant women assessing the concentration in the blood serum should be done at the beginning of pregnancy. In case of a low result, one should give a supplementary dose of not more than 10 000 iu/twenty-four hours. One should carefully control the concentration of vitamin A in serum, because too high levels, particularly in the first term of pregnancy, are teratogenic for the fetus [5.6].

Vitamin D

The proper concentration of vitamin D in the blood serum varies between 7.5–75.0 ng/ml. The optimum and recommended concentration in women with CF is > 30 ng/ml. In the case of liver damage it is necessary to supply calcifediol [8,9]. The concentration of vitamin D must be controlled and a proper dose established considering its content in food, sunlight exposure and the dose in supplemented vitamin products [6].

Vitamin K

The recommended dose of vitamin K is 1––20 mg/week. The concentration of vitamin K is assessed by measuring the level of protein induced by its deficiency. A too low concentration in blood serum leads to disorders in blood coagulation and a rise in the risk of osteoporosis [5,6]

No research has been conducted to consider the necessary consumption of calcium, iron, magnesium and zinc in CF patients. It is recommended to supply them in the same amounts as in healthy patients [5,6,8].

Physiotherapy and physical activity

Physiotherapy should be applied in all CF patients, even in ones not showing respiratory symptoms. This activity should be treated as obligatory hygiene. The aim of physiotherapy is the systematic removal of mucus lying in the lungs. Its basic form is postural drainage consisting of patting, shaking and pressing the chest. During the treatment 6–10 positions are used [7]. In physiological pregnancy, changes concerning the respiratory system occur, consisting in respiration with the diaphragm path and accretion of the transverse diameter of the chest, rise in the ventilation of lungs and inhalation capacity. In CF lung function is limited, therefore the increase in inhalation capacity can be slight [7,8]. Pregnant women with cystic fibrosis should modify therapy proceedings, expanding them with exercises suitable in individual terms of pregnancy. An expectant mother applying postural drainage must remember to assume the appropriate body position. Lying on the left side is recommended in order not to make the patient faint through pressure of the pregnant womb on the inferior vena cava.

Physical activity is an integral part of physiotherapy. It should be adapted to the patient's functional capacity. A combination of exercises might be undertaken by pregnant patients. Cycling is recommended, as well as jogging and swimming, if there are no gynecological contraindications. The increased amount of mucus is expectorated during physical activity, yet regular postural drainage needs to be performed [5,7].

Contraindications against applying physical activity with expectant mothers having cystic fibrosis: placenta previa, high body temperature, placental abruption, waters breaking early, high hypertension, imminent abortion, preeclampsia, nephropathies, thyroid diseases, diabetes, postmaturity, fetal pulse disorders or acute circulation problems [7].

Therapy of respiratory tract disease exacerbations

Standard action in exacerbating respiratory tract diseases is antibiotic therapy. The scope of recommendations including introducing antibiotics in the CF population has greatly widened. In selecting an appropriate preparation, one should conduct a throat swab or analyse expectorated spit and determine the antibiogram. On account of the pharmacokinetic and pharmacodynamic properties of medicines, applying larger doses is necessary, as well as the time of applying is extended to a minimum 14 days of therapy [1,12]. Depending on the degree of respiratory disease exacerbation in a pregnant patient, one should consider the degree of disease progress. Using antibiotics from the D group is necessary in difficult cases, because the danger for the mother is high. Making a decision on antibiotic treatment is often difficult. In such cases it is important to discuss every change in the treatment with the patient showing the side effects and expected effects. Aerosol therapy is recommended for treating pregnant women on account of limiting permeation of the medicine to the fetus by blood. Applying nebulization reduces the degree of teratogenic influence. Both inhalatory antibiotics, as well as bronchodilators have an impact on the respiratory system without the need to introduce medicines to blood.
Macrolithiums, nonsteroidal anti-inflammatory drugs and system glucocorticosteroids are applied in anti-inflammatory treatment. A specialist centre leading both the pregnancy and illness of the patient always issues recommendations for the use of these medicines. Regular monitoring of the concentration of medicines in the blood of the mother is necessary. The proven therapeutic effect of macrolithiums, among others, anti-inflammatory, anti-adhesion, suppressing the production of bacterial exoenzymes, as well as reducing the movement of cells, supports applying this group of medicines in pregnant women [12,13].

Delivery methods

In CF patients spontaneous delivery is the optimal manner of completing pregnancy (with extradural anaesthetization) on account of the shorter recovery time and smaller number of complications. Caesarean section should be performed only in the case of obstetric recommendation. It was proved that spontaneous childbirth has a better influence on the function of lungs than childbirth by caesarean section [7]. In patients in a good or average constitution, spontaneous delivery most often takes place in the 35–36th week of pregnancy. In patients with the cystic fibrosis, controlling saturation is necessary in the course of childbirth on account of the possibility of lowering saturation indicators and the need to apply oxygen therapy during labor [8]. In a correct course of childbirth and confinement, preparing the pregnant woman with antenatal classes will matter greatly.

Confinement and cystic fibrosis

In the first days after physiological childbirth, minimizing perinatal tiredness is essential. Early verticalization after childbirth contributes to correct functioning of the lungs as well as prevents the lying of mucus and infection. One should begin exercises 10–12 hours after physiological childbirth. After childbirth via caesarean section, early verticalization should begin after 12–24 hours [7].
In the case of women with recognised cystic fibrosis, pelvic floor muscle exercises are very important since manifestations of urinary incontinence appear as complications in this illness, even in women who have not given birth. Amongst the causes, coughing, intensive physiotherapy and undernourishment are mentioned. Very childbirth can increase manifestations of the urinary incontinence in patients with recognised CF. After natural childbirth or a caesarean it is necessary to prevent urinary tract inflammations and teach patients e pelvic floor muscle exercises. Applying drainage after childbirth is necessary, however, it can be postponed until the moment perinatal tiredness subsides. After a caesarean section, one should minimize pain through using painkillers, thanks to which the patient can be subjected to drainage and exercises streamlining the respiratory system more quickly [7,8,13].

Breastfeeding

Breastfeeding is not contraindicated in CF patients, however, not taking medicines penetrating into breast milk is a condition. The breast milk of a woman with recognised cystic fibrosis does not differ in composition from that of a healthy woman. One should pay special attention to appropriate additional energy supply, at least 500 kcal/day [5,9].

Contraception

In spite of the problems observed in CF patients in conception, coincidences in which pregnancy was not planned, happen. The unpreparedness of the organism for pregnancy carries far-reaching results including the death of the woman [9,14,15]. Hence, contraception is recommended. Methods of natural regulation of conception are inadvisable on account of the lack of changes in the consistency of cervical mucus, as well as numerous cycles without – and multi-ovulation. Using mechanical barriers is recommended [15]. Attention should be paid to taking contraception pills, which can worsen the medical condition. In current scientific news reports, changes concerning the lungs or exacerbation of patients taking

OCP were not stated. A highly recommended contraception method is the intrauterine application of progestogen, levonorgestrel released into the uterus which causes no changes in the organs afflicted by the disease [14,15].

CONCLUSION

Managinging pregnancy in cystic fibrosis patients, on account of the multiorgan expression of the illness, requires multispecialist and comprehensive care. One should remember about the psychological consequences for women with cystic fibrosis and their families. Literature data shows that 20% of women with CF do not live to the tenth birthday of their own child [5,11]. Managing pregnancy in CF patients is undoubtedly difficult, however, progress of the iatrology and the cooperation of interdisciplinary teams in perinatal care lets women with cystic fibrosis have healthy offspring more and more often, while a decade ago it was impossible [5].

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