

ABSTRACT

Title: Premature delivery and cannabinoid receptor expression in the placenta.

Introduction

Fortunately, premature delivery concerns a minority of births around the world. Nevertheless, the occurrence of this pathology is associated with significant complications for not prepared to an extrauterine life newborn in the form of prolonged hospitalization and their stay in the neonatal intensive care unit. It is also the leading cause of infant mortality. The significant progress in the field of molecular biology made in recent years has allowed analyzing many unexplored mechanisms of preterm labor. The role of the developing inflammatory response within the uterine cavity and the pro-inflammatory cytokine profile in the pathogenesis of preterm labor appears to be very likely. Direct mechanisms combining the appropriate cytokine profile with the production of prostaglandins that triggers uterine contractile function are not yet studied. A significant fixation point seems to be the endocannabinoid system, which has a proven effect on the pathogenesis of the inflammatory response. Expression of cannabinoid receptors, which are a crucial link in the endocannabinoid system, is present in almost every cell of the human body.

Study objectives

To investigate the relationship between cannabinoid receptor expression within the placenta after delivery and the problem of preterm delivery.

To investigate the relationship between the expression of CB1, CB1a and CB2 receptors in the placenta, and the duration of pregnancy / gestational age at delivery and the occurrence of preterm delivery, as well as the occurrence of selected pregnancy complications.

Material and methods

The study was conducted on multicenter material of 150 women giving birth in the period from March 2004 to December 2012. 115 women were diagnosed with premature delivery and were qualified to the Study Group, 35 women had a delivery at the physiological time and were qualified to the Control Group.

In order to determine the expression of cannabinoid CB1, CB1a, and CB2 receptors in the placenta, immediately after the end of the 3rd delivery period and excretion of the postpartum, 4 sections were taken from the placenta; one from each quadrant, from macroscopically unchanged locations. Sections were placed in RNA-Later for 24 hours and then, after drying, material was frozen at -80 ° C. The following techniques were then used: RNA isolation, followed by reverse transcription (RT) and real-time polymerase chain reaction (Real-Time PCR) to assess the expression of cannabinoid receptors in the tested material. The obtained results were compared to the expression of the reference genes GAPDH (3-phosphoglyceroldehyde dehydrogenase) and ACT (β -actin).

Results

In statistical analysis following differences between the study group and control group showed that CB2 receptor expression was lower in the placenta from women who undergo preterm delivery. In the study, uterine tenderness correlated with the expression of CB1 and CB1a receptors and was reported statistically more often by patients from the study group. Stimulation of CB1 and CB2 receptors causes a decrease in pain perception observed in animal models, which may be a mechanism for a different perception of pain in women during childbirth.

In the study group, the history of preterm labor, history of intrauterine fetal deaths, and pregnancies terminated by Caesarean section correlated with lower expression of the CB1 and CB1a receptors in the placenta in patients from the study group. These complications are well-known risk factors for preterm labor in subsequent pregnancies.

Urinary tract infection and bleeding reported by patients at any stage of pregnancy statistically more frequently occurred in the study group and correlated with CB2 receptor expression.

Conclusions

1. Expression of cannabinoid receptors could be an essential tool in the pathogenesis of preterm labor. The lower CB2 receptor expression more often occurs in the placenta delivered after preterm labor.
2. The occurrence of uterine pain during pregnancy correlates with the expression of cannabinoid receptors in the placenta. The lower level of the

CB1 and CB1a expression was connected with more painful contraction perception of the uterus during labor.

3. The correlation between CB1, CB1a, CB2 receptors expression and pregnancy complications found in the study, such as the occurrence of preterm delivery occurrence in the past, intrauterine death of the fetus in the past, vaginal bleeding during pregnancy, increased body temperature during delivery, and urinary tract infections, justifies that the diagnosis of cannabinoid receptor expression in pregnant women at various stages of pregnancy should be performed.