Abstract

Endometriosis is a prevalent disease associated with late diagnosis and greatly impairs women's lives in many ways. Therefore, researchers and doctors should put great emphasis on understanding the pathogenesis of this disease and also on finding a sufficiently sensitive and specific diagnostic test that would allow for early diagnosis. This study analysed the mechanisms involved in the pathogenetic processes of endometriosis with a focus on sphingolipids, which are compounds that determine cell fate by affecting cell proliferation, growth and apoptosis. Sphingolipid profiles in the endometrium, ovarian cysts and serum of patients with moderate to severe endometriosis were then characterised. Concentrations of sphinganine, sphingosine, sphingosine-1- phosphate, C14 Ceramide, C16 Ceramide, C18:1 Ceramide, C18 Ceramide, C20 Ceramide, C22 Ceramide, C24:1 Ceramide, C24 Ceramide, Lactosylceramide 16 were determined in the serum, eutopic endometrium and ovarian cyst fragments. The group of patients with endometriosis was compared with a group of women with other non endometrial ovarian cysts. Furthermore, the diagnostic value of the tested sphingolipids for distinguishing patients with endometrial ovarian cysts from patients with an ovarian cyst of non-endometriosis origin was also assessed. The concentration of individual sphingolipids was determined using ultra-high performance liquid chromatography (Agilent 1290) coupled to a triple quadrupole tandem mass spectrometer (Agilent 6460) with electrospray ionisation (ESI) (UHPLC ESI MS/MS). After taking into account the inclusion and exclusion criteria, 44 patients with endometriosis and 30 patients with other non-endometrial ovarian cysts were enrolled in the study. When comparing the endometriosis group with the control group a statistically significant increase in concentrations of C18:1- Cer, C18-Cer and C20-Cer in the serum; Sph, SPA, S1P, C20-Cer, C22-Cer, C24: 1-Cer, C24-Cer and LacCer 16 in the endometrium; Sph, SPA, SPA, C16-Cer, C18:1- Cer, C18-Cer, C20-Cer, C22-Cer, C24- 88 Cer and LacCer 16 in ovarian cysts was observed. In addition, a statistically significant decrease in serum Sph and C18-Cer concentrations in the endometrium were also observed in the endometriosis group compared to the control group. An increase in eutopic endometrial C24 Ceramide and serum C18:1 Ceramide concentrations were associated with a greater than 13-fold and 5-fold increased risk of endometriosis, respectively, in the group of women with ovarian cysts; while a decrease

in serum sphingosine concentrations increased this risk by more than 7-fold. The study also revealed that the evaluation of serum C18:1 Ceramide and endometrial C24 Ceramide concentrations makes it possible to distinguish between patients with endometrial ovarian cysts from patients with other non-endometrial ovarian cysts. The results obtained in this study indicate the involvement of sphingolipids in the pathogenesis of endometriosis. It can be assumed that some sphingolipids could be used as biomarkers in the creation of new diagnostic methods and also to differentiate between patients with endometrial and non-endometrial ovarian cysts. Hence, the findings of this study make a case for further research on a larger group of patients with less severe endometriosis.