INTISARI

Latar belakang: Endometriosis didefinisikan dengan adanya sel endometrium (kelenjar dan stroma) yang berlokasi di luar cavum uteri. Inflamasi dan neoangiogenesis merupakan tanda yang umum pada penyakit tersebut. Pada perempuan dengan endometriosis, tingkat fertilitasnya menurun dibandingkan dengan perempuan non endometriosis. Hal ini disebabkan oleh berbagai faktor. Salah satu faktor yang berpengaruh adalah faktor folikulogenesis. Dalam proses inflamasi dan angiogenesis, suatu Reaktif Oksigen Spesies (ROS) terlibat. Seperti NO, 8-OH-dG dan sitokin seperti IL-1β (Interleukin I Beta) mempengaruhi perkembangan oosit. NO disintesis oleh sekelompok enzim yang dikenal sebagai Oksida Nitrit Sintase (NOS) dan eNOS adalah salah satu dari Isoform Oksida nitrit Sintase yang menunjukkan peran dalam endometriosis.

Metode penelitian: Penelitian ini menggunakan metode *cross-sectional* dengan variabel bebas Endometriosis. Stadium/*grade* endometriosis yang diukur pada saat terdiagnosis. Pemeriksaan klinis dan laparoskopi serta Metode Operasi Wanita (MOW) dilakukan terhadap seluruh responden. Variabel terikat adalah kadar IL-1β, NO, dan 8-OH-dG di dalam cairan folikuler dan polimorfisme gen eNOS. Penelitian ini bertujuan mengkaji hubungan ekspresi gen eNOS pada pasien endometriosis. Sampel penelitian diambil dari pasien endometriosis yang menjalani laparoskopi dan pasien normal saat dilakukan MOW dengan sampel masing-masing 27 untuk pasien endometriosis dan 27 pasien normal. Pemeriksaan kadar IL-Iβ, NO, dan 8-OH-dG menggunakan metode ELISA dari cairan folikuler ovarium. Pemeriksaan polimorfisme eNOS dengan *Polymerase Chain Reaction Restriction Fragment Length Polymorphism* (PCR-RFLP).

Hasil: Hasil penelitian menunjukkan peningkatan kadar IL-1β pada penderita endometriosis dengan p=<0,05 dengan CI 95%=12,09-41,51 dengan selisih rerata 26,81. Kadar IL-1β lebih tinggi pada pasien endometriosis. Hasil pengukuran NO pada pasien endometriosis berbeda bermakna dengan p=<0.05 dengan CI 95%= 0,89-2,60 dibanding non endometriosis (rerata perbedaan 1,78). Kadar 8-OH-dG pada endometriosis lebih tinggi dari non endometriosis dengan nilai p=<0,05 dengan C1 95%= 220,57-2787,47 (selisih rerata 1504,03). Hasil PCR-RFLP gen eNOS genotipe GG, GT dan TT ada perbedaan bermakna antara pasien endometriosis dan non endometriosis (p=<0,05, OR=24,50 dan CI 95%= 1,31-1256,13. Genotype gabungan GG/GT dengan TT signifikan (p=< 0,05, OR= 5,68 dan CI 95%= 0,76-65,43. Distribusi Alel G dan T menunjukkan perbedaan bermakna (p=0,005, OR=4,66 dan CI 95%= 1,39-16,05). Gabungan genotipe GG/GT atau genotipe GG menunjukkan alel yang sering ditemukan pada endometriosis.

Kesimpulan: Kadar IL-1β, NO dan 8-OH-dG pada pasien endometriosis adalah lebih tinggi dibanding pasien normal. Polimorfisme gen eNOS dengan alel GG dan gabungan GG/GT tersering ditemukan pada endometriosis endometriosis.

Kata kunci: IL-1β, NO, 8-OH-dG , eNOS, endometriosis, stadium endometriosis

ABSTRACT

Background: Endometriosis is the presence of endometrial glands and stroma located outside the uterine cavity. Inflammation and neoangiogenesis is a common feature of the disease. In women with endometriosis, fertility levels are decreased compared with non endometriosis women. It is caused by various factors. One influential factor is the folliculogenesis factor. In the process of inflammation and angiogenesis, a Reactive Oxygen Species (ROS) is involved. Like NO, 8-OH-dG and cytokines such as IL-1β (Interleukin I Beta) affect oocyte development. NO is synthesized by a group of enzymes known as Nitric Oxide Synthase (NOS) and eNOS is one of the isoforms of nitric oxide synthase which indicates a role in endometriosis.

Methods: This study used a cross-sectional method with Endometriosis as the independent variable. Grade in endometriosis and types of endometriosis were measured at the time of diagnosis of endometriosis conducted with clinical examination and laparoscopy. The control group was normal patients who underwent MOW, while the dependent variables were the levels of IL-1β, NO, and 8-OH-dG in follicular fluid and eNOS polymorphism. This study aimed to examine the relationship of the expression of independent variables in patients to endometriosis. Samples were taken from endometriosis patients who underwent laparoscopy and normal patients when performed MOW with each 27 samples for endometriosis patients and 27 for controls. The examination of level of IL-Iβ, NO, and 8-OH-dG was with ELISA method through retrieval of ovarian follicular fluid. ENOS polymorphism examination was by the Polymerase Chain Reaction Restriction Fragment Length Polymorphism (PCR-RFLP).

Results: The results showed there were elevated levels of IL-1β in patients with endometriosis with p = 0.00 (95% CI: 12.09 to 41.51) with a mean difference of 26.81. IL-1β high levels in patients with endometriosis affected the NO levels in follicular fluid indirectly. NO excretion measurement results in patients with endometriosis were significantly different with p of 000 (95% CI 0.89 to 2.60) with the control. The difference in the mean value was 1.78. Higher NO in the follicular fluid would cause damage to DNA and cause degenerative oocytes. Levels of 8-OH-dG in endometriosis was higher than those in the control with p = 0.02 (95% C1 220.57 to 2787.47) with a mean difference of 1504.03. Like NO, 8-OHD-G would cause degeneration of oocytes and apoptosis to disrupt meiotic spindle. On eNOS examination, between genotype GG, GT and TT, there were no significant differences between patients with endometriosis and controls with p = 0.007 and OR = 24.50 (CI95% 1.31 to 1256.13). On a combined GG / GT with TT, the p-value was 0.046 with OR = 5.68 (95% CI 0.76 to 65.43). Distribution of allele G and T also showed significant differences with p = 0.004 and OR = 4.66 (CI95 and 1.39 to 16.05). Combined genotype GG / GT or genotype GG showed the most risk to the occurrence of endometriosis in Javanese women.

Conclusions: Levels of IL-1β, NO and 8-OH-dG in patients with endometriosis were higher than those in normal patients, while the polymorphisms frequency distribution in eNOS in genotype GG and combined genotype GG / GT was higher in patients with endometriosis compared with the controls.

Keywords: IL-1β, NO, 8-OH-dG, eNOS, endometriosis, endometriosis grade