

INTISARI

PERBEDAAN EKSPRESI mRNA eNOS, RESEPTOR ESTROGEN DAN ppET-1/ET_BR BERDASARKAN JENIS KELAMIN DI GINJAL TIKUS [*Rattus norvegicus* (Brekenhout, 1769)] PADA TAHAP AWAL DIABETES MELITUS

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Latar Belakang: Endothelin-1 (ET-1) menginisiasi vasodilatasi dan ekspresi eNOS melalui aktivasi ET_BR. Meskipun diabetes melitus (DM) menyebabkan aktivasi ET-1 dan kerusakan endothelium, estrogen melewati reseptor estrogen memiliki kemampuan vasoproteksi sehingga dapat memproteksi kerusakan endothelium yang dapat menginduksi nefropati diabetika. Informasi tahap awal diabetes belum banyak diketahui. Oleh karena itu, perlu penyelidikan fungsi vaskular pada tahap awal penyakit ginjal. Hubungan antara ppET-1 melalui ET_BR dan reseptor estrogen berdasarkan jenis kelamin belum diketahui pada kondisi awal diabetik.

Tujuan: Penelitian ini bertujuan untuk mengkaji ekspresi mRNA reseptor estrogen, ERa and ERb, dan ppET-1/ ET_BR sebagai vasoprotektif pada tikus DM jantan dan betina.

Metode: DM diinduksi pada tikus betina (DMB, n=6) dan jantan (DMJ, n=6) dengan *Streptozotocin* injeksi tunggal 60mg/Kg.BB. Kelompok kontrol betina (KB, n=6) dan jantan (KJ, n=6) diinjeksi NaCl 0,9% . Tikus determinasi setelah 1 bulan. Proteinuria diukur pada semua kelompok. *Reverse Transcription-PCR* (RT-PCR) dilakukan untuk mengetahui ekspresi mRNA eNOS, ET_BR, ERa and ERb dari jaringan ginjal.

Hasil: Hasil pengukuran proteinuria dan struktur histologis menunjukkan tidak ada perbedaan yang mencolok antar kelompok. Hal ini dapat dikorelasikan dengan ekspresi eNOS yang tetap pada masing-masing kelompok yang telah dikonfirmasi dengan analisis RT-PCR. Tidak ada perbedaan yang signifikan ekspresi mRNA eNOS pada kelompok DM dibandingkan dengan kontrol pada masing-masing gender. Selanjutnya, ekspresi ERa and ERb pada DMB lebih tinggi daripada DMJ. Namun, tidak ada perbedaan ekspresi ERa and ERb antara kelompok kontrol dan DM pada masing-masing jenis kelamin. Sedangkan ekspresi mRNA ET_BR DMJ lebih tinggi daripada DMB.

Kesimpulan: Peningkatan regulasi ER pada tikus DM betina dan ET_BR pada jantan diasosiasikan dengan ekspresi mRNA eNOS pada kondisi awal diabetes.

Kata Kunci: ppET-1, Diabetes Melitus, eNOS, ET_BR, Reseptor estrogen.

ABSTRACT

DIFFERENT CONTRIBUTION OF ppET-1/ET_BR AND ESTROGEN RECEPTORS IN eNOS AVAILABILITY BASED ON SEXUAL DIMORPHISM IN EARLY STAGE OF DIABETIC RATS

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Background: The ET-1 promotes vasodilation and eNOS expression through ET_BR activation. However, diabetes mellitus causes ET-1 activation and endothelial cell injury, then leads to diabetic nephropathy. Estrogen in females that has vasoprotector property may protect from endothelial injury in diabetes. Information on the early stages of diabetes is not widely known. Therefore, it is necessary to investigate vascular function in the early stages of kidney disease. There are different relationship between ppET-1/ ET_BR and estrogen receptors based on gender in early diabetic condition.

Objective: This research aims to elucidate the expression of Estrogen Receptor, ER α and ER β and ET_BR as vasodilator properties in male and female DM rats.

Methods: Diabetes Mellitus was induced in male (DMM group, n=6) and female (DMF group, n=6) rats with Streptozotocin 60mg/Kg.BB single injection. Control group was injected with NaCl 0.9% in male (CM group, n=6) and female (CF group, n=6) rats. Rats were terminated at the 1st month. Proteinuria score were measured in all groups. Reverse Transcription-PCR (RT-PCR) was performed to determine mRNA expression of eNOS, ET_BR, ER α and ER β from kidney.

Results: All groups showed that there were no significant differences in proteinuria score and histological structure related to persistent of eNOS mRNA expression which confirmed by RT-PCR analysis, there were no significant differences between eNOS mRNA expression in DM to control groups in each gender. Furthermore, ER α and ER β mRNA expression in DMF were significantly higher than DMM group. But, there were no significant differences in ER α and ER β mRNA expression between control and DM groups in male and female. Nevertheless, ET_BR mRNA expression was significantly higher in DMM compared to DMF.

Conclusions: ERs upregulation in female early diabetic rats and ET_BR upregulation in male early diabetic rats might be associated with persistent eNOS expression in early diabetic condition.

Key Words : ppET-1, Diabetes Mellitus, eNOS, ETBR, Estrogen Receptors