INTISARI

Latar belakang: Diabetes mellitus dengan hiperglikemia dapat menyebabkan gagal ginjal yang ditandai dengan cedera tubulus. *Epithelial-Mesenchymal Transition (EMT)* dengan peningkatan ekspresi mRNA vimentin dan mRNA fibronectin dapat memperparah cedera tubulus. Asam klorogenat diketahui mempunyai efek renoprotektif pada beberapa model gagal ginjal tetapi efeknya terhadap *Epithelial-Mesenchymal Transition (EMT)* dan cedera tubulus pada gagal ginjal sebagai akibat progresivitas diabetes mellitus belum diketahui.
Tujuan : Penelitian ini bertujuan untuk mengkaji peran asam klorogenat terhadap cedera tubulus dan *Epithelial-Mesenchymal Transition (EMT)* pada tikus model diabetes mellitus tipe 1.
Metode: Penelitian ini menggunakan metode quasi-eksperimental dengan sampel yang digunakan adalah tikus jantan Wistar (n=30) berusia 2 bulan. Tikus dibagi menjadi 6 kelompok yaitu kelompok kontrol, kelompok DM yang diinduksi streptozotocin 60 mg/kgBB selama 1,5 bulan (Kelompok DM1,5 n=5) dan 2 bulan (Kelompok DM2 n=5). Kelompok DM 1,5 bulan diberikan suplementasi asam klorogenat dengan dosis 12,5 mg/kgBB (kelompok CGA1 n=5), 25 mg/kgBB (kelompok CGA2 n=4), dan 50 mg/kgBB (kelompok CGA3 n=6) selama 14 hari. Setelah itu, tikus diterminasi untuk memeriksa progresivitas cedera organ pasca diabetes mellitus. Jaringan ginjal diwarnai dengan *Periodic Acid-Shiff (PAS)* untuk melihat skor cedera tubulus. *Reverse Transcription-Polymerase Chain Reaction (RT-PCR)* digunakan untuk memeriksa ekspresi marker *Epithelial-Mesenchymal Transition (EMT)* yaitu mRNA vimentin dan mRNA fibronectin sebagai indikator regenerasi tubulus.
Hasil: Hasil skor cedera tubulus pada kelompok CGA1 lebih rendah dibandingkan dengan kelompok DM1,5 dan DM2 (p = 0,009 dan p = 0,007), kelompok CGA2 lebih rendah dibandingkan dengan kelompok DM2 (p = 0,011), dan kelompok CGA3 lebih rendah dibandingkan dengan kelompok DM2 (p = 0,005) yang semuanya bermakna secara statistik. Ekspresi mRNA vimentin pada kelompok CGA1 lebih rendah dibandingkan dengan kelompok DM2 yang bermakna secara statistik (p = 0,021). Ekspresi mRNA fibronectin pada kelompok CGA2 lebih rendah dibanding kelompok DM1,5 (p = 0,907) dan DM2 (p = 0,565), walaupun tidak bermakna secara statistik.
Kesimpulan: Asam klorogenat mampu menurunkan atau memperbaiki skor cedera tubulus ginjal serta mampu mereduksi proses *Epithelial-Mesenschymal Transition (EMT)* yang ditandai dengan penurunan ekspresi marker mesenkim, yaitu mRNA vimentin dan mRNA fibronectin.

Kata kunci : Diabetes mellitus tipe 1, cedera tubulus, asam klorogenat, *Epithelial-Mesenchymal Transition (EMT)*, vimentin, fibronectin.

ABSTRACT

Background: Diabetes mellitus with hyperglycemia can cause kidney failure which is characterized by tubular injury. Epithelial-Mesenchymal Transition (EMT) with increased expression of mRNA vimentin and mRNA fibronectin can exacerbate tubular injury. Chlorogenic acid is known to have a renoprotective effect in several models of renal failure but its effect on Epithelial-Mesenchymal Transition (EMT) and tubular injury in renal failure as diabetes mellitus progresses is unknown.
Objective: This study aimed to examine the role of chlorogenic acid on tubular injury and Epithelial-Mesenchymal Transition (EMT) in a rat model of type 1 diabetes mellitus.
Methods: This study used a quasi-experimental method with the sample used was male Wistar rats (n=30) aged 2 months. Rats were divided into 6 groups : control group, DM group induced by streptozotocin 60 mg/kgBW for 1.5 months (DM1,5 group n=5) and 2 months (DM2 group n=5). The 1.5 month DM group was given chlorogenic acid supplementation at a dose of 12.5 mg/kgBW (CGA1 group n=5), 25 mg/kgBW (CGA2 group n=4), and 50 mg/kgBW (CGA3 group n=6) for 14 days. After that, the rats were terminated to examine the progression of organ injury after diabetes mellitus. Kidney tissue was stained with Periodic Acid-Schiff (PAS) to see the tubular injury score. Reverse Transcription-Polymerase Chain Reaction (RT-PCR) was used to examine the expression of Epithelial-Mesenchymal Transition (EMT) markers, mRNA vimentin and mRNA fibronectin, as indicators of tubular regeneration.
Results: The result of the tubular injury score in the CGA1 group was lower than the DM1,5 dan DM2 group ($p = 0.009$ and $p = 0.007$), the CGA2 group was lower than the DM2 group ($p = 0.011$), and the CGA3 group was lower than the DM2 group ($p = 0.005$), all of which were statistically significant. The mRNA expression of vimentin in the CGA1 group was lower than that in the DM2 group, which was statistically significant ($p = 0.021$). The mRNA expression of fibronectin in the CGA2 group was lower than that in the DM1,5 group ($p = 0.907$) and DM2 group ($p = 0.565$), although not statistically significant.
Conclusion: Chlorogenic acid is able to reduce or improve renal tubular injury score and is able to reduce the Epithelial-Mesenchymal Transition (EMT) process which is characterized by a decrease in the expression of mesenchymal markers, mRNA vimentin and mRNA fibronectin.

Keywords: Type 1 diabetes mellitus, tubular injury, chlorogenic acid, Epithelial-Mesenchymal Transition (EMT), vimentin, fibronectin.