Efek kuersetin terhadap ginjal tikus model penyakit ginjal kronik melalui jalur nuclear factor-erythroid-2 related factor 2 (NRF2) = The effect of quercetin on kidney in rat model of chronic kidney disease via activating the nuclear factor erythroid-2 related factor-2 (NRF2) pathway

Kamalia Layal, author

Abstrak

Latar Belakang: Penyakit ginjal kronik (PGK) merupakan penyakit progresif dan ireversibel yang mempunyai berbagai komplikasi serius serta belum ada terapi yang dapat memperbaiki kerusakan ginjal yang telah terjadi. Beberapa studi menunjukkan stres oksidatif berperan dalam patogenesis penyakit ini. Stres oksidatif terjadi akibat ketidakseimbangan produksi ROS dan pertahanan antioksidan. Nrf2 merupakan faktor transkripsi yang terlibat dalam mekanisme pertahanan sel dalam mengatasi stres oksidatif. Penelitian ini bertujuan untuk mengetahui aktivitas kuersetin sebagai aktivator Nrf2 dalam menghambat progresivitas penyakit ginjal yang diinduksi nefrektomi 5/6.
Metode: Tikus Sprague-Dawley jantan dikelompokkan secara acak dalam kelompok kontrol normal (C), kontrol nefrektomi 5/6 (Nx), nefrektomi 5/6 yang diberi kuersetin dengan dosis 100 mg/kgbb/hari/p.o. (NxQ), nefrektomi 5/6 dan diberi kaptopril dengan dosis 10 mg/kgbb/hari/p.o. (NxK). Hewan coba diterminasi diakhir perlakuan untuk diambil darah, urin, dan organ ginjalnya. Pemeriksaan yang dilakukan adalah pemeriksaan proteinuria, kreatinin urin dan plasma, ureum plasma, kadar MDA plasma dan jaringan, aktivitas glutation peroksidase (GPx), kerusakan jaringan (histopatologi) dan ekspresi Nrf2 (imunohistokimia).
Hasil: Hasil penelitian menunjukkan bahwa nefrektomi 5/6 dapat menimbulkan peningkatan proteinuria, ureum plasma, dan derajat fibrosis ginjal secara signifikan. Nefrektomi 5/6 cenderung meningkatkan kreatinin plasma, kadar MDA ginjal, aktivitas GPx, dan menurunkan MDA plasma serta ekspresi Nrf2. Kuersetin tidak mempengaruhi proteinuria, ureum dan kreatinin plasma, dan derajat fibrosis ginjal. Kuersetin cenderung menurunkan kadar MDA dan meningkatkan aktivitas enzim GPx serta ekspresi Nrf2.
Kesimpulan: Kuersetin tidak mempengaruhi proteinuria, ureum dan kreatinin plasma serta kerusakan struktur jaringan atau fibrosis ginjal. Kuersetin cenderung menurunkan kadar MDA dan meningkatkan aktivitas enzim GPx serta cenderung meningkatkan ekspresi Nrf2.
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Background: Chronic Kidney Disease (CKD) is a progressive and irreversible condition that has several serious complications and currently there has no single therapy that can repair kidney damage was occurred. Some studies suggest a role of oxidative stress in the pathogenesis of this disease. Oxidative stress is caused by an imbalance of ROS production and antioxidant defenses. Nrf2 is a transcription factor involved in cell defense mechanisms againts oxidative stress. This study was aimed to determine the quercetin activity as Nrf2 activator in inhibit the progression of 5/6 nephrectomy induced CKD in male rats.
Method: Sprague-Dawley rats were randomly divided into normal control group (C), untreated 5/6 nephrectomy (Nx), quercetin-treated 5/6 nephrectomy, NxQ (100 mg / kg / day orally), captopril-treated 5/6 nephrectomy, NxK (10 mg / kg / day orally). Animal models was sacrificed at the end of intervention to take

blood to measure creatinine, urea, and MDA, urine to measure protein and creatinine, and kidney organ to measure levels of MDA, glutathione peroxidase (GPx) activity, and renal damage (histopathology) and Nrf2 expression (immunohistochemistry).
Results: The results showed that 5/6 nephrectomy may cause an increased of proteinuria, plasma urea, and grade of renal fibrosis significantly. 5/6 nephrectomy has trend to increased plasma creatinine, renal MDA levels, GPx activity, and decreased plasma MDA and Nrf2 expression. Quercetin did not decrease proteinuria, plasma urea and creatinine, and renal fibrosis grading. Quercetin tend to reduced levels of MDA, increased GPx enzyme activity, and expression of Nrf2.
Conclusion: Quercetin does not affect proteinuria, plasma urea,plasma creatinine, and tissue damage or kidney fibrosis. Quercetin tend to reduced levels of MDA and increased the activity of GPx and Nrf2 expression.