Studi Patofisiologi Sindroma Metabolik pada Skizofrenia Berbasis Pendekatan Polimorfisme Gen GCLC GAG TNR Terhadap Aktivitas Stres Oksidatif dan Metabolisme Seluler = Metabolic Syndrome Patophysiology Study in Schizophrenia on GCLC GAG TNR Gene Polymorphism Towards Oxidative Stress and Cellular Metabolism

Kresna Septiandy Runtuk, author

Abstrak

Latar Belakang: Skizofrenia merupakan gangguan jiwa berat yang kompleks dengan angka harapan hidup yang rendah karena penyakit kardiovaskular. Orang dengan skizofrenia rentan mengalami sindroma metabolik meskipun tidak mendapat pengobatan antipsikotika. Sebuah penelitian di RSUPN Cipto Mangunkusumo menunjukkan prevalensi sindroma metabolik sebanyak 3,3% sampai 68% yang berhubungan dengan stress oksidatif dan berpotensi menurunkan produksi ATP. Penelitian ini berusaha menjelaskan patofisiologi sindroma metabolik pada skizofrenia dan hubungannya terhadap polimorfisme gen GCLC GAG TNR, stres oksidatif dan aktivitas metabolisme seluler.
Metode: Penelitian merupakan penelitian observasional analitik. Subjek sebanyak 25 pasien skizofrenia dan 25 pasien kontrol sehat dilakukan pengambilan fibroblas dan PBMC kemudian dilakukan pengamatan polimorfisme gen GCLC GAG TNR, stres oksidatif (kadar MDA, MnSOD, GSH, GSSG, dan rasio GSH/GSSG), aktivitas metabolisme seluler (kadar ATP), dan parameter sindroma metabolik (lingkar pinggang, Indeks Massa Tubuh (IMT), LDL-c, HDL-c, TG, HbA1C, dan tekanan darah). Hubungan dianalisis dengan uji komparasi atau uji korelasi.
Hasil: Terdapat korelasi pada sel fibroblas dengan PBMC yaitu korelasi kuat pada MnSOD (r=0.797) dan korelasi sedang pada GSSG (r=0.581). Didapatkan perbedaan yang bermakna pada kadar stres oksidatif yaitu MDA (p=0.013), GSH (p0.001), GSSG (p0.001), dan rasio GSH/GSSG (p0.001) pada kelompok skizofrenia dan kontrol serta didapatkan hubungan polimorfisme gen GCLC GAG TNR terhadap MDA (p=0.054) dan GSSG (p=0.010) pada kelompok skizofrenia tetapi tidak ditemukan perbedaan kadar ATP dan hubungan antara polimorfisme GCLC GAG TNR terhadap kadar ATP. Pada orang dengan skizofrenia didapatkan lingkar pinggang, IMT, LDL-c, dan HDL-c yang lebih rendah (p=0.025;p=0.003;p=0.022;p=0.010) dan TG yang lebih tinggi (p=0.038) dibandingkan kelompok kontrol.
Simpulan: Polimorfisme gen GCLC GAG TNR memiliki hubungan terhadap stres oksidatif tetapi tidak ada hubungan terhadap aktivitas metabolisme seluler. Tidak terdapat perbedaan aktivitas metabolisme seluler pada orang dengan skizofrenia dan tidak ditemukan hubungan antara metabolisme seluler dengan sindroma metabolik. Terjadi perubahan kadar penanda stres oksidatif yang memiliki

hubungan terhadap sindroma metabolik pada orang dengan skizofrenia
.....Background: Schizophrenia is a complex severe mental disorder with low life expectancy due to cardiovascular disease. People with schizophrenia is prone to metabolic syndrome even if they do not receive antipsychotic. One study in Cipto Mangunkusumo General Hospital showed the prevalence of metabolic syndrome as much as 3.3% to 68% which correlate with oxidative stress and has the potential to reduce ATP production. This study aims to explain the pathophysiology of the metabolic syndrome in schizophrenia and its relationship to the GCLC GAG TNR gene polymorphism, oxidative stress and metabolic activity.
Methods: This research is an observational analytic study. Twenty five schizophrenic patients and 25 healthy control patients were admitted to study. Fibroblast and PBMC (peripheral blood mononuclear cell) were taken to measure GCLC GAG TNR gene polymorphism, oxidative stress (levels of MDA, MnSOD, GSH, GSSG, and GSH/GSSG ratio), cellular metabolic activity (ATP levels), and metabolic syndrome parameters (waist circumference, body mass index (BMI), LDL-c, HDL-c, TG, HbA1C, and blood pressure). Relationship between variables were analyzed by comparison test or correlation test.
Results: There is a correlation in fibroblast cells with PBMC with a strong correlation in MnSOD (r=0.797) and a moderate correlation in GSSG (r=0.581). There were significant differences in the levels of oxidative stress, namely MDA (p=0.013), GSH (p0.001), GSSG (p0.001), and GSH/GSSG ratio (p0.001) in the schizophrenia and control groups. There was correlation found for the polymorphism of the GCLC GAG TNR gene towards MDA (p=0.054) and GSSG (p=0.010) in the schizophrenia group but found no difference in ATP levels in the schizophrenia and control groups alongside with GCLC GAG TNR polymorphism and ATP levels. In people with schizophrenia, waist circumference, BMI, LDL-c, and HDL-c were lower (p=0.025;p=0.003;p=0.022;p=0.010) and higher TG (p=0.038) than the control group.
Conclusion: GCLC GAG TNR gene polymorphism has correlation to oxidative stress but not to cellular metabolic activity. There is no difference in metabolic activity in people with schizophrenia and no relationship between cellular metabolism and the metabolic syndrome. There is alteration of oxidative stress markers which have an association with metabolic syndrome in people with schizophrenia.