Pengaruh likopen terhadap kerusakan hati tikus akibat alkohol

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Abstrak

Ruang lingkup dan metode penelitian:
Alcoholic liver disease (penyakit hati alkoholik, ALD) merupakan salah satu komplikasi utama dari penyalahgunaan alkohol. Konsumsi alkohol kronik dapat menginduksi stres oksidatif pada jaringan hati dan ekstrahati karena ketidakseimbangan antara pro-oksidan dan antioksidan, menghasilkan radikal bebas yang dapat merusak komponen selular dan menyebabkan peroksidasi lipid yang mengakibatkan steatosis (perlemakan hati), steatohepatitis (hepatitis alkoholik) sampai sirosis. Penelitian sebelumnya memperlihatkan pemberian likopen sebelum etanol kronik memberikan efek perlindungan pada kerusakan mitokondria hati tikus in vivo.

Penelitian ini bertujuan untuk menguji hipotesis bahwa likopen yang diberikan bersamaan dengan alkohol kronik dapat melindungi kerusakan hati tikus akibat alkohol. Untuk menilai efek proteksi likopen sehubungan dengan stres oksidatif yang ditimbulkan alkohol, dilakukan pengukuran kadar peroksida lipid (malondiatdehid, MDA), glutation (GSH), glutamat piruvat transaminase (GPT) jaringan hati dan plasma, serta pemeriksaan histopatologi jaringan hati.

Penelitian ini menggunakan 25 ekor tikus putih galur Sprague-Dawley, yang dibagi menjadi 5 kelompok secara acak, masing-masing terdiri dari 5 ekor. Kelompok I (kontrol), diberikan CMC (Carboxy Methyl Celulose) 1% (b/v) 1 ml/100 gBB/hari; kelompok II diberikan etanol 25% (b/v) 1 ml/gBB (2,5 g/kgBB)/hari; kelompok III, 1V, dan V, masing-masing diberikan etanol (2,5 g/kgBB/hari) dan likopen 50; 100; 200 mg/kgBB/hari selama 4 minggu.

Seluruh hewan coba diterminasi dengan cara dekapitasi pada hari ke-28, sebelumnya tikus dipuasakan selama 24 jam. Darah diambil untuk pengukuran kadar MDA, GSH,dan GPT had dan plasma. Selain itu hati lobus kiri diambil untuk pemeriksaan histopatologis, sisanya untuk pengukuran MDA, GSH, dan GPT. Nilai rerata data ± SD kadar MDA, GSH, dan GPT dianalisis dengan uji Anova satu arah dan bila bermakna, dilanjutkan dengan analisa antar kelompok dengan uji Bonferroni. Skor patologi diuji dengan uji Kruskal-Wallis, dan bila bermakna dilanjutkan dengan perbandingan antara kelompok dengan uji Mann-Whitney. Seluruh uji statistik dilakukan dengan menggunakan SPSS.

Hasil
- Pertambahan berat badan kelompok EtOH lebih kecil dibandingkan kelompok lainnya (kontrol dan likopen 200 mg/kg BB/hari, $p<0.01$; likopen 100 mg/kgBB/hari, $p<0.05$; likopen 50 mg/kgBB/hari $p>0.05$).
- Kadar MDA hati dan plasma meningkat lebih dari 2x lipat pada kelompok EtOH secara bermakna (0.001) dibandingkan dengan kelompok kontrol. Likopen berbagai dosis dapat menurunkan peningkatan kadar MDA hati dan plasma ini secara bermakna ($p<0.001$). Di samping itu, likopen dosis sedang dan tinggi dapat

menurunkan kadar MDA hati dan plasma sampai setara dengan kontrol.
- Penurunan kadar GSH hati dan plasma pada kelompok EtOH ($p<0.001$) dibandingkan dengan kelompok kontrol, dapat ditingkatkan oleh likopen berbagai dosis secara bermakna ($p<0.001$). Likopen dosis sedang dan tinggi meningkatkan penurunan ini mencapai nilai kelompok kontrol.
- Penurunan kadar GPT hati pada kelompok EtOH ($p<0.001$) dibandingkan dengan kelompok kontrol, dapat ditingkatkan oleh likopen berbagai dosis ($p<0.001$), likopen dosis tinggi dapat mengembalikan kadar GPT hati setara dengan kelompok kontrol. Peningkatan kadar GPT plasma pada kelompok EtOH walaupun secara klinik tidak bermakna (<3x lipat nilai normal), tapi secara statistik bermakna ($p<0.001$) dibandingkan dengan kelompok kontrol. Likopen dosis sedang dan tinggi dapat mengembalikan kadar GPT hati setara dengan nilai kelompok kontrol.
- Pemberian etanol kronik menyebabkan akumulasi lemak sedang-berat dan nekrosis pada hati (skor patologi 3±0), perubahan patologi ini dicegah secara bermakna oleh likopen dosis rendah (skor patologi 2±0, $p<0.01$); likopen dosis sedang (skor 1.6± 0.55, $p<0.005$), dan dosis tinggi (1.4±0.55, $p<0.005$). Hanya likopen dosis sedang dan tingi yang dapat mengembalikan nilai skor patologi setara dengan kontrol.

Kesimpulan
1. Likopen dapat mencegah cedera hati akibat alkohol melalui aktivitas antioksidannya (scavenger radikal peroksida dan quenching oksigen singlet) yang diperlihatkan oleh adanya penurunan stres oksidatif dan perbaikan fungsi hati.
2. Suplementasi likopen dosis sedang (100 mg/kgBB/hari) dan tinggi (200 mg/kgBB/hari) dapat mengembalikan fungsi hati kembali setara dengan kelompok kontrol. Suplementasi likopen dosis kecil (50 mg/kgBB/hari) walaupun sudah dapat memberikan perlindungan dibandingkan dengan kelompok EtOH, tetapi belum dapat mengembalikan fungsi hati kembali setara dengan kelompok kontrol.
<hr><i>Alcoholic liver disease is one of the main complications of alcohol abuse. Consumption of chronic alcohol may induce oxidative stress in liver and extra hepatic tissues because of imbalance between pro-oxidant and antioxidant, this would result in free radical accumulation which destroy cellular component and lipid per oxidation leading to steatosis (fatty liver), steatohepatitis (alcoholic hepatitis), and sirosis. Previous studies showed that lycopene supplementation giving prior to chronic ethanol administration gave protection of liver mitochondria damage in rats in vivo.

This study was designed to investigate the effects of lycopene on liver damage in rats given at the same time with chronic alcohol by measuring the MDA, GSH, and GPT of liver tissue and plasma, as well as pathological change of liver tissue.

Twenty-five Sprague-Dawley rats were divided randomly into five groups. The first group received CMC 1%, 1ml/100 gBW daily (control); the second group received etanol 25%, 1 ml/gBW (2.5 g/kgBW) daily; the third, fouth, and fift group received ethanol and likopen 50; 100; 200 mg/kgBW daily respectively for 4 weeks.

All rats were scarified by decapitation at day 28, after over night fasting. Blood samples were used for measuring MDA, GSH, and GPT. The left lobe of liver was used for histopathological analysis and the remaining liver tissues were used for measuring MDA, GSH, and GPT.

One-way ANOVA with Bonferroni's posthoc tests were used for the determination of statistical significance as appropriate; data represented as mean SD. For comparison of pathological scores, the Kruskal-Wallis rank sum test and Mann-Whitney's posthoc test were used. A p value less than 0.05 was selected before the study as the level of significance. All statistical tests were carried out by means of SPSS.

Result

- Body weight gains in EtOH group was the smallest compared to other groups (control vs lycopene 200 mg/kgBW/d, $p<0.01$; lycopene 100 mg/kgBW/d, pe0.05; lycopene 50 mg/kgBW/d, $p>0.05$).
- Liver and serum MDA levels in EtOH group were increased significantly ($p<0.001$) more than 2-fold over control value; various doses of lycopene blunted this increase significantly. Moderate and high doses of lycopene ecreased liver and serum MDA levels, which were not significantly different from that of control values.
- Liver and serum GSH levels in EtOH group were decreased significantly ($p<0.001$) compared to control value; various doses of lycopene blunted this decrease significantly ($p<0.001$). Moderate and high doses of lycopene increase liver and serum GSH levels, which were not significantly different from that of control values.
- Liver GPT levels in EtOH group were decreased significantly ($p<0.001$) compared to control group; lycopene in various doses blunted this decrease significantly ($p<0.001$), lycopene high dose blunted this decrease which were not significantly different from that of control values. Serum GPT levels in EtOH group were increased significantly ($p<0.001$) compared to control group, although not clinically significant (less than 3-fold over control value). Moderate and high doses of lycopene blunted this increase which was not significantly different from that of control values,
- Chronic ethanol consumption caused moderate-severe fatty liver and necrosis (pathology score: 3 ± 0). These pathological changes were blunted significantly by small dose (pathological score 2 ± 0, $p<0.01$); moderate dose (pathological score 1.6 ± 0.55, $p<0.005$) and high dose (pathological score 1.4 ± 0.55, $p<0.005$) of lycopene. Only moderate and high doses of lycopene reversed pathologcal score which were not significantly different from that of control values.

Conclusions:

1. Lycopene prevented liver injury induced by alcohol through its antioxidant activities (scavenging peroxide radical and quenching singlet oxygen), showed by decreased oxidative stress and improvement of liver function.
2. Lycopene of moderate dose (100 mg/kgBW daily) and high dose (200 mg/kgBW daily) supplementation reversed liver functions which were not significantly different from that of control values. Although low dose of lycopene (50 mg/kgBW daily) gave protection compare to EtOH group, but it couldn't reverse liver functions which were not significantly different from that of control values.</i>