Prekondisi dan hipotermia untuk proteksi cedera reperfusi hepar pada oryctolagus cuniculus = Precondition and hypothermia for protection from hepatic reperfusion injury on oryctolagus cuniculus

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Abstrak

Pendahuluan: Cedera iskemia reperfusi CI/R merupakan masalah serius yang dihadapi pascahipoksia menyebabkan kerusakan sel yang letaknya berjauhan remote organ injury. Strategi yang digunakan untuk mengurangi kerusakan hepar pascaiskemia adalah melalui penerapan ischemic pre conditioning PI/R dan hiportemia. PI/R telah terbukti mengurangi kerusakan jaringan melalui mekanisme resistensi terhadap iskemia dan kebutuhan energi lebih rendah. Sedangkan hipotermia menghambat laju kematian sel sehingga dapat diterapkan sebagai terapi awal pada tatalaksana trauma dengan tujuan mencegah kerusakan bertambah berat. Penelitian ini bertujuan untuk diketahuinya efek protektif PI/R dan hipotermia terhadap perubahan morfologi jaringan hepar dan peningkatan kadar malondialdehyde MDA sebagai respon stress oksidatif.
Metode: Studi eksperimental pada 24 ekor Oryctolagus cuniculus. Kelompok iskemia dilakukan ligasi arteri femoralis komunis dalam pembiusan selama empat jam untuk menginduksi iskemia, kemudian ligasi dibuka dan kelinci dibiarkan beraktivitas selama delapan jam. Pada kelompok PI/R dilakukan ligasi berulang arteri femoralis komunis kanan selama dua menit, dilepaskan tiga menit sebanyak dua siklus, kemudian diligasi selama empat jam. Kelompok hipotermia, dilakukan iskemia disertai membungkus ekstremitas bawah kanan dengan es, suhu antara 31-33oC Kemudian dilakukan laparotomi, dan diambil organ hepar. Pemeriksaan histopatologi hepar dilihat dari 3 zona, sentral, midzonal, perifer. Untuk menilai stress oksidatif jaringan dilakukan pemeriksaan biokimia dengan malondialdehyde MDA. Dilakukan uji statistik terhadap variabel tersebut dengan kemaknaan.
Hasil: Pada pemeriksaan histomorfologi terdapat perbedaan perubahan histomorfologi pada sampel kontrol PI/R, dan Hipotermia terhadap iskemia ($p<0,05$). Derajat kerusakan histomorfologi pada kelompok PI/R lebih rendah dibandingkan kelompok iskemia reperfusi pada semua zona (p sentral = 0,015, p medial = 0,019, p perifer = 0,026). Analisis kadar MDA memperlihatkan terjadi peningkatan pada kelompok iskemia reperfusi menujukkan adanya stress oksidatif. Kadar MDA pada kelompok PI/R dan hipotermia lebih rendah dibandingkan kelompok iskemia.($p = 0,002$).
Konklusi: Keadaan iskemia reperfusi menyebabkan perubahan histomorfologi dan stres oksidatif sel–sel hepar. PI/R dan hipotermia mempunyai efek protektif pada cedera iskemia reperfusi. Efek protektif PI/R lebih baik dari hipotermia.
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Introduction: Ischemia-reperfusion injury IRI is a serious problem occuring after hypoxia it causes injuries to cells located remotely from one another remote organ injury. Strategies used to decrease hepatic injuries post ischemic condition are composed as ischemic pre-conditioning IPC and hypothermia management procedures. IPC has been proven to decrease tissue injuries through resistance mechanisms towards ischemia and lower energy requirements. Meanwhile, hypothermia detained the rate of cell deaths, therefore, it can be used as initial therapy on trauma management in order to prevent worsening of the injuries. This research aims to evaluate the protective effects of IPC and hypothermia towards morphological changes of

hepatic tissues and the increase of malondialdehyde MDA level as a response to oxidative stress.Methods. Methods: This research is an experimental, descriptive-analytical study on 24 Oryctolagus cuniculus. The specimens were divided into four groups, with one group as control. The ischemia group underwent femoral artery ligations under anesthesia for four hours to induce ischemia. Afterwards, the ligations were released and the rabbits were free to roam for eight hours. The IPC group underwent repeated ligations of right communal femoral artery for two minutes and three minutes of release in two cycles. Afterwards, the arteries were ligated for four hours. The hypothermia group underwent ischemia and wrapping of right lower extremities using ice, with temperature around 31-33oC. Afterwards, laparotomies were conducted on all groups to obtain and evaluate the liver. Hepatic histopathology assessment were conducted from 3 zones, the central, midzone, and peripheral zone. To evaluate the effects of oxidative stress on the tissue, a biochemical assessment with malondialdehyde MDA was conducted. Statistical tests were then conducted to assess the relationship between the variables with significance level $p < 0.05$.
Results: On histomorphological assessment, there were histomorphologic changes on control samples for IPC and hypothermia compared to ischemia $p < 0.05$. On MDA level analysis, there were increases in all four groups $p < 0.05$. However, there were no significant differences for the histomorphological changes when compared between central, medial, and peripheral zones.
Conclusion: Ischemic reperfusion condition causes histomorphological changes and oxidative stress on hepatic cells. IPC and hypothermia have protective effects from ischemia-reperfusion injuries. The protective effects of IPC was better than hypothermia.