Pengaruh pemberian pentoksifilin terhadap perubahan kadar platelets activating factor pada cedera reperfusi-iskemik tungkai akut

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Abstrak

Latar Belakang. Cedera Reperfusi Iskemia merupakan eksaserbasi paradoks mengakibatkan disfungsi dan kematian sel setelah aliran darah direstorasi ke jaringan yang sebelumnya iskemia. Pada iskemia tungkai akut, reperfusi menimbulkan reaksi kompleks melibatkan inflamasi lokal maupun sistemik dengan dampak lokal sindroma kompartemen dan dampak sistemik berupa disfungsi hingga kegagalan multi organ. Platelets activating factors (PAF) sebagai mediator inflamasi pospholipid mempunyai efek fisiologis yang poten dan beragam, sehingga meningkatkan respon inflamasi pada cedera reperfusi iskemik.

Berbagai upaya untuk mencegah dan memperingan cedera reperfusi iskemik, antara lain penggunaan prosedur ischemic preconditioning, antioksidan dan terapi anti-sitokin telah diteliti namun hasil dan manfaat klinisnya belum memuaskan. PTX, phosphodiesterase nonspesifik derivat xanthine, memperlihatkan efek penekanan inflamasi dan menghambat interaksi lekositendotel yang menjanjikan dalam mencegah cedera reperfusi. Namun hasil penelitian mengenai peran pentoxifylinne dalam menekan reaksi inflamasi melalui penekanan PAF pada iskemia tungkai akut tidak konsisten. Sehingga penelitian ini bertujuan untuk menilai peran PTX dalam mengurangi cedera reperfusi melalui penekanan mediator inflamasi PAF pada hewan coba kelinci dengan Reperfusi Iskemia tungkai akut.

Metodologi. Dilakukan tindakan iskemik tungkai kiri selama 3 jam yang diikuti 2 jam periode reperfusi pada 10 ekor kelinci New Zealand White jantan yang dibagi menjadi 2 kelompok (kelompok pentoksifin dan kelompok kontrol) secara acak. Pada kelompok perlakuan diberikan PTX 30 menit sebelum reperfusi dengan dosis initial bolus 40 mg/kgBB diikuti dengan dosis rumatan 1 mg/kg BB/jam hingga 3 jam periode reperfusi. Pada kelompok kontrol diberikan cairan garam fisiologis dengan kecepatan dan volume yang sebanding. Tindakan Iskemik dilakukan dengan oklusi arteri iliaka komunis sinistra mengunakan klem selama 3 jam kemudian dilanjutkan dengan restorasi aliran darah. Pengambialn sampel untuk pemeriksaan kadar PAF dilakukan pada 2,5 jam iskemik dan pada 2 jam reperfusi.

Hasil. Pada periode Iskemik dua jam tiga puluh menit tidak mengakibatkan perbedaan bermakna (p=0,754), kadar rerata PAF pada kelompok PTX 13,09 ± 0,41 pg/mL dan kelompok kontrol I3,38 ± 0,28 pg/mL. Pada jam ke dua tindakan reperfusi ditemukan perbedaan bermakna (p=0,009) kadar rerata PAF dari kelompok PTX menurun menjadi 11,36±0,78 pg/mL dan kelompok kontrol meningkat menjadi 25,5±0,78 pg/dL.

Kesimpulan. PTX menurunkan kadar PAF plasma kelinci dengan cedera reperfusi iskemikia tungkai akut. <hr><i>Background. Ischemic reperfusion injury is a paradoxical exacerbation of cell dysfunction and death following the restoration of blood flow to previously ischemic tissue. Restoration of blood flow is essential to salvage ischemic tissue, however reperfusion itself paradoxically causes further damage to the ischemic

tissue, threatening function and viability both organ local and distal through the inflammation response.

In Acute limb ischemia, there are essentially two components: a local component that can result in increasing the regional damage from ischemia inflammatory responses which may result in local syndrome, compartment syndrome, and systemic syndrome, multi organ dysfunction and failure.

Several method and attempt had been studied and performed to prevent and attenuate reperfusion injury such as, ischemic preconditioning, antioxidant, and anti-cytokine therapy, but their clinical benefit were not satisfactory. Pentoxifylline has emerged as an agent that may attenuate inflammation response through several mechanisms. However, studies on PTX and its function to prevent and attenuate inflammation response through attenuating PAF in acute limb ischemic were not consistent. In this study the role of PTX and its function to prevent and attenuate inflammation response through attenuating PAF in acute limb ischemic was investigated.

Methods. Acute limb ischemia in the left lower limbs of 10 New Zealand White male rabbit were performed for 3 hour followed by 2 hours period of ischemia. The rabbits were randomly separated into 2 groups of five (group pentoxifylinne and group control). The Pentoxifylline group was given PTX 40 mg/kg bolus half an hour prior to reperfusion followed by maintenance dose 1 mg/kg/hour until 2 hour post reperfusion, while the control group was given normal saline solution with comparable volume and rate administration. Acute limb Ischemic procedure was performed by direct occlusion of the left femoral artery using non traumatic clamp and followed by releasing the clamp after 3 hours of occlusion. Level of PAF were measured after 2.5 hour of ischemic period and after 2 hours of reperfusion period.

Results. After 2.5 hours of ischemic period, the mean PAF levels did not show any significant difference (p=0.754). The mean PAF level of pentoxifylline group 13.09f0.41 pg/mL, while the mean PAF level of control group 13.38±0.28 pg/mL, After 2 hours period of reperfusion, there were significant differences of mean PAF level between the two groups (p=0.009). The mean PAF level in the control group increase by 12.1 110.79 to became 25.5±0.78 pg/dL, while the mean PAF level of the PTX group decrease by 1.73f1.1 pg/mL and became 11.36±0.78 pg/m L.

Conclusion. PTX decreased the PAF level in rabbits with acute limb ischemic reperfusion injury.</i>