ABSTRAK

Latar belakang: Terapi trauma uretra saat ini dilakukan setelah striktur uretra terjadi dengan tingkat keberhasilan yang tidak memuaskan. Gen yang berperan dalam perkembangan striktur uretra antara lain TGF-β1, MMP-1, CTGF dan PAI-1. Tujuan penelitian ini adalah menilai efek docetaxel dan captopril pada ekspresi mRNA gen-gen tersebut dan gambaran histologi jaringan.
Metode: 28 kelinci jantan *New Zealand* berusia 230 ± 20 hari dengan berat 4 hingga 5 kg yang mengalami ruptur uretra dengan reseksi endoskopik dalam kondisi teranestesi. Subjek dibagi menjadi 5 kelompok; kelompok kontrol negatif, kelompok ruptur+tanpa obat, kelompok ruptur+captopril (captopril 0,05 mg/kelinci/hari), kelompok ruptur+docetaxel (docetaxel 0,1 mg/kelinci/hari) dan kelompok ruptur+docetaxel+captopril (docetaxel 0,1 mg dan captopril 0,05 mg/kelinci/hari). Kelinci mendapat gel transuretral larut air yang mengandung obat sesuai kelompoknya selama 28 hari. Setelah masa perlakuan, kelinci di-*sacrifice* dengan penthotal 200mg, kemudian dilakukan pemeriksaan *real time* PCR dan histologi corpus spongiosum.
Hasil: Ekspresi mRNA TGF-β1 pada kelompok ruptur+tanpa obat lebih tinggi dari kelompok kontrol negatif, kelompok ruptur+docetaxel dan kelompok ruptur+docetaxel+captopril.
Ekspresi mRNA MMP-1 tidak berbeda pada semua kelompok penelitian.
Ekspresi mRNA CTGF kelompok ruptur+tanpa obat lebih tinggi dari kelompok kontrol negatif, kelompok ruptur+captopril, kelompok ruptur+docetaxel, dan kelompok ruptur+docetaxel+captopril.
Ekspresi mRNA PAI-1 kelompok ruptur+tanpa obat lebih rendah dari kelompok kontrol negatif dan kelompok ruptur+docetaxel.
Luas lumen kelompok ruptur+tanpa obat lebih sempit dibanding kelompok kontrol negatif, dan kelompok ruptur+captopril.
Perimeter lumen kelompok ruptur+tanpa obat lebih pendek dibanding kelompok kontrol negatif, kelompok ruptur+captopril.
Perimeter membrana basalis kelompok ruptur+tanpa obat lebih pendek dari kelompok kontrol negatif, kelompok ruptur+captopril, kelompok ruptur+docetaxel.
Luas area yang dibatasi membrana basalis kelompok ruptur+tanpa obat lebih sempit dibanding kontrol negatif,
Panjang perimeter sentral tidak berbeda pada semua kelompok penelitian.
Luas epitel tidak berbeda dengan semua kelompok penelitian.
Ketebalan epitel rata-rata tidak berbeda dengan semua kelompok penelitian
Fraksi area fibrosis kelompok ruptur+tanpa obat lebih banyak dibanding kelompok kontrol negatif, kelompok ruptur+captopril, kelompok ruptur+docetaxel, kelompok ruptur+docetaxel+captopril
Kesimpulan: Docetaxel dan captopril adalah agen yang menjanjikan untuk menghindari perkembangan striktur uretra pada ruptur uretra anterior.

Kata kunci: docetaxel, captopril, TGF-β1, CTGF, PAI-1, MMP-1.

ABSTRACT

Background: Treatment of urethral trauma is currently done after urethral stricture occurs, which gives an unsatisfactory success rate. There are several genes that have been shown to play a role in the development of urethral stricture such as TGF-β1, MMP-1, CTGF and PAI-1. The aim of this study was to assess the effects of docetaxel and captopril on mRNA expression of these genes and tissue histology.

Methods: The subjects of this research were 28 male New Zealand rabbits aged 230 ± 20 days weighing 4 to 5 kg who underwent urethral rupture by endoscopic resection in anesthetized condition. Subjects were divided into 5 groups; negative control group, positive control group, captopril group (0.05 mg captopril / rabbit / day), docetaxel group (docetaxel 0.1 mg / rabbit / day) and docetaxel+captopril group (docetaxel 0.1 mg / rabbit / day and 0.05 mg captopril / rabbit / day). Rabbits get water-soluble transurethral gel that contains drugs according to their group for 28 days. After the treatment period, rabbits were sacrificed with penthotal 200mg, then corpus spongiosum was prepared for real time PCR and histology examination.

Results: TGF-β1 mRNA expression in the rupture+drug-less group was higher than the negative control group, the rupture+docetaxel group and the rupture + docetaxel + captopril group.

MMP-1 mRNA expression did not differ in all study groups.

The expression of CTGF mRNA in rupture+drug-less group was higher than the negative control group, the rupture + captopril group, the rupture + docetaxel group, and the rupture + docetaxel + captopril group.

MRNA expression of PAI-1 rupture+drug-less group was lower than the negative control group and the rupture + docetaxel group.

The lumen area of rupture+drug-less group was narrower than that of the negative control group and the rupture + captopril group.

Lumen perimeter of the the rupture+drug-less group was shorter than the negative control group, the rupture + captopril group.

The basal membrane perimeter of the rupture+drug-less group was shorter than the negative control group, the rupture + captopril group, the rupture + docetaxel group.

The area limited by the basement membrane of the rupture+drug-less group was narrower than the negative control group.

The length of the central perimeter, the epithelial and the mean epithelial thickness area did not differ in all study groups.

The fraction of the fibrosis area in the the rupture+drug-less group was higher than the negative control group, the rupture + captopril group, the rupture + docetaxel group, the rupture + docetaxel + captopril group.

Conclusion: Docetaxel and captopril are promising agents to avoid the development of urethral strictures in anterior urethral rupture.

Keywords: docetaxel, captopril, TGF-β1, CTGF, PAI-1, MMP-1.