Peningkatan kolagen total pada model striktur uretra Kelinci New Zealand : Kajian perubahan kadar enzim matriks metaloproteinase tissue inhibitor of metalloproteinase dan transforming growth factor = Total collagen increase in New Zealand Rabbit : Urethral stricture model study of expression changes in matrix metalloprotein tissue inhibitor of metalloprotein and transforming growth factor / Johannes Cansius Prihadi

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Abstrak

[ABSTRAK
Latar Belakang : Striktur uretra adalah kelainan berupa penyempitan lumen uretra akibat terbentuknya jaringan parut yang melibatkan epitel dan jaringan erektil korpus spongiosum. Patofisiologi kelainan ini belum sepenuhnya diketahui. Degradasi matriks ekstraselular diduga berperan penting dalam terjadinya striktur uretra. Matriks metaloproteinase (MMP-1), Tissue inhibitor of metalloproteinase (TIMP-1) dan Transforming growth factor (TGF-β) berperan pada degradasi matriks ekstraselular. Tujuan penelitian ini adalah untuk mengetahui peran MMP-1, TIMP-1, rasio TIMP- 1/MMP-1 dan TGF-β pada fase remodeling striktur uretra dan hubungannya dengan kolagen total dan kolagen tipe-I.
Metode : Penelitian eksperimental ini dilakukan pada kelinci New Zealand jantan dewasa yang dibagi menjadi dua kelompok, yaitu kelompok kelinci yang dilakukan insisi mukosa dan elektrokoagulasi untuk menimbulkan striktur uretra (Kelompok kelinci striktur uretra) dan kelompok kelinci kontrol. Dilakukan pengamatan dan eutanasia pada empat kelinci pada masing-masing kelompok pada hari ke-7, 14, 21, 28, dan 56. Dilakukan pemeriksaan adanya hambatan pada uretra dengan kateter no 8F selanjutnya dilakukan pemeriksaan hematoksilin-eosin untuk melihat gambaran histopatologi, pemeriksaan Trichrome-Masson untuk melihat kolagen total, pemeriksaan imunohistokimia untuk melihat kolagen tipe-I. Pemeriksaan ELISA untuk mengukur kadar MMP-1, TIMP-1dan TGF-β. Rasio MMP-1/TIMP-1 dihitung dengan membagi kadar MMP-1 dengan kadar TIMP-1. Persentase kolagen total dan persentase kolagen tipe-1 dihitung dengan menggunakan program image J 1,46q. Uji statistik dengan General Linear Model.
Hasil: Pada kelompok striktur uretra didapatkan kadar MMP-1 yang lebih rendah, TIMP-1 yang lebih tinggi, rasio MMP-1/TIMP-1 yang lebih rendah, dan TGF-β yang lebih tinggi bila dibandingkan dengan kelompok kontrol. Terdapat korelasi positif kuat antara kadar TGF-β dengan persentase kolagen total (r = 0,617, p: 0,004) dan korelasi lemah antara kadar MMP-1 dengan persentase kolagen total (r = 0,561, p: 0,010).
Simpulan: Striktur uretra tidak hanya disebabkan oleh dekomposisi kolagen tetapi juga oleh ketidakseimbangan degradasi matriks ekstraselular yang ditandai oleh menurunnya MMP-1, meningkatnya TIMP-1 dan menurunnya rasio MMP-1/TIMP-1.;
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ABSTRACT
Background: Urethral stricture is a narrowing of urethral lumen due to scar formation involving epithelium and corpus spongiosum. The pathophysiology process of this abnormality is not fully understood.

Extracellular matrix degradation supposed to play an important role as the etiology of urethral stricture. Matrix metalloprotein (MMP-1), Tissue inhibitor of metalloprotein (TIMP-1) and Transforming growth factor-β (TGF-β) are involved in matrix extraselular degradation. The purpose of this study was to investigate the role of MMP-1, TIMP-1, MMP-1/TIMP-1 rasio and TGF-β at remodeling phase of urethral stricture and their correlations to total collagen and collagen type I.
Metode: This study was an experimental study in adult male New Zealand rabbits, divided into two groups, namely the urethral stricture group and the control group. Euthanasia was performed in four rabbits of each group on days 7, 14, 21, 28, and 56. Urethral stricture was confirmed by urethral catether no 8F. Several laboratory examination were done, including haematoxylin-eosin, trichrome-masson, immune-histochemistry and ELISA to determine levels of MMP-1, TIMP-1, TGF-β, MMP- 1/TIMP-1 rasio, total collagen and collagen type-1. Percentage of total collagen and collagen type I were counted with image J 1.46q programme. General linear model was used for statistical analysis
Results : This study found level of MMP-1 was lower, TIMP-1 was higher, MMP-1/ TIMP-1 rasio was lower, and TGF-β was higher in the urethral stricture group compared with control. There was a strong positif correlation between TGF-β level and total collagen percentage (r = 0.617; p = 0.004) and weak positive correlation between MMP-1 level with total collagen percentage (r = 0.561; p = 0.010).
Conclusions : Urethral stricture is not only caused by collagen decomposition but also by imbalance of extracellular matrix degradation which is marked by decreased MMP-1 level and MMP-1/TIMP-1 rasio, increased TIMP-1 level., Background: Urethral stricture is a narrowing of urethral lumen due to scar formation involving epithelium and corpus spongiosum. The pathophysiology process of this abnormality is not fully understood. Extracellular matrix degradation supposed to play an important role as the etiology of urethral stricture. Matrix metalloprotein (MMP-1), Tissue inhibitor of metalloprotein (TIMP-1) and Transforming growth factor-β (TGF-β) are involved in matrix extraselular degradation. The purpose of this study was to investigate the role of MMP-1, TIMP-1, MMP-1/TIMP-1 rasio and TGF-β at remodeling phase of urethral stricture and their correlations to total collagen and collagen type I.
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