Drug influence on intra-renal oxygenation estimated by BOLD-MRI

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Introduction

Acute renal failure induced by drugs or radiocontrast media is a common cause of hospital acquired renal failure [1]. One mechanism leading to nephropathy involves renal ischemia. The aim of this study was to investigate the acute effect of several drugs (indometacin, cyclosporine and tacrolimus) and iodinated radiocontrast media on renal oxygenation measured by BOLD-MRI [2,3] in healthy volunteers.

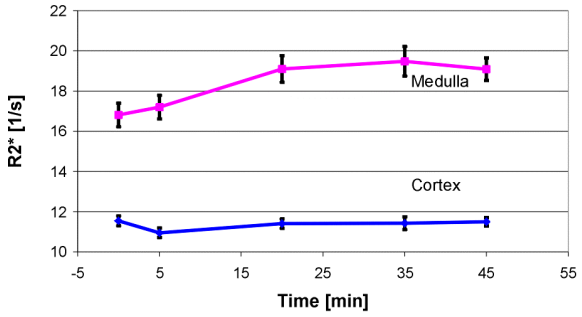
Methods

All measurements were carried out on a 1.5 T scanner (SONATA, Siemens, Germany) using a body coil for transmission and a phased array surface coil for reception. A modified Multi Echo Data Image Combination sequence (TR: 65 ms, TE: 6-52.31 ms, flip angle: 30°) was used to acquire 12 T_2* weighted images within a breath-hold. Forty volunteers were involved. Measurements were repeated 0, 5, 20, 35, and 45 min after administration of indometacin and radiocontrast media, and 0, 120 and 240 min after taking cyclosporine or tacrolimus. R_2* maps were calculated by fitting ln(signal intensity) vs. echo time to linear function [4]. ROIs were selected in medulla and cortex, and a mean value of R_2* index was estimated.
Statistical significance of the results was analyzed using MANOVA for repeated measures (time) and 3 variables (volunteer, medulla/cortex, left/right kidney) with Bonferroni adjustment for multiple comparison (R), and 2-sided paired t-test of the area under the curve (A) using SPSS11.0.

Results

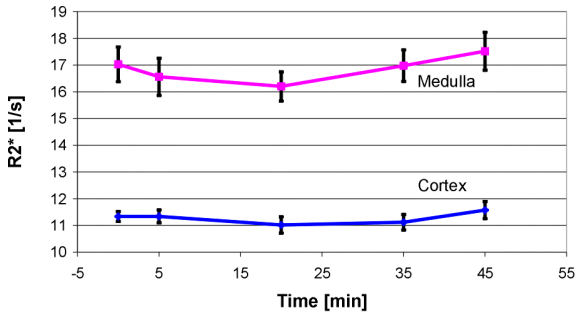
For all drugs no significant differences between right and left kidney were found.

Fig.1: Effects of radiocontrast media (mean ± sem; n=10)



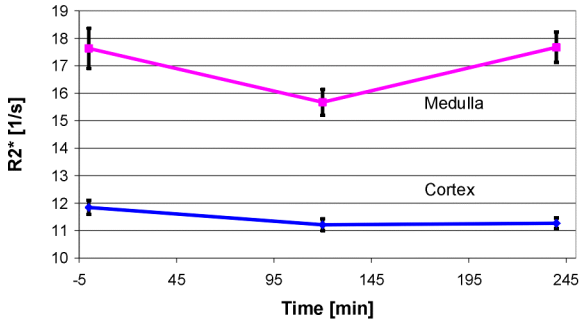
A: Highly significant effect in medulla, not in cortex
R: Significant changes in medulla and tendency to change in cortex over the time

Fig.2: Effects of indometacin (mean ± sem; n=10)



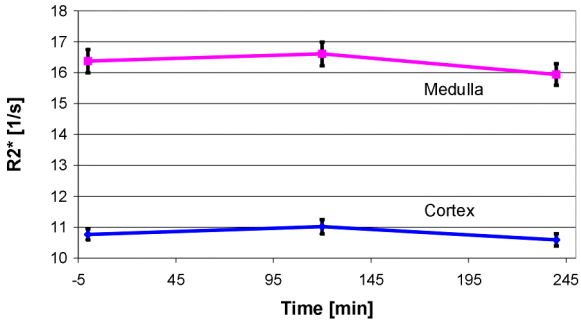
A: No significant effect, neither in medulla nor in cortex
R: Tendency to change with time

Fig.3: Effects of cyclosporine (mean ± sem; n=10)



A: Highly significant effect in cortex, only tendency in medulla
R: Significant changes in medulla and cortex over the time

Fig.4: Effects of tacrolimus (mean ± sem; n=10)



A: No significant effect, neither in medulla nor in cortex
R: No significant changes in medulla or cortex over the time

Discussion/Conclusion

This study shows for the first time the acute effects of different drugs in human healthy kidneys. The conversion of the mean R_2* values to oxygen tension [5] gives pO_2 of 39.3 mmHg for medulla and 61.7 mmHg for cortex, which are in agreement with literature [6]. Iodinated radiocontrast media induced a vasoconstriction and therefore a decrease in medullary oxygenation. Indometacin and tracrolimus didn't show any effect on renal hemodynamics. Cyclosporine showed an opposite effect (better medullary oxygenation) than expected.

References

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