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The Role of Genetic Polymorphisms of Renin-Angiotensin System in Renal Diseases: A Meta-analysis

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***Abstract*— Renal Failure has a complex phenotype resulting from an underlying kidney disease as well as environmental and genetic factors. In the present study we performed meta-analyses to evaluate the association of the A1166C polymorphism of Angiotensin II type 1 Receptor gene (AGTR1) with Renal Diseases. We found that AGTR1 A1166C, is neither associated with Chronic Kidney Disease (CKD), nor with End Stage Renal Disease (ESRD). Moreover, AGTR1 A1166C polymorphism is not associated with either IgA nephropathy (IgAN) or Vesicoureteral Reflux (VUR). Finally, we could not find evidence for the association of AGTR2 A1332G polymorphism with (VUR).**

I. Introduction

Chronic Kidney Disease (CKD) is the final result of many renal diseases, characterized by a slow, progressive and irreversible deterioration of renal function which is usually asymptomatic. In the last stage of CKD, called End Stage Renal Disease (ESRD), dialysis or kidney transplantation is required. IgA nephropathy (IgAN) and Vesicoureteral Reflux (VUR) are diseases that can lead to Chronic Kidney Disease. Arterial hypertension (HT) is the most important risk factor for the progression of renal failure and is largely regulated by the Renin-Angiotensin System [1,2]. In the present study, we attempted to clarify the genetic association of polymorphisms of the angiotensin receptors with renal diseases and discus the possibility that these polymorphisms may be used as prognostic markers for renal failure.

II. Material and Methods

A comprehensive literature search was performed and 30 independent studies were retrieved, that could fulfil all the eligible criteria. More precisely, eight studies were included for CKD (4252 controls, 812 cases), 17 studies for ESRD (3866 controls, 2596 cases), five studies for IgAN (1373 controls, 785 cases) and three studies for VUR (216 controls, 174 cases) to asses their association with AGTR1 A1166C polymorphism. Three studies (790 controls, 654 cases) were used to examine the association of AGTR2 A1332G polymorphism with VUR. The effect size, odds ratio, and the confidence interval 95% CI were calculated in meta-analyses, using STATA, according to the random effects model [3].

III. Results

In a meta-analysis to test the putative association of the A1166C polymorphism of the AGTR1 gene with ESRD, no statistical significant association was revealed for the per-allele contrast since OR was 1.12 (95%CI: 0.90-1.38). Similarly, non-significant association was revealed when dominant and recessive models were analyzed. Association of CKD and A1166C polymorphism of AGTR1 gene could not be proven neither with per allele contrast nor with genotypes contrasts [OR 1.16 (95% CI: 0.83-1.64) for the per allele contrast]. Additional meta-analyses to search for associations of the same A1166C polymorphism of AGTR1 gene with IgAN and VUR were also performed. Testing all models of inheritance, no significant associations could be proven. Another gene polymorphism, A1332G of the AGTR2 was also analyzed for its association with VUR. No statistical significant association could be proven since OR was 1.02 (95% CI: 0.67-1.55) for the per allele contrast.

IV. Conclusions

Our results imply that the A1166C polymorphism of the AGTR1 gene is not significantly associated with any of the renal diseases we tested i.e. CKD, ESRD, IgAN and VUR. Furthermore, the A1332G polymorphism of AGTR2 gene is also not associated with VUR. Because in most of the meta-analyses we performed, few populations were included, it seems that more studies will improve the significance of our results. Moreover, in view of the probability that gene-gene interactions may be master regulators of renal disease development, new multigenic studies are also needed to shed light on the roles of AGTR1 and AGTR2 polymorphisms in renal diseases.

References

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