

## 13. Summary

### 13.1. English Summary

**This thesis deals with the evaluation of U-NAG in various disease states, in order to underline the important role of this enzyme in patients with kidney disorders.**

#### **Chapter 1**

Chapter 1 gives brief information on renal anatomy and physiology, and in particular on anatomy, physiology and pathophysiology of renal tubules, including diagnostic procedures. This introduction is essential for the integrity of the thesis.

#### **Chapter 2**

Chapter 2 gives basic information concerning this thesis, its primary and secondary aims. This thesis gives a detailed account of various studies, not necessarily in the sequence in which these were carried out.

#### **Chapter 3**

Chapter 3 gives a state-of-art overview of the diagnostic role of U-NAG in the detection of renal tubular impairment and its clinical applicability. 92 articles are evaluated in this review in a critical way. U-NAG activity is a useful marker of renal tubular impairment in various disease states. When compared to other urinary enzymes, U-NAG is the most frequently used urinary enzymatic marker when it comes to the evaluation of tubular function. However, the routine evaluation of enzymuria is much less frequently used when compared to the routine evaluation of enzymes in serum or plasma.

#### **Chapter 4**

Chapter 4 presents reference data of U-NAG for all paediatric age groups. In conclusion, the U-NAG/Cr values of 262 healthy children aged 0-18 years, obtained with fluorimetric assay, are strongly age-dependent. The establishment of U-NAG/Cr reference paediatric values is a potentially useful tool for proper evaluation of renal tubular impairment in childhood, because knowledge of normal physiological variation is necessary to identify pathological changes.

#### **Chapter 5**

Chapter 5 gives information on U-NAG/Cr values in 20 paediatric patients with idiopathic hypercalciuria. High U-NAG suggests renal tubular injury, however the absence of correlation between U-NAG/Cr and U-Ca/24h also suggests that increased urinary concentration of calcium might lead to damage of tubular cells, even in the absence of lithiasis. In conclusion, children with IH have some degree of secondary renal tubular impairment. The tubular impairment is most probably aggravated by the increased urinary concentration of calcium, and, in particular, by the cell-crystal interactions. There doesn't seem to be a direct relationship between this tubular impairment and the degree of calcium leakage.

#### **Chapter 6**

Chapter 6 analyses the relationship among bone mineral density, body height and U-NAG/Cr values in 15 children with idiopathic hypercalciuria (IH). High U-NAG/Cr, low BMD and a tendency to short stature were observed in children with IH. We found inverse and significant correlation between BMD and U-Ca/24 h, and a similar correlation between U-Ca/24 h and body height. There was no correlation between U-NAG/Cr and U-Ca/24 h. It seems likely that hypercalciuria can contribute to the skeletal demineralization and to the development of nephrocalcinosis, both resulting in stunted growth. In conclusion, tubular impairment is highly probable in children with IH, as high U-NAG/Cr was observed, but there seems to be a poor relationship with the degree of calcium leakage. Idiopathic hypercalciuria should be considered

as a risk factor for stunted growth and low bone mass, however it doesn't correlate with U-NAG/Cr.

#### **Chapter 7**

Chapter 7 presents data on calciuria and U-NAG/Cr activity in 14 children with NE. The values of U-Ca/Cr did not differ significantly from the reference data, however U-NAG/Cr values were significantly higher compared to reference values. There was no correlation between U-NAG/Cr and U-Ca/Cr. In conclusion, hypercalciuria was not found in children with NE. The presence of elevated urinary levels of U-NAG/Cr suggest that tubular dysfunction might be present in patients with NE.

#### **Chapter 8**

Chapter 8 presents U-NAG activity in 22 children with various grades of vesicoureteral reflux (VUR). The U-NAG/Cr values were significantly higher in the VUR patients in comparison to the reference data. There was no difference in U-NAG/Cr between children with unilateral and bilateral VUR and no significant difference between VUR I-III and VUR IV-V subgroups. The U-NAG/Cr activity was high in patients with RN when compared to reference data, but there was no difference in comparison to children with VUR but without RN. We found no correlation between U-NAG/Cr and grade of VUR, without statistical significance. Number of pyelonephritic episodes in patients' personal history was not related to U-NAG/Cr or VUR grade. In conclusion, tubular dysfunction is common in children with VUR. U-NAG/Cr should be considered as a useful marker of renal tubular impairment in patients with VUR, however there is a very weak relationship with the grade of VUR. This might further support more recent observations that severity of VUR doesn't always fully correspond with the degree of kidney damage.

#### **Chapter 9**

Chapter 9 gives data on U-NAG activity in 31 patients with hydronephrosis (HN). The U-NAG/Cr values were significantly higher in the patients with HN in comparison to the reference data. There was no difference in U-NAG/Cr between children with unilateral and bilateral HN. There was no significant difference in U-NAG/Cr between children with HN grade 1-3 and grade 4, respectively. No correlations were observed between U-NAG/Cr and the grade of hydronephrosis. The renal functions, as assessed by the  $^{99m}\text{Tc}$  MAG3 renography, were not severely impaired. These results might suggest that the renal function, as assessed by  $^{99m}\text{Tc}$  MAG3 renography might not be solely related to the grade of hydronephrosis, and that U-NAG in hydronephrosis is not dependent on the amount of affected renal tissue. We can't rule out that the U-NAG can reflect even very mild changes in renal tubular function, which might occur even in low-grade non-obstructive hydronephrosis. In conclusion, U-NAG/Cr is increased in children with hydronephrosis grade 1-4, however there is no relationship with the grade of hydronephrosis or with the amount of affected renal tissue. U-NAG/Cr is a useful marker of renal tubular impairment, however there is no relationship with the degree of kidney damage in patients with hydronephrosis.

### **10. General conclusions and recommendations**

5. U-NAG/Cr is an important marker of renal tubular dysfunction.
6. U-NAG/Cr can reflect even very mild changes in renal tubular function.
7. U-NAG/Cr is significantly increased in the following urinary tract disorders: idiopathic hypercalciuria, nocturnal enuresis, vesicoureteral reflux and hydronephrosis.
8. In the above mentioned disease states affecting the uropoetic system, the U-NAG/Cr is elevated, but not correlated with the severity of the disease.