Canterbury Medical Research Foundation

Final report for Grant in Aid GIA2 2018

Grant recipient

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Grant details

GRANT TYPE	Grant in Aid	FUNDING ROUND	2018 Grant In Aid
GRANT REFERENCE	GIA2 2018	GRANT AMOUNT	$5,000

Final report

1. Scientific Assessing Committee report

Thank you for your support of the project: ***C-type natriuretic peptide: a potential marker of chronic kidney disease in diabetes.***

Sample collection and preliminary data analysis went according to the plan outlined in the grant application, with a total of 202 participants recruited for this study. An abstract was presented at the EASD (European Association for the Study of Diabetes) meeting, Berlin, October 2018 (a copy of poster enclosed below as a file). Useful feedback was given at the poster/oral question time about the best way of undertaking more detailed statistical analyses. A paper is being prepared for submission to a peer reviewed journal.

In conclusion, results show that C-type natriuretic peptide remains a potential candidate marker for kidney damage in diabetes and we are seeking further funding to undertake a longitudinal study.

2. Photographs

View an attachment by double clicking the icon to the left of the file name. Icons are not displayed and attachments are not accessible when this PDF is viewed in a web browser; you must open it in PDF reader software.

EASD poster - Copy.pdf
294.0 KiB

4. Feedback

C-TYPE NATRIURETIC PEPTIDE AS A CANDIDATE MARKER OF DIABETIC KIDNEY DISEASE

P1002

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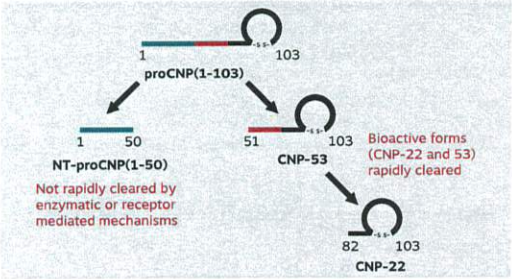
What is CNP and how is it measured?

- C-type natriuretic peptide (CNP) belongs to a family of structurally related peptides (including ANP and BNP) that have important roles in regulating blood volume and vascular tone. CNP also inhibits fibrosis in many tissues.
- CNP is synthesized as a prohormone (Fig 1) and processed intracellularly.
- C-terminal (bioactive) forms (CNP22 and CNP53) are rapidly degraded in contrast to NTproCNP which is easily measured in plasma but has not previously been reported to be present in urine.

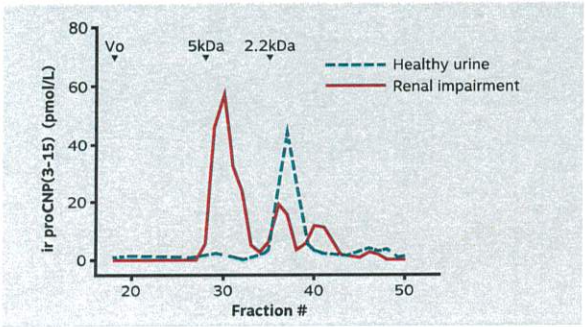
Fig 1. proCNP processing pathway



What does CNP do in the kidney?

- CNP is expressed in the renal glomerulus, podocytes, tubules and interstitial matrix – where it inhibits inflammation and is reno-protective.
- Experimental models suggest that CNP excretion in urine is an early marker of renal inflammation and fibrosis, and increases before albumin is affected[1].
- Pilot data indicates that in healthy subjects NTproCNP found in urine is degraded, whereas the 5kDa intact NTproCNP is present in urine from diabetic participants with impaired renal function (Fig 2).

Fig 2. Size exclusion HPLC — NTproCNP forms in urine



How does CNP compare to traditional markers of kidney injury?

Current markers of diabetic kidney disease (DKD) lack sensitivity and specificity.
This study aimed to evaluate the utility of urine NTproCNP, compared to urine albumin as a marker of renal disease in subjects with diabetes.

Study Design:
Adult participants (n=200) with Type 1 Diabetes (duration T1DM >5y) or with Type 2 DM were selectively recruited from an outpatient clinic population to encompass a wide range of ACR and eGFR values.
A random spot urine sample was obtained for measurement of albumin creatinine ratio (ACR) and intact NTproCNP creatinine ratio (NCR).
A second urine sample was collected within three weeks to assess replication.
Urine NTproCNP was analysed by a radioimmunoassay that specifically measures intact NTproCNP in urine.

Table 1 *Summary of study participants' clinical characteristics*

	T1DM	T2DM	*p*
n	100	100	
Gender (% female)	55%	44%	*0.16*
Age (years) ‡	46 (30 – 64)	58 (51 – 68)	*<0.001*
HbA1c (mmol/mol) ‡	66 (56 – 80)	69 (58 – 90)	*0.14*
ACR (g/mol) ‡	1.4 (0.7 – 5.0)	5.8 (1.2 – 48)	*<0.001*
eGFR (ml/min/1.73m²) ‡	76 (66 – 93)	83 (63 – 99)	*0.30*
NCR (pmol/µmol) ‡	0.13 (0.09 – 0.19)	0.14 (0.09 – 0.22)	*0.51*

‡Results are expressed as medians (interquartile ranges)

Results:
- The coefficient of variation for repeat spot urine measurements for NCR and ACR in individuals was 36% vs 50% respectively.
- eGFR and NCR levels were not significantly different between the T1DM and T2DM cohorts.
- Median NCR was 0.22 (0.14-0.47, IQR) pmol/µmol in participants with impaired eGFR (<60ml/min/1.73m²) compared to 0.12 (0.08-0.17) pmol/µmol in participants with normal eGFR (>70ml/min/1.73m²), p<0.001.
- The inverse association of NCR with eGFR (Spearman's rho, r= -0.37) was stronger than that observed between ACR and eGFR, r= -0.14 (Fig 3).

Fig 3a Association of NTproCNP:creatinine ratio (NCR) with eGFR

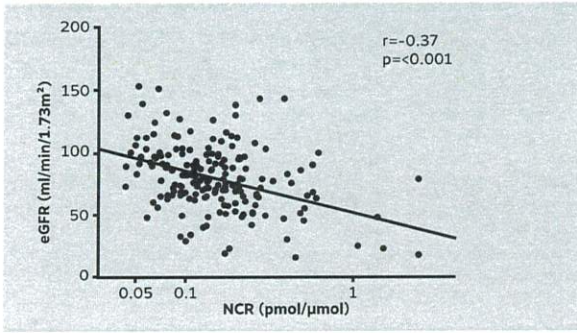
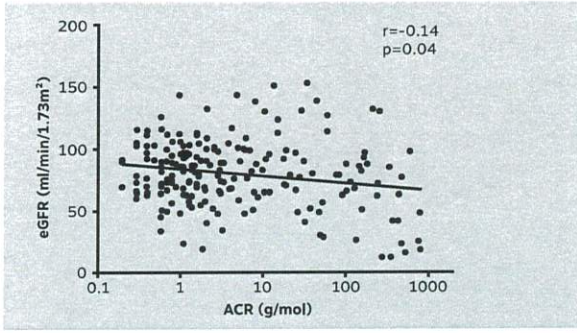


Fig 3b Association of albumin:creatinine ratio (ACR) with eGFR



Summary and Conclusions

These preliminary results support the hypothesis that urine NTproCNP excretion reflects declining renal function and may be superior to urinary albumin excretion as a marker of kidney injury in diabetes.

Reference: (1) Hu P, Wang J, Hu B, Lu L, Xuan Q, Qin YH. Increased urinary C-type natriuretic peptide excretion may be an early marker of renal tubulointerstitial fibrosis. Peptides. 2012;37:98-105.

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University of Otago Christchurch
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