The detection of obesity-related nephropathy using novel urinary biomarkers.

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Abstract

The aetiology of obesity-related nephropathy (ORN) is proposed to involve glomerular hyperfiltration and inflammation. We aimed to characterise the regional damage in ORN using novel urinary biomarkers.

Methods: Urines were collected from 17 obese non-diabetic subjects. Samples were assayed for biomarkers of proximal tubular damage (Alpha GST), distal tubular damage (Pi GST) and glomerular fibrosis (Collagen IV).

Results: The obese subjects all had normal serum creatinine and eGFR and median BMI 47kg/m2. Three obese subjects had microalbuminuria. Compared to controls, 59% of obese subjects had elevated urinary Alpha GST, 29% had elevated urinary Pi GST and 24% had elevated urinary collagen IV. One subject requiring temporary dialysis 3 months prior to the study did not have elevated Alpha GST, but instead had elevated Pi GST and Collagen IV.

Conclusion: In subjects with obesity and normal serum creatinine there is a high prevalence of detectable renal damage. This ORN appears to be more related to the proximal renal tubule rather than the distal tubule or glomerulus. This suggests additional mechanisms to hyperfiltration as contributing to ORN.

Introduction

Obesity is a growing epidemic affecting around one quarter of the Western European and one third of the North American populations. The prevalence of ESRD has more than doubled in the last decade.

Obesity increases the risk of ESRD, even when other co-morbidities such as hypertension and diabetes have been corrected for .

The entity of Obesity Related Nephropathy (ORN) has become widely recognized.

The pathological renal changes have been widely described but the aetiology is uncertain and may involve hyperfiltration and systemic inflammation.

Aim

To define ORN using novel urinary biomarkers that can identify damage to specific regions of the nephron.

Method

Clinical data, blood and urine samples were collected from a consecutive series of 22 patients attending a weight-management clinic, and from a control group of 19 healthy volunteers. Urine samples were assayed for biomarkers of proximal tubular damage (Alpha GST), distal tubular damage (Pi GST) and glomerular fibrosis (Collagen IV) using commercial ELISAs (Biotrin International, Dublin, Ireland). Results are in µg/mmol Urinary Creatinine.

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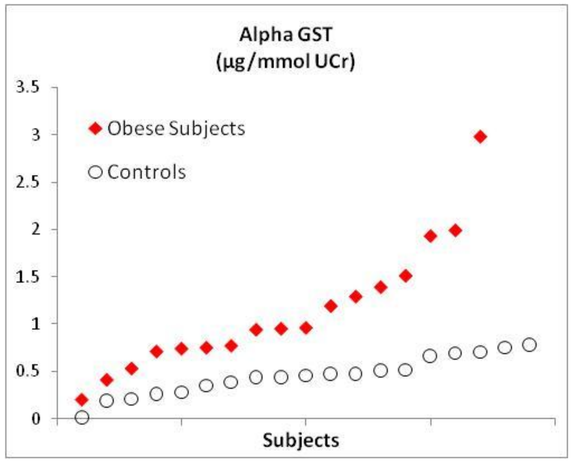
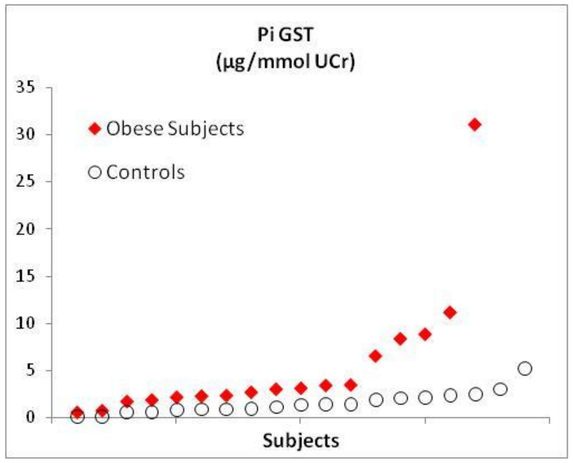
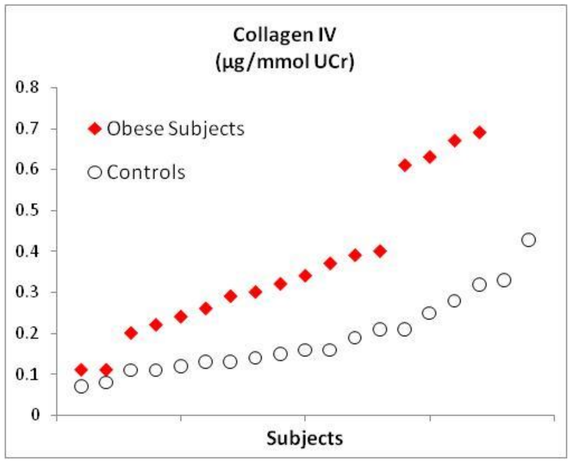
Results

The control group had mean age 35 years, 15/19 were male, mean weight 77.9 kg. Five obese subjects had diabetes and were excluded from the analysis. The remaining 17 obese subjects had mean age 44 years, 7/17 were male, median BMI was 45 kg/m^2 (range 35–78 kg/m^2). All non-diabetic obese subjects had normal serum creatinine (mean 75.1µmol/l) and eGFR (mean 90.3 ml/min). One patient had acute renal failure requiring temporary renal dialysis 3 months prior to the study.

Compared to the control group 10/17 obese patients (59%) had elevated urinary alpha GST (median 0.95, range 0.2-2.98, control 0.46, range 0.01-0.79, P<0.0005). Five of 17 obese patients (29%) had elevated urinary Pi GST (median 3.0, range 0.56-31.1, control 1.26, range 0.0-5.2, P<0.001), whilst 4/17 obese patients (24%) had elevated urinary collagen IV (median 0.32, range 0.11-0.69, control 0.16, range 0.07-0.43, P<0.05). The patient requiring temporary dialysis had grossly elevated pi GST (203.5, control<5.2) and elevated collagen IV (12.2, control<0.43).

Conclusion

In patients with obesity and normal serum creatinine there is a high prevalence of detectable renal damage compared to a healthy control group. This ORN appears to be related more to the proximal renal tubule rather than the distal tubule or the glomerulus. This suggests alternative mechanisms to hyperfiltration as the cause of Obesity Related Nephropathy.