PROTEINURIA DETECTED BY ALBUMIN DIPSTICK TEST PREDICTS THE SEVERITY OF ACUTE KIDNEY INJURY IN PUUMALA HANTAVIRUS-INDUCED NEPHROPATHIA EPIDEMICA

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INTRODUCTION AND OBJECTIVES

Puumala hantavirus induced nephropathia epidemica (NE) is common in Finland, where 1,000-3,000 cases are serologically diagnosed annually. The disease is likewise common in several other European countries.

Acute tubulointerstitial nephritis is the renal histologic lesion in NE. Acute kidney injury (AKI) in NE is self-limiting and has a favorable prognosis. Transient proteinuria (PU) is present in > 90% of the patients and is often quite massive. The pathogenesis of PU is not known. Thrombocytopenia and increased capillary leakage are the other main manifestations of NE.

Here we studied prognostic significance of PU detected by albumin dipstick test for the severity of AKI and other clinical and laboratory findings of NE, as well as time relationship of glomerular and tubular PU to AKI.

METHODS

205 patients with serologically confirmed acute NE treated in Tampere University Hospital, Finland, during 1997-2014 were studied.

The amount of PU detected by albumin dipstick test on hospital admission was graded to three categories: 0-1+ (n=54), 2+ (n=73), 3+ (n=78).
In 70 patients 24-hour urinary protein excretion and overnight excretion of albumin as well as α1-microglobulin were also studied during the three consecutive days in hospital.

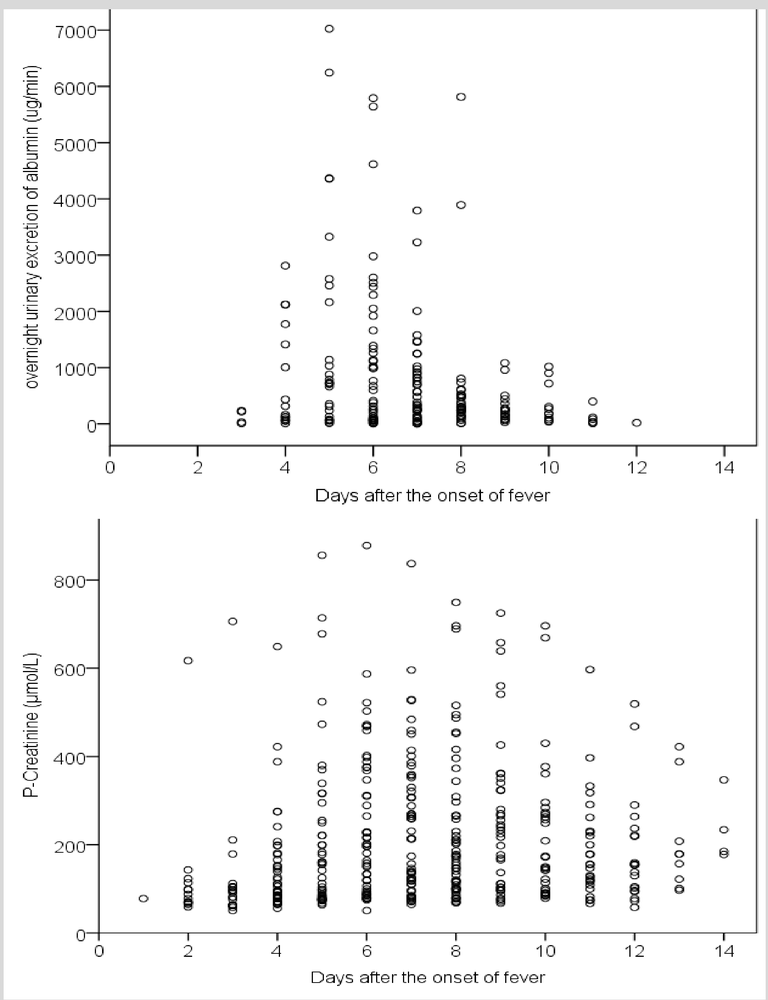
The severity of AKI was defined by maximum plasma creatinine (crea-max). The other variables studied were minimum platelet count (thromb-min), maximum leukocyte count (leuk-max), maximum C-reactive protein (CRP-max), weight change (reflecting fluid accumulation) and duration of hospitalization. The onset of NE was the day when fever commenced.

Clinical and laboratory findings in 205 patients with acute Puumala hantavirus infection categorized according to urine dipstick test at hospital admission

	U-alb 0/1+ (n=54)	U-alb 2+ (n=73)	U-alb 3+ (n=78)	p-value
Age, years	41 (22-77)	43 (22-74)	40 (15-65)	0.294
Length of hospital stay, days	5 (3-22)	6 (3-15)	7 (2-14)	0.026
Weight change during hospital stay, kg	1.6 (0-10.8)	2.2 (0-10.0)	3.7 (0-12.0)	<0.001
Platelets min, ×10⁹/L	68 (3-249)	61 (15-198)	56 (5-187)	0.232
Leukocytes max, ×10⁹/L	9.2 (5.1-38.6)	9.0 (4.2-31.2)	13.0 (5.7-45.0)	<0.001
Plasma CRP max, mg/L	74 (16-236)	92 (20-269)	68 (21-214)	0.012
Plasma creatinine max, µmol/L	98 (52-1447)	139 (71-829)	363 (51-1285)	<0.001
Urinary protein excretion max, g/24h (n=70)	0.57 (0.14-9.50)	1.75 (0.18-17.78)	2.22 (0.30-10.00)	0.077
Overnight urinary albumin excretion max, µg/min (n=70)	104 (4-4617)	756 (12-6246)	1016 (136-7026)	0.007
Overnight urinary α1microglobulin excretion max, µg/min (n=70)	20 (10-89)	38 (9-209)	30 (2-130)	0.693

Values are expressed as medians (range)

Overnight urinary albumin excretion and plasma creatinine according to the onset of fever



RESULTS

Median crea-max values were significantly different between different dipstick categories: the more albuminuria detected by dipstick at admission, the more severe AKI was developed (table). Albumin dipstick test was positive in 87% of patients.
Significant differences between albumin dipstick categories were also found in duration of hospitalization, weight change and leuk-max but not in thromb-min.

24-hour protein excretion ranged from 0.14 to 17.8 (median 1.78) g and it was of nephrotic range (>3.5 g) in 34% of patients.
Maximum 24-hour protein excretion and overnight albuminuria medians were observed 5 days and median crea-max 9 days after the onset of fever.
There was no clear time peak of urinary excretion of α1-microglobulin. Increased urinary α1-microglobulin levels (>7µg/min) were found in 90% of patients.

Glomerular proteinuria i.e. urinary albumin excretion correlated with crea-max (P<0.001), while tubular proteinuria i.e. α1-microglobulin excretion did not (P=0.291).

CONCLUSIONS

The amount of PU detected by albumin dipstick test at hospital admission clearly predicts the severity of AKI in NE. It also associates with several other variables reflecting the severity of NE.This quick and easy assessment is highly useful in daily clinical work.

Moreover, maximum excretion of glomerular PU occurs some days before the most severe phase of AKI. Association of tubular proteinuria with the severity of AKI is less clear.

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53 ERA
198--SP
Acute Kidney Injury. Clinical.
Paula Mantula
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS VIENNA AUSTRIA MAY 21st-24th 2016
Held jointly with Österreichische Gesellschaft für Nephrologie
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