Technical Report

Pseudo-proteinuria following gelofusine infusion

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Abstract

Transient massive proteinuria following cardiopulmonary bypass surgery was observed. It was characterized and attributed to post-operative gelofusine infusion. Gelofusine was found to interfere with dye binding but not immunochemical assays of proteinuria. Proteinuria following gelofusine infusion may not reflect underlying glomerular pathology.

Key words: gelofusine; proteinuria

Introduction

The association between the development of proteinuria and severe tissue injury following trauma [1,2] and major surgery [3] is recognized, with evidence of both increased glomerular permeability and reduced proximal tubular reabsorption reflecting epithelial cell injury. Similarly, elevated levels of urinary albumin and N-acetyl-glucosaminidase (NAG, a marker of tubular injury) following cardiac surgery have been documented previously [4]. In this study, we investigated apparent massive proteinuria following elective cardiopulmonary bypass surgery.

Methods

Twenty-four-hour urine samples were collected before and during the first postoperative day in patients undergoing elective cardiopulmonary bypass surgery. Samples were analysed for total protein (UTP, molybdate pyrogallol red method, Randox) and selectivity was assessed by urine protein electrophoresis (Beckman Paragon using Coomassie blue stain).

In a subgroup of patients, serial urine samples were collected from patients on the day before operation and on days 1, 2 and 4 after cardiopulmonary bypass surgery. Samples were analysed for total protein (UTP, albumin (U Alb, immunoturbidimetry, Incstar SPQ), creatinine (UCr, kinetic Jaffe reaction) and protein.

These assays were repeated using urine from healthy volunteers and diabetic patients with established microalbuminuria to which gelofusine had been added.

Results

Proteinuria following cardiopulmonary bypass

During the first postoperative day, patients demonstrated nephrotic-range proteinuria (median 2.84 g/day, range 0.64–21.9 g/day, n = 45). Urine electrophoresis revealed a dense transzonal band.

Comparison of urinary assays of total protein and albumin

In six patients who underwent serial urinalysis over four postoperative days, negligible albuminuria could be demonstrated despite gross proteinuria (Table 1).

Effect of gelofusine on albuminuria and proteinuria in healthy volunteers and diabetics with microalbuminuria

Urine from three healthy volunteers was spiked with gelofusine to achieve concentrations between 5 and 40 g/l. Strong positive interference (35% cross-reactivity relative to albumin) was noted when the pyrogallol red method was used to measure UTP. There was no interference in measurement of U Alb in samples from patients with microalbuminuria (32–156 mg/mmol creatinine) which had been spiked with gelofusine. Only urine samples from patients and controls which contained gelofusine demonstrated a dense transzonal band on electrophoresis. Gelofusine did not affect UCr measurement.

Discussion

Our initial results provided evidence of massive proteinuria following elective cardiopulmonary bypass surgery which implied a glomerular leak, although this occurred in the absence of albuminuria. The unusual finding of a dense transzonal band on urine electrophoresis suggested the renal clearance of a therapeutic agent, such as gelofusine, of which patients undergoing cardiopulmonary bypass routinely receive 1.0–1.5 l peri-operatively. The subsequent experiments provided evidence that the addition of gelofusine to normal and microalbuminuric urine interfered with assays based on dye binding but not immunochemical techniques. Significant proteinuria in the absence of albuminuria may also occur in patients with Bence-Jones proteinuria.
Pseudo-proteinuria following gelofusine infusion

Table 1. Comparison of urinary assays of total protein and albumin

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<thead>
<tr>
<th></th>
<th>Pre-operative</th>
<th>Post-operative</th>
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<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>$U_{TP}$</td>
<td>6</td>
<td>4.9 (2.7–7.5)</td>
</tr>
<tr>
<td>$U_{alb}$</td>
<td>6</td>
<td>0 (0–2.9)</td>
</tr>
</tbody>
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All data given as median (range). $U_{TP}$ (normal range 0–13) and $U_{alb}$ (normal range 0–2) expressed as mg per mmol urinary creatinine.

although under these circumstances, urine electrophoresis will reveal a monoclonal light-chain excess.

Gelofusine is composed of gelatin with a mean molecular mass of 30 000 Da formed by hydrolysis and succinylation of bovine collagen. This colloid solution is widely used to achieve plasma expansion. The observation of pseudo-proteinuria following the infusion of gelofusine may mislead and has not been reported previously. Clinicians and chemical pathologists should be aware that this plasma expander interferes with urine protein assays based on dye binding, although not with immunochemical assays. This is of particular relevance given the current debate regarding the use of synthetic colloids in place of albumin.

References


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