Use of NGAL in intensive care unit

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A/ Our faculty hospital provides healthcare for 170,000 inhabitants

B/ Our ICU is specialized in nephrological, hepatological and metabolic disorders

C/ Nephrotoxic antibiotics are often necessary

A + B + C = ACUTE KIDNEY INJURY (AKI) IS AN ORDINARY MATTER
Why is prediction of emerging AKI important in real life?

■ A/ Medication management
  ■ choice and dosage of nephrotoxic therapy

■ B/ Determination of the extent of kidney damage

■ C/ Evaluation of the patient’s prognosis
Urinary NGAL preference

- Urinary NGAL is more specific for kidney injury (professor Hollmen – Transplant center in Helsinki)
- Other urinary biomarkers of AKI are examined – α1microglobulin, in the future - KIM-1, L-FABP, IL18
Case report no. 1

- A 62 year old woman was admitted in ICU for severe hypo-osmolar dehydration
- Confusion and amention
- Normal renal function
Adenom of hypophysis diagnosed (verified by CT and MRI, hypothyreosis and low somatomedin (IGF1))

Therapy: hormonal substitution (levothyroxine) and mineral and volume substitution
The course of the disease was complicated bronchopneumonia and respiratory failure requiring mechanical ventilation

ATB therapy – change to gentamicine + ceftazidime + fluconazole according to microbiological examination of sputum (Klebsiella pneumoniae)
Monitoring of renal parameters

Following nephrotoxicity, gentamicin, renal parameters and uNGAL was monitored
## Monitoring of renal function and urinary NGAL during antibiotic therapy

<table>
<thead>
<tr>
<th></th>
<th>Aug 26(^{th})</th>
<th>Sep 9(^{th})</th>
<th>Sep 13(^{th})</th>
<th>Sep 15(^{th})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (µmol/l)</td>
<td>129</td>
<td>124</td>
<td>167</td>
<td>179</td>
</tr>
<tr>
<td>NGAL (ng/ml)</td>
<td>55</td>
<td>1285</td>
<td>660</td>
<td>355</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>76.4</td>
<td>256</td>
<td>191</td>
<td>57.4</td>
</tr>
<tr>
<td>Gentamicine level before administr. N&lt;2 mg/l</td>
<td>-</td>
<td>3.6</td>
<td>1.88</td>
<td>-</td>
</tr>
<tr>
<td>Gentamicine 160mg/24hrs</td>
<td>Gentamicine 80 mg/24hrs</td>
<td>Gentamicine stopped</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Mech. vent. Aug 26-30 Amoxicilin claritromyc.</td>
<td>Gentamicine Ceftazime Fluconazole Since Sep 8(^{th})</td>
<td>Without antibiotics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Dynamics of creatinine and urinary NGAL during antibiotic therapy
Conclusions on case report no. 1

Monitoring of NGAL and serum levels of nephrotoxic antibiotic therapy (gentamicine) facilitates the management and adjustment of therapy (early reduction of dosage) and thus prevention of worsening of AKI.
Case report no. 2

- The patient is a 55 year old woman
- Case history:
  - *Sclerosis multiplex including paraparesis of lower extremities and urinary incontinence*
  - *Permanent urinary catheter inserted chronically*
  - *Home care provided*
Hospitalization

- Admission in ICU for urosepsis due to obturation of permanent urinary catheter including hydronephrosis of both kidneys
- Replacement of urinary catheter – cloudy and smelly urine derived
- Empirical antibiotic therapy started (Amoxicillin/clavulanate + gentamycin)
Course of the disease

- Laboratory findings (creatinine, levels of gentamicine, CRP)
- Microbiological examination – Escherichia coli in the urine and hemocultures
- Ultrasonography – regression of hydronephrosis, without dilatation of urinary tract
Monitoring of renal function and urinary NGAL during antibiotic therapy

<table>
<thead>
<tr>
<th></th>
<th>January 6(^{th})</th>
<th>January 8(^{th})</th>
<th>January 10(^{th})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (umol/l)</td>
<td>55</td>
<td>37</td>
<td>40</td>
</tr>
<tr>
<td>NGAL (ng/ml)</td>
<td>891</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>351</td>
<td>267</td>
<td>60.3</td>
</tr>
</tbody>
</table>
Dynamics of creatinine, NGAL and CRP during ATB therapy
Conclusions on case report no. 2

- High initial value of NGAL was caused by urinary tract infection
- No acute kidney injury was developed
- No signs of gentamicine nephrotoxicity was revealed
- Differentiation between monomer and dimer forms of NGAL was not available in our hospital
Case report no. 3

- The patient is a 70 year old man
- Case history:
  - *Diabetes mellitus*
  - *Arterial hypertension*
  - *MGUS (monoclonal gammopathy uncertain significance)*
  - *Ischemic heart disease*
Nephrological history

- St. p. left nephrectomy in 2002 due to infiltrating adenocarcinoma of colon
- Stenosis of urethra – permanent epicystostomy introduced since 2009
- Repeated urinary infection
Hospitalization and renal treatment

- Worsening of chronic kidney disease (hyperkalemia 6.35 mmol/l and creatinine 893 umol/l)
- START OF HEMODIALYSIS at August 14th, regular hemodialysis required
Hospitalization and antibiotic therapy

- Before hospitalization: nitrofurantoinum, trimetoprim
- August 14th-17th: gentamicin
- Since August 17th: mertapenem (diagnosed ESBL type of Klebsiella pneumoniae)
- Since August 26th: norfloxacin
Monitoring of renal function and urinary NGAL during antibiotic therapy

<table>
<thead>
<tr>
<th></th>
<th>August 15th</th>
<th>August 17th</th>
<th>August 28th</th>
<th>September 4th</th>
</tr>
</thead>
<tbody>
<tr>
<td>NGAL ng/ml</td>
<td>556</td>
<td>679</td>
<td>462</td>
<td>1336</td>
</tr>
<tr>
<td>Creatinine µmol/l</td>
<td>893</td>
<td>hemodialysis</td>
<td>hemodialysis</td>
<td>hemodialysis</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>165</td>
<td>76,4</td>
<td>68,2</td>
<td>56,5</td>
</tr>
<tr>
<td>Gentamicine level before admin. N &lt;2 mg/l</td>
<td>0,6</td>
<td>5,83</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Treatment</td>
<td>Gentamicine</td>
<td>Gentamicine stopped, started ertapenem</td>
<td>norfloxacin</td>
<td>norfloxacin</td>
</tr>
</tbody>
</table>
Conclusions on case report no. 3

- Patient with chronic kidney disease – start of regular hemodialysis
- Persisting high levels of NGAL
- Levels of NGAL – without dynamic development following nephrotoxic antibiotics
Case report no. 4

- A 65 year old patient abuses beer, spirits and sleeping pills (zolpidem 4x 10 mg!)

- Case history:
  - *Severe acute steatohepatitis with cholestatic component of toxonutritive etiology*
Hospitalization

- Severe withdrawal syndrome developed after reducing zolpidem and alcohol withdrawal
- Urinary infection (Escherichia coli) persisted despite antibiotic therapy (amoxycilin + sulbactam), therefore gentamycin was added – with good effect
Monitoring of renal function and urinary NGAL during antibiotic therapy

<table>
<thead>
<tr>
<th></th>
<th>August 24&lt;sup&gt;th&lt;/sup&gt; 2012</th>
<th>August 28&lt;sup&gt;th&lt;/sup&gt; 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>NGAL ng/ml</td>
<td>108</td>
<td>5</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>168</td>
<td>20,4</td>
</tr>
<tr>
<td>creatinine umol/l</td>
<td>59</td>
<td>71</td>
</tr>
<tr>
<td>Gentamicine level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>before administration</td>
<td>0,72</td>
<td>0,94</td>
</tr>
<tr>
<td>&lt; 2 mg/l</td>
<td></td>
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</tbody>
</table>
Conclusions on case report no. 4

- Initial elevation of NGAL was probably the consequence of urinary infection.
- No negative effect of nephrotoxic gentamicin on kidney parenchyma revealed.
NGAL is very useful for management of the antibiotic therapy – especially in polymorbid patients in risk of AKI development.

It is quickly available in everyday clinical work in our hospital.