Basics and Decontamination in Clinical Toxicology

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Theoretical Considerations

• Theoretically: reduced poison load = reduced morbidity and mortality

• Is there evidence that decontamination improves survival?

• Risk/Benefit-ratio of different procedures?

• Is there a chance to reach the poison?
## Primary & Secondary Decontamination

<table>
<thead>
<tr>
<th>Primary Decontamination</th>
<th>Secondary Decontamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced emesis</td>
<td>Alkaline diuresis</td>
</tr>
<tr>
<td>Gastric lavage</td>
<td>Gastrointestinal dialysis</td>
</tr>
<tr>
<td>Single dose activated charcoal (SDAC)</td>
<td>Multiple dose activated charcoal (MDAC)</td>
</tr>
<tr>
<td>Whole bowel irrigation (WBI)</td>
<td>Hemodialysis / Hemoperfusion</td>
</tr>
</tbody>
</table>
Primary decontamination
Forced (induced) emesis

• Sirup ipecacuanhae: 10-30 mL p.o.
  • marked reduction of tracer substances in GIT
  • high variability in recovery, time-dependency
  • No improvement of clinical outcome: „...The use should be abandoned...“

• to be considered: within the first hour after ingestion of a lethal dose of a truculent poison

Eddleston et al., 2003; Krenzelok et al., 2002 & 2004
Primary decontamination
Gastric lavage

• „Cornerstone in the management of poisoning emergencies“

• Many studies focused primarily on the recovery of marker substances, not on outcome

• If lavage is considered appropriate...it is essential...that the stuff...should be experienced in its execution...

• No study demonstrated any clinical benefit yet

• to be considered: within the first hour after ingestion of a lethal dose of a truculent poison

  Kulig et al., 2004; Vale et al., 1997 & 2004; Merigian et al., 1990
Primary decontamination
Gastric lavage

Krenzelok et al., 2002
Primary decontamination
Gastric lavage

- Position: left-side, head down (20°)
- Tube 36-40 Fr (Adults) or 24-28 Fr (Infants)
- 200-300 mL NaCl 0.9% or plain water, 37°

- Contraindications
  - compromised airway
  - Ingestion of caustics and solvents
Primary decontamination

Gastric lavage
Primäre Giftelimination

“Hazards of gastric lavage in a resource poor location“

Median reduction of drug exposure (%)
Gastric lavage: "a lack of beneficial effect"
Single Dose Activated charcoal

SDAC

- Surface: 500 - 3000 m² / g
- Binds most of all toxins (not: metals, alcohols)
- Dose: 1 g/kg b.w. as a slurry or ratio AC:poison=10:1
  - usually, 30-50 g bolus is sufficient and tolerable
  - administer as early as possible (e.g. nasogastric tube)
- Seems to be inferior to MDAC
- Don´t use cathartics together with AC ever

Chyka et al., 1997 & 2005; Barceloux et al., 1997
Whole bowel irrigation (WBI)

- performed with osmotic-balanced PEG-ES; 500-2000 ml/h
- Interference with absorption capacity of activated charcoal?
- No „standard care option“
- No data regarding improvement of patient´s outcome
- To be considered: Ingestion of slow-release formulations or in the treatment of „body packers“

Tennenbein et al., 2004; Krenzelok et al., 2002
Secondary Elimination Techniques
Forced alkaline diuresis

• Rationale

  • Increased filtrate flow results in shorter time for reabsorption

  • Modifying urine pH results in ionisation of acidic or alkaline drugs becoming not absorbable

  • effective ionisation requires: Urin-pH = Blood-pH + 1

• Forced renal elimination has been shown for:

  • Diflunisal, barbiturates, MTX, fluorides, salicylates

Proudfoot et al., 2004
Secondary Elimination
Multiple dose activated charcoal

- 25-50 g AC every 4-6 hours up to 300 g total load
- may prevent primary absorption and trapping of poison with relevant enterohepatic or enterovascular circulation
- contradictory results of two prospective randomized trials in Sri Lanka
  - de Silva et al.: significant reduction in mortality & morbidity (n=400)
  - Eddleston et al.: no significant benefit comparing NoAC vs SDAC vs MDAC regarding primary & secondary endpoints (n=4500)
    Eyer et al., 2007 & 2008; de Silva et al., 2003; Eddleston et al., 2008
Secondary Elimination
Multiple dose activated charcoal

• Effectiveness in vitro regarding t1/2 and Clearance shown for:
  
  • Carbamazepine
  
  • Dapsone

  • Phenobarbital

  • Chinin / Chinidin

  • Theophylline

• Don`t use MDAC together with cathartics

• Interruption of seromucosal transport seems to be clinically irrelevant
  
  Vale et al., 1999; Brahmi et al., 2006; Eyer et al., 2007 & 2008
Secondary Elimination
Hemodialysis / Hemoperfusion
Secondary Elimination
Hemodialysis / Hemoperfusion

- Premises for effective elimination
  - low protein binding
  - slow endogenous clearance
  - small volume of distribution
  - small molecule size
  - adsorbable to AC (HP)
Secondary Elimination
Hemodialysis / Hemoperfusion

• Consensus for effective elimination for:
  • Salicylates (HD)
  • Methanol, Ethyleneglycol, Isopropanol (HD)
  • Valproic acid (HD), Carbamazepine (HP)
  • Lithium (HD)
  • Phenobarbital (HD/HP)
  • Theophylline (HP)
  • Phenytoin (HP)

Shalkam et al., 2006
Facts to remember - Decontamination
(Take Home Message)

• Primary decontamination (if ever) only in cases of massive ingestion of a truculent poison within one hour

• Alkaline diuresis seems to be theoretically reasonable for few poisons...

• HD & HP is indicated for a small number of poisons and can be lifesaving

• MDAC seems (still) justifiable for most poisons with respect to precautions
Identification of the poisoned patient at risk for ICU transfer

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Introduction (1)

- Admissions due to poisonings are frequent in the ED
- Only the minority of patients will develop signs of serious toxicity calling for ICU-transfer
- Due to shortness in ICU-capacity, to outweigh both patient safety and economic aspects, predicting factors for serious toxicity in the course of overdose are urgently needed
- It is unclear, however, which patients should be subject for aggressive monitoring and/or ICU-treatment
Introduction (2)

- Patients with intoxications may present critically ill and warrant ICU admission.

- Many other patients who are initially stable have the potential for rapid deterioration and require continuous cardiopulmonary or neurologic monitoring.

- ICU admission in these patients is thus frequently required.
ICU-transfer in poisonings

• Critical illness of poisoned patients may result from
  
  • direct toxic effects: e.g. cardiodepressants, sedatives, acute liver or renal failure
  
  • indirect, non-specific complications due to poisoning
    
    • aspiration pneumonia (e.g. OD with antidepressants, neuroleptics, sedatives, opiates)
    
    • anoxic encephalopathy after opioid-OD
    
    • renal failure due to rhabdomyolysis
Points favoring ICU transfer (1)

• Close hemodynamic and/or laboratory monitoring after massive overdose

• Significant comorbidity of the poisoned patient (e.g. chronic diseases like heart failure, diabetes, immunosuppression, chronic pulmonary diseases)

• Life threatening symptoms occurring during poisoning
  • loss of consciousness
  • Inability to allow a pertinent safe airway
  • respiratory insufficiency or arrest
  • cardiovascular instability or failure
Points favoring ICU transfer (2)

- Abnormal signs of microcirculation resulting from hypotension warrant close monitoring of
  - urine output
  - serum creatinine, transaminases
  - venous plasma lactate ($\text{Lactate}^* > 3.0 \text{ mmol/L}$ was associated with a 15-fold increase in odds of fatality)

Points favoring ICU transfer (3)

- Overdoses with β-Blockers or CCB with hypotension not readily improved by careful fluid administration and/or vasopressors/inotropes in standard doses

- Tricyclic- or Neuroleptic overdoses with
  - QRS-prolongation above 120ms
  - T40ms vector between 130-270° (complicated, not readily available*)

*Eyer et al., 2009 Hum Exp Toxicol 28(8):511-519
Predicting a patient’s low risk

• if none of the following criteria was present in the ED
  • need for intubation
  • seizures
  • unresponsive to verbal stimuli
  • $\text{paO}_2 < 45 \text{ mmHg}$
  • second- or third-degree AV-block
  • $\text{QRS} > 120 \text{ msec}$
  • systolic pressure < 100mmHg

Brett et al., Arch Intern Med 1987; 147
Problems

- in the majority no close (if any) relation between ingested dose, serum level and severity of overdose

- patients with absent signs of toxicity (e.g. in the ED) may develop serious toxicity in the further course

- instant lab-analysis to exclude serious OD is frequently not readily available (e.g. AAP- or Salicylate toxicity)

- Intoxications with cardiotoxicants and occurrence of hypotension neither necessarily mean the need for vasopressor use nor ICU-transfer - but can even mandate for extracorporeal life support in the most severe cases

- clear prognosticators predicting a severe course of poisoning remain unclear
Serum concentration of toxins

Table 3—Specific Serum Concentrations That May Affect Management

<table>
<thead>
<tr>
<th>Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Cooximetry (carboxyhemoglobin, methemoglobin, sulfhemoglobin)</td>
</tr>
<tr>
<td>Digoxin</td>
</tr>
<tr>
<td>Selected metals (iron, lead, mercury; based on history and clinical findings)</td>
</tr>
<tr>
<td>Lithium</td>
</tr>
<tr>
<td>Phenytoin</td>
</tr>
<tr>
<td>Salicylate</td>
</tr>
<tr>
<td>Theophylline, caffeine</td>
</tr>
<tr>
<td>Toxic alcohol (ethylene glycol, isopropanol, methanol)</td>
</tr>
<tr>
<td>Valproic acid</td>
</tr>
</tbody>
</table>
Risk identification

- Should account for
  - time and dose ingested
  - formulation (e.g. immediate-release or sustained-release preparations)
  - co-ingestions (synergistic or protective effects?)
  - delay in treatment since exposure (e.g. AAP)
  - patients medical condition at onset of overdose
  - drug elimination (e.g. impaired renal function, poor- or fast metabolizers, hepatic insufficiency, enterohepatic circulation)
Prognostic scores

• APACHE-II, SAPS-II, PSS or SOFA-scores are useful (e.g. for retrospective or prospective trials) to quantify critical illness (at the time when the score is captured) but is limited to predict ICU-transfer

• Glasgow coma scale (GCS)

  • e.g. GCS score of 5 certainly persuade ICU-transfer but not necessarily mandate intubation
Prognostic factors - children

• Predictors of outcome in children with acute poisonings admitted to PICU with kerosene, iron, carbamates, OP´s

• Significant predictors for PICU-admission (implicating increased mortality) in a recent multivariate analysis (n=225) were:
  • Hypotension at admission
  • higher PRISM-score (Pediatric risk of mortality)

Jayashree M et al., Journal of Trop Pediatrics 2011;57
<table>
<thead>
<tr>
<th>Variable</th>
<th>Age Restrictions and Ranges</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>Infants 130-160</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>55-65</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>&gt;160</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>40-54</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>&lt;40</td>
<td>7</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>all ages &gt;110</td>
<td>6</td>
</tr>
<tr>
<td>HR (beat/min)</td>
<td>Infants &gt;160</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>&lt;90</td>
<td>5</td>
</tr>
<tr>
<td>Respiratory rate (breath/min)</td>
<td>Infants 61-90</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;90</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Children 51-70</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Apnea</td>
<td>5</td>
</tr>
<tr>
<td>PaO₂/Fio₂</td>
<td>all ages 200-300</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&lt;200</td>
<td>3</td>
</tr>
<tr>
<td>Paco₂ (torr)</td>
<td>all ages 51-65</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;65</td>
<td>5</td>
</tr>
<tr>
<td>Glasgow Coma Score</td>
<td>all ages &lt;8</td>
<td>6</td>
</tr>
<tr>
<td>Pupillary reactions</td>
<td>unequal or dilated fixed and dilated</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>all ages</td>
<td>10</td>
</tr>
<tr>
<td>PT/PTT</td>
<td>1.5 × control</td>
<td>2</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>&gt;1 mo</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>&gt;3.5</td>
<td>6</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>all ages 3.0-3.5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>6.5-7.5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>&lt;3.0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>&gt;7.5</td>
<td>5</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>all ages 7.0-8.0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>12.0-15.0</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>&lt;7.0</td>
<td>6</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>all ages 40-60</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>250-400</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>&lt;40</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>&gt;400</td>
<td>8</td>
</tr>
<tr>
<td>Bicarbonate (mEq/L)</td>
<td>all ages &lt;16</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt;32</td>
<td>3</td>
</tr>
</tbody>
</table>
**Prognostic factors - children**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivors (N=205)</th>
<th>Non-survivors (N=20)</th>
<th>95% CI for mean difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean)</td>
<td>3.1 ± 3.0</td>
<td>4.8 ± 3.8</td>
<td>-3.1</td>
<td>0.021*</td>
</tr>
<tr>
<td>PRISM (mean)*</td>
<td>7.2 ± 8.6</td>
<td>20.7 ± 13.8</td>
<td>-23.9</td>
<td>0.011*</td>
</tr>
<tr>
<td>Length of PICU stay (days; mean)</td>
<td>5.7 ± 7.8</td>
<td>3.4 ± 5.1</td>
<td>-1.8</td>
<td>0.348</td>
</tr>
<tr>
<td>Interval between ingestion and reaching hospital</td>
<td>13.5 ± 26.1</td>
<td>10.4 ± 16.3</td>
<td>-9.0</td>
<td>0.609</td>
</tr>
<tr>
<td>Hb (g/dl; mean)</td>
<td>10.7 ± 2.1</td>
<td>12.2 ± 2.3</td>
<td>-3.0</td>
<td>0.066</td>
</tr>
<tr>
<td>Total leukocyte count (mean)</td>
<td>13 204 ± 6093</td>
<td>11 504 ± 8875</td>
<td>-5680.2</td>
<td>0.650</td>
</tr>
<tr>
<td>Platelet count (mean)</td>
<td>298 005 ± 117 328</td>
<td>258 005 ± 167 320</td>
<td>-87 076.7</td>
<td>0.524</td>
</tr>
<tr>
<td>Male:female</td>
<td>141:64</td>
<td>14:6</td>
<td></td>
<td>0.910</td>
</tr>
<tr>
<td>Hypotension at admission</td>
<td>11</td>
<td>6</td>
<td></td>
<td>0.001**</td>
</tr>
<tr>
<td>O₂ requirement</td>
<td>86</td>
<td>13</td>
<td></td>
<td>0.029**</td>
</tr>
<tr>
<td>Ventilation requirement</td>
<td>27</td>
<td>15</td>
<td></td>
<td>0.0001**</td>
</tr>
</tbody>
</table>

*The PRISM scores are available for 84 patients only.
*p < 0.05 by Students’ t-test; **p < 0.05 by Chi Square test.
Conclusion

- Identification of patient’s at risk for ICU transfer in case of intoxication is a predominantly individual decision

- ICU-transfer may be warranted
  - Organ failure
  - need for invasive monitoring or symptomatic treatment (e.g. ventilation, hemodialysis)
  - ECG and occasionally serum drug concentrations may provide rare prognosticators in poisonings
Thank you for your kind attention!