Acidosi metabolica e danno cardiaco

Ivo Casagranda.

AO di Alessandria
Agenda

- Introduzione
- Acidosi metabolica ed alterazioni cardiovascolari
  - Acidosi metabolica: da acidi inorganici
    - da acidi organici
    - da tossici
  - Quale terapia?
- Conclusioni
Introduzione
Introduction

Disturbances in acid-base balance are commonly met problems in clinical medicine and decision about their treatment are of great importance in patients with cardio-pulmonary problems, in whom acid-base disturbances may be especially critical.

Similarly, cardiopulmonary function may be significantly compromised even in patients with no intrinsic heart or lung disease, in the face of acid-base disturbance.

Mitchell JH et al. Kidney Internat 1972
Figure 1 Adverse effects of a | acute metabolic acidosis and b | chronic metabolic acidosis


Figure 2 Schematic representation of cellular and functional consequences in myocardial and vascular smooth muscle cells in instances of severe lactic acidosis. The same mechanisms are involved in both cell types but with specific functional consequences. PFK, phospho-fructo-kinase; pHe, extracellular pH; pH, intracellular pH.
Acidosi metabolica ed effetti cardiovascolari
Effect of metabolic acidosis on cardiac output

Metabolic acidosis: mean values from eight animals receiving 8.5% lactic acid

Control studies with NaCl. Mean values from five animals are illustrated.

Effect of metabolic acidosis on cardiac output

Metabolic acidosis induced by lactic acid injection, with reduction of pH to 6.8, resulted in a consistent increase in cardiac output and fall in peripheral resistance


Isolated cardiac muscle and heart preparation in vitro invariably exhibit decreased contractile force during either metabolic or respiratory acidosis. The difference between the response of isolated hearths and intact animals are due primarily to sympathoadrenal factors.

Mitchell JH et al. Kidney Internat 1972
Effect of metabolic acidosis on myocardial contractility

Old experimental works show that acidosis depresses myocardial contractility. However, this effect is significant only when intracellular pH is less than 6.4.


Some Authors evaluated myocardial contractility using ultrasound examination during severe diabetic ketoacidosis and they find any significant sign of cardiac depression.


Cardiac failure may occur in a patient with severe hypoxic acidosis, but it is likely that the depressant myocardial effect is linked to hypoxia and not to acidosis.

Levraut J and Grimaud D. Curr Opin Crit Care 2003
Effect of metabolic acidosis on myocardial contractility

It is generally agreed that myocardial contractility is depressed and the cardiovascular system becomes less responsive to catecholamines such as adrenaline or noradrenaline in the presence of acidosis, especially when the pH decreases less than 7.2.

In a study dobutamine, but not adrenaline and noradrenaline, retains its inotropic effect in anesthetized dogs subjected to metabolic acidosis (pH 7.0) by infusing HCL or lactic acid.

Huang YG et al. Br J Anaesth 1995
Cause di acidosis metabolica
ANION GAP METABOLIC ACIDOSIS

- Ketosis: β-OH-Butyric & Ac Ac
- Uremia: Multiple organic & In acids
- Salicylate: Multiple Organic Acids
- Methanol: Formic Acid
- Aldehydes: Acetic Acid
- Lactate: L-Lactic Acid (d-Lactate)
- Ethylene Glycol: Glyoxylic & Oxalic Acid
  
  Pyroglutamic acid
# HYPERCHLOREMIC METABOLIC ACIDOSIS

## Causes:

<table>
<thead>
<tr>
<th>GI Disorders</th>
<th>Kidney Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Early Kidney Failure</td>
</tr>
<tr>
<td>Pancreatic Fistula</td>
<td>RTA</td>
</tr>
<tr>
<td>Ureteroenterostomy</td>
<td>• Proximal (Type II)</td>
</tr>
<tr>
<td></td>
<td>• Distal (Type I)</td>
</tr>
<tr>
<td></td>
<td>• Type IV</td>
</tr>
<tr>
<td>Drugs</td>
<td>Other</td>
</tr>
<tr>
<td>HCl &amp; HCl Precursors</td>
<td>Post-Hypocapnia</td>
</tr>
<tr>
<td>Acetazolamide</td>
<td>Recovery from DKA</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>Toluene</td>
</tr>
<tr>
<td>CaCl₂</td>
<td></td>
</tr>
</tbody>
</table>
ACIDOSI METABOLICHE

Quando vanno trattate?
ACIDI INORGANICI

\[ \text{HCl} \]
\[ \text{H}_2\text{SO}_4 \]
\[ \text{H}_3\text{PO}_4 \]
H⁺ IS BAD

ALKALI-THERAPY IS GOOD
ACIDOSI INORGANICHE (Cl⁻, SO₄²⁻, PO₄²⁻)

**GAP ANIONICO NORMALE**
- Perdita di NaHCO₃
  - Gastroenterica
  - Diarrea
  - Fistole
- Renale
  - RTA prossimale
  - ACZ
  - IRC precoce
  - US-stomia

**GAP ANIONICO ELEVATO**
- Perdita di sali di Na con ridotto Hₑ/H₁/GFR
- Perdita nefroni
- IRA
- IRC

**ALCALI**
ACIDI INORGANICI

$\text{H}_2\text{SO}_4$

$\text{H}_3\text{PO}_4$
Renal failure
Renal Failure and metabolic acidosis

• Moderate degree of RI (serum creatinine 2-4 mg/dl) causes a significant decline in serum bicarbonate although it remains within normal ranges; Once GFR declines to about 20 ml/min frank acidosis supervenes.

Physiopathology:

• In milder degrees of RI the organic ions that comprise the anion gap are excreted normally and the acidosis is hypercloremic;

• When renal failure worsens the kidney loses its ability to excrete sulfate, phosphates, and others anions, which results in their accumulation and an increased anion gap.

Gauthier PM, Szerlip HM. Crit Care Med 2002
Renal Failure and metabolic acidosis

Treatment.

Anion gap metabolic acidosis

- Hemodialysis corrects acidosis by replacing bicarbonate while also maintaining euvolementia and normal serum concentration;
- In the rare patient with severe acidosis who does not have any other indication for dialysis, bicarbonate can be administered;

Hyperchloremic metabolic acidosis

- Type I (classic distal): bicarbonate is indicated;
- Type II: bicarbonate administration results in renal wasting;
- Type IV: correct hyperkalemia and replace bicarbonate if necessary.

Gauthier PM, Szerlip HM. Crit Care Med  2002


H$^+$ IS BAD

IS ALKALI-THERAPY GOOD?

IS ALKALI-THERAPY ALWAYS GOOD?
Chetoacidosi diabetica
Gestione della chetoacidosi diabetica

1. Ripristinare di liquidi persi
2. Somministrare insulina e.v.
3. Correggere il potassio
4. Valutare se è il caso di correggere l’acidosi metabolica (bicarbonato)
Perché non somministrare bicarbonato

- Stimola, a livello epatico, la chetogenesi con aumento della chetonemia

- Determina acidosi intracellulare nei tessuti

- Aumento dell’affinità per l’ossigeno da parte dell’emoglobina con ipossia tessutale periferica
  BellingamAJ et al. Trans Assoc Am Phys1970;83:113-120
Perché non somministrare bicarbonato

- I bicarbonati sono rigenerati dal metabolismo del lattato, dei chetoacidi e dell’aceto-acetato con il trattamento patogenetico

  Halperin ML et al. Metabolism 1983;32:308-15

- Il pH risponde rapidamente al trattamento con fluidi e insulina.

### Terapia con bicarbonato

#### L’evidenza

<table>
<thead>
<tr>
<th>Studio</th>
<th>Disegno</th>
<th>Conclusione</th>
<th>Livello di evidenza</th>
</tr>
</thead>
</table>
| Gamba G. Osguerra J  
Bicarbonate therapy in severe diabetic ketoacidosis. A double blind, randomized, placebo controlled trial.  
Random  
(pH <7.15) | Nessuna differenza | A |
| Lever E, Jaspan JB  
Sodium bicarbonate therapy in severe diabetic ketoacidosis  
AM J Med 1983;75:263-8 | 73pz  
Retrospettivo | Nessuna differenza | B |
| Morris LR, Murphy MB, Kitabachi AE  
Bicarbonate therapy in severe diabetic ketoacidosis  
Diabetes Care 1980;3: 53-56 | 21 pz  
Random  
(ph 6.9-7.14) | Nessuna differenza | A |
Bicarbonate in diabetic ketoacidosis – a systematic review

From 508 potentially relevant articles, 44 were included in the systematic review, including three adult randomized controlled trials (RCT) on bicarbonate administration versus no bicarbonate in DKA. We observed a marked heterogeneity in pH threshold, concentration, amount, and timing for bicarbonate administration in various studies. Two RCTs demonstrated transient improvement in metabolic acidosis with bicarbonate treatment within the initial 2 hours. There was no evidence of improved glycemic control or clinical efficacy. There was retrospective evidence of increased risk for cerebral edema and prolonged hospitalization in children who received bicarbonate, and weak evidence of transient paradoxical worsening of ketosis, and increased need for potassium supplementation. No studies involved patients with an initial pH < 6.85.

Conclusions: The evidence to date does not justify the administration of bicarbonate for the emergent treatment of DKA, especially in the pediatric population, in view of possible clinical harm and lack of sustained benefits.

Chua HR, Schneider A, Bellomo R. Annals of Intensive Care 2011, 1:23
Terapia con bicarbonato

Somministrare sodio bicarbonato solo se:

- pH < 6,9

Continuare la somministrazione fino a che:

- Il valore del bicarbonato sierico si raddoppia
- Il valore del bicarbonato si avvicina a 8 mEq/l
- Δ bicarbonatemia x 0,5 x peso corporeo

La concentrazione di HCO₃ non aumenta per qualche ora per la titolazione degli H⁺ intracellulari e per la diluizione secondaria alla somministrazione di soluzione salina.
Conclusioni

L’evidenza

Per la gestione della chetoacidosi diabetica la letteratura offre un certo numero di RCT’s anche se le casistiche inserite sono piccole.
Acidosi lattica
Lactic acidosis, defined as a lactate concentration > 5mmol/L and a pH < 7.35, commonly complicates critical illness. Its causes are legion, including sepsis, cardiogenic shock, severe hypoxemia, hepatic failure, and intoxication. Many of these share reduced delivery of oxygen to cells or impaired use of oxygen mitochondria, yet some are based in more complex derangements.

Forsyte SM and Schmidt GA. Chest 2000
## Causes of Lactic acidosis

**Type A**

<table>
<thead>
<tr>
<th>Decreased oxygen delivery</th>
<th>Increase oxygen demands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>Exercise</td>
</tr>
<tr>
<td>Volume depletion</td>
<td>Seizures</td>
</tr>
<tr>
<td>Blood loss</td>
<td>Shivering</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td></td>
</tr>
<tr>
<td>Severe anemia</td>
<td></td>
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<tr>
<td>Severe hypoxemia</td>
<td></td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td></td>
</tr>
</tbody>
</table>

Fall PJ, Szerlip HM. J Intensive Care Med 2005;
Causes of Lactic acidosis
Type B

Inadequate oxygen utilization

- SIRS
- Diabetes mellitus
- Malignancy
- Total parenteral nutrition
- Thiamine deficiency

Congenital lactic acidosis
Mitochondrial myopathies
HIV infection
Malaria
Drug/toxins

Other

D-lactic acidosis

Causes of Lactic acidosis
Type B

Drugs/toxins

- Biguanids
- Propofol
- Salicylate
- Simvastatin
- Lactulose
- Propylene glicole
- Theophylline
- Nalidix acid
- Nitroprusside
- Ethanol
- β-2 Agonists
- Niacin
- Cyanide
- Antiretroviral drugs
- Vasoactive drugs
- Isoniazide
- Acetaminophen
- Linezolid

Those who continue to advocate the use of sodium bicarbonate for lactic acidosis generally use the following chain of reasoning.

1. A low pH, in and of itself, is harmful (most notably by impairing cardiovascular function).

2. Sodium bicarbonate can increase the pH when infused IV.

3. Raising the pH with sodium bicarbonate improves cardiovascular function or some other relevant outcome.

4. Any adverse effects of sodium bicarbonate are outweighed by its benefits.

Forsythe SM and Schmidt GA. Chest 2000
1. A low pH, in and of itself, is harmful (most notably by impairing cardiovascular function).

- Numerous studies, concerning very different cells, have shown that anoxic or ischemic cells placed in a buffer of pH 6.5 to 7 are able to survive during several hours.
  
  If the same anoxic cells are incubated in a buffer of pH 7.40, they all die in less than an hour.

- Anoxic cells placed in a acidic buffer begin to die when the pH of the medium (pH paradox) increases.

Levraut J and Grimaud Curr Opin Crit Care 2003
2. Raising the pH with sodium bicarbonate improves cardiovascular function or some other relevant outcome.

No controlled study has shown improved hemodynamics attributable to sodium bicarbonate infusion regardless of effect on pH, and many show worsening of some hemodynamic variable.

It is significant that such negative findings include two studies in critically ill humans receiving infused catecholamines, subset of patients who might be expected to benefit most dramatically.

Forsyte SM and Schmidt GA. Chest 2000
2. Raising the pH with sodium bicarbonate improves cardiovascular function or some other relevant outcome.

- Paradoxical lowering of intracellular pH despite a rise in extracellular pH when bicarbonate is administered.
- This is due to the fact that when bicarbonate combines with hydrogen ions, it forms carbonic acid.

\[ \text{H}_2\text{CO}_3 \rightarrow \text{CO}_2 + \text{H}_2\text{O} \]

CO₂ diffuses into cells, worsening intracellular pH.

Gauthier PM, Szerlip HM. Crit Care Med 2002
Hemodynamic consequences of severe lactic acidosis in shock states: from bench to bedside.

Deleterious hemodynamic effects of severe lactic acidosis are largely suggested by experimental data, although not fully confirmed by human studies. Pending the effectiveness of an etiological treatment, there is no efficient and validated symptomatic therapy at hand to correct a lifethreatening metabolic acidosis. Upcoming research in this field should be focused on the optimal strategy to treat severe metabolic acidosis, including symptomatic therapy.

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental (E) or human (H)</th>
<th>Methodology (intervention/subjects/protocol/measurements)</th>
<th>Increased PaCO₂ after alkalinization in HCO₃⁻ group?</th>
<th>Decreased or unchanged pHe or phi after alkalinization in HCO₃⁻ group or compared with other groups?</th>
<th>Shock associated lactic acidosis?</th>
<th>Positive effects of sodium bicarbonate on hemodynamics (arterial pressure/cardiac index)³</th>
<th>Positive impact of sodium bicarbonate on mortality⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim <em>et al.</em> 2013 [112]</td>
<td>H</td>
<td>Retrospective. 103 patients with lactic acidosis. Effects of HCO₃⁻ on survival</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Wilson <em>et al.</em> 2013 [81]</td>
<td>H</td>
<td>Retrospective series. Severe acidotic trauma patients. Effects of HCO₃⁻ on survival, PaCO₂, pH</td>
<td>Yes</td>
<td>pHe: no</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Levraut <em>et al.</em> 2000 [113]</td>
<td>H</td>
<td>Mild metabolic acidosis in non-shock patients. Effects of a bicarbonate load on CO₂ generation depending on non-bicarbonate buffer</td>
<td>Yes</td>
<td>phi: no</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Fanconi <em>et al.</em> 1993 [117]</td>
<td>H</td>
<td>Neonatal acidosis. HCO₃⁻ before-after study. Effect on hemodynamics, pH, PaCO₂, PtCO₂</td>
<td>Yes</td>
<td>pHe: no</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Mathieu <em>et al.</em> 1991 [92]</td>
<td>H</td>
<td>Septic shock. HCO₃⁻ vs. saline. Effect on arterial pH, PaCO₂, hemodynamics</td>
<td>Yes</td>
<td>pHe: no</td>
<td>Yes</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>Cooper <em>et al.</em> 1990 [89]</td>
<td>H</td>
<td>Septic shock. HCO₃⁻ vs. saline. Effect on arterial pH, PaCO₂, hemodynamics</td>
<td>Yes</td>
<td>pHe: no</td>
<td>Yes</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>Bersin <em>et al.</em> 1989 [118]</td>
<td>H</td>
<td>Congestive heart disease. HCO₃⁻ vs. saline. Effect on acidosis, PaCO₂, hemodynamics (myocardial oxygen consumption)</td>
<td>Yes</td>
<td>pHi: no</td>
<td>No</td>
<td>No</td>
<td>NA</td>
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<td>Kimmoun <em>et al.</em> 2014 [60]</td>
<td>E</td>
<td>Hemorrhagic shock. Rats. HCO₃⁻ with calcium adjuvance and increased respiratory rate. Effect on pHe, muscle phi, hemodynamics</td>
<td>No</td>
<td>pHe: No</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
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</table>


<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Model/Precondition</th>
<th>Intervention</th>
<th>Outcome</th>
<th>pHe</th>
<th>pHl</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valenza et al. 2012 [84]</td>
<td>E</td>
<td>Lactic acid infusion. Rats. Lactic acidosis vs. lactic acidosis + sodium bicarbonate. Effects on hemodynamics, pHe, lactate, phosphofructokinase.</td>
<td>Yes</td>
<td>pHe: No</td>
<td>No</td>
<td></td>
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<tr>
<td>Beech et al. 1994 [87]</td>
<td>E</td>
<td>Hypovolemic shock. Rats. Carbicarb vs. HCO$_3^-$, Muscle pHl, PaCO$_2$ and hemodynamics</td>
<td>Yes</td>
<td>pHe: No</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Bollaert et al. 1994 [79]</td>
<td>E</td>
<td>Endotoxic shock. Rats. HCO$_3^-$ vs. saline. Effect on arterial pH, PaCO$_2$, muscle pHl, hemodynamics</td>
<td>Yes</td>
<td>pHe: No</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Rhee et al. 1993 [83]</td>
<td>E</td>
<td>Hypoxic lactic acidosis. Mongrel dogs. HCO$_3^-$ vs. Carbicarb vs. saline. Effects on PaCO$_2$, hemodynamics</td>
<td>Yes</td>
<td>pHe: Yes</td>
<td>No</td>
<td></td>
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<tr>
<td>Cooper et al. 1993 [88]</td>
<td>E</td>
<td>L-Lactic infusion. Pigs. HCO$_3^-$ vs. saline. Effects on pH, hemodynamics</td>
<td>Per protocol ventilation adjustment</td>
<td>pHe: No</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Shapiro et al. 1990 [119]</td>
<td>E</td>
<td>Ammonium chloride-induced metabolic acidosis. HCO$_3^-$ vs. Carbicarb. Effects on PaCO$_2$, pHe, hepatic pHl, hemodynamics</td>
<td>Yes</td>
<td>pHe: No</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iberti et al. 1988 [91]</td>
<td>E</td>
<td>Hemorrhagic shock. Dogs. HCO$_3^-$ vs. saline. Effect on hemodynamics, pH, PaCO$_2$</td>
<td>Yes</td>
<td>pHe: Yes</td>
<td>No</td>
<td></td>
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</tr>
<tr>
<td>Hope et al. 1988 [121]</td>
<td>E</td>
<td>Incomplete cerebral ischemia in lamb. Effects of glucose and HCO$_3^-$ on cerebral pHl, PaCO$_2$ and PtiCO$_2$</td>
<td>Yes</td>
<td>pHe: No</td>
<td>No</td>
<td></td>
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</tr>
<tr>
<td>Sessler et al. 1987 [122]</td>
<td>E</td>
<td>Lactic acidosis treatment in neonatal rabbits. Effect of HCO$_3^-$ on pHe and pHl and PaCO$_2$</td>
<td>Yes</td>
<td>pHe: no</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graf et al. 1985 [90]</td>
<td>E</td>
<td>Hypoxic lactic acidosis. Dogs. HCO$_3^-$ vs. saline vs no therapy. Effects on pHe and hemodynamics</td>
<td>NA</td>
<td>pHe: yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graf et al. 1985 [123]</td>
<td>E</td>
<td>Hypoxic lactic acidosis. Dogs. HCO$_3^-$ vs. saline. Effects on pHe and hepatic pHl</td>
<td>Yes</td>
<td>pHe: yes</td>
<td>No</td>
<td></td>
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<tr>
<td>Arieff et al. 1982 [82]</td>
<td>E</td>
<td>Phenformin-induced lactic acidosis. Dogs. HCO$_3^-$ vs. saline vs placebo. Effects on pHe, pHl, hemodynamics</td>
<td>NA</td>
<td>pHe: yes</td>
<td>No</td>
<td></td>
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</tr>
</tbody>
</table>

*Only applicable in comparative studies with critical patients or experimental models. ‡Only applicable in comparative studies with critical patients or experimental models. NA, not applicable; pHe, extracellular pH; pHl, intracellular pH.
Conclusion

- Sodium bicarbonate is clearly effective in raising the arterial pH in critically ill patients with lactic acidosis;
- The impact on intracellular pH is unknown in such patients, but extrapolation from extensive animals studies suggests that it’s negative;
- Despite the correction of arterial acidemia, sodium bicarbonate has no favorable effects, even for patients with severe acidemia and receiving continuous infusion of catecholamines.
- Clinicians universally agree that the most important step in the treatment of lactic acidosis is to treat the underlying conditions.
ACIDI ORGANICI

ESODOGENI

Tossici
Salicylate overdose
Gestione dell’intossicazione da aspirina

1. Gastrolusi anche dopo ore dall’ingestione
2. Carbone attivato per ridurre l’assorbimento
3. Ripristino del deficit di liquidi
4. Induzione dell’eliminazione dei salicilati
5. Emodialisi se: salicilati sierici > 800 mg/l (700 mg/l nel bambino), pH < 7,2, edema polmonare ac., IRA, interessamento del SNC
Ripristino dei liquidi e induzione dell’eliminazione

1. Espandere il volume con soluzione salina NaCl 0,9% a 10-20 ml/kg/h fino ad ottenere un flusso urinario stabilizzato di 1-1,5 ml/kg/h

2. Alcalinizzazione delle urine

3. La diuresi forzata non è raccomandata

4. Più elevato è il flusso urinario, più è difficile mantenere l’alcalinizzazione

5. Cautela nell’infondere liquidi per la possibile comparsa di edema polmonare da aspirina
Alcalinizzazione delle urine

1. Bolo iniziale di bicarbonato a 1-2 mEq/kg
2. Infusione continua con sol. glucosata 5% + bicarbonato 100-150 mEq/l + KCl 20-40 mEq/l
   Velocità di infusione: 1,5-2,5 ml/kg/h
   Flusso urinario atteso: 0,5-1 ml/kg/h
3. Mantenere il pH urinario tra 7,5 e 8
4. Monitorare gli elettroliti e glucosio nel siero
Toxic alcohol poisoning
Treatment of alcohol ingestion

Stop formation of toxic substances

Ethanol

• High dose ethanol, which has a higher affinity for the ADH:
  Loading of 0.6 g/Kg, maintenance of 66 mg/Kg/hour in non-drinkers
• Monitor serum ethanol: between 100 and 200 mg/dl

Fomepizole

• More potent than ethanol
• Never use concomitantly with ethanol
• Loading 15 mg/Kg over 30 min, followed by 10 mg/Kg/12 hours
• Expensive
Treatment of alcohol ingestion

Remove already formed toxic substances

Hemodialysis

• Hemodialysis is very effective to remove both toxic metabolites as the alcohols

Others

• Folic acid (50 mg IV per 4 hours) promotes break-down of formate the H₂O and CO₂
• Piridoxine (50 mgIM/6 hrs and thiamine (100mgIM/6 hrs promote conversion of glyoxalate to glycine instead of oxalate
The treatment of the metabolic acidosis with base has been recommended by most experts. Base administration has also been postulated to increase renal excretion of formate and glycolate. Base can be given intravenously or via dialysis. The delivery of base with dialysis might be preferred to lesser complications of base therapy.

Conclusions - 1

• It is difficult to claim that acidosis by itself is able to deeply depress the myocardial activity;

• In the acidotic models there is a reduction in myocardial responsiveness to adrenaline or noradrenaline but not to dobutamine;

• Several electrophysiologic studies have shown that acidosis promote some arrhythmia, notably the reentrant arrhythmia
Conclusions

- Alkali therapy should be restricted to severe mineral metabolic acidosis (BE ≤ 10 mmol/L) because it seems to be safe.

- The benefit of alkali therapy has never been clinically demonstrated during severe organic metabolic acidosis.

- Metabolic acidosis and the systematic symptomatic correction of all severe organic metabolic acidosis by alkali is undoubtedly a serious mistake.

- In toxic metabolic acidosis the alkali therapy is recommended by most experts.