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Use and Abuse of Bicarbonate in the Emergency Department

When we stopped using bicarbonate in ACLS, did we throw away the baby with the bath water? There are still many good, scientifically valid reasons to use this old agent. This session will discuss the rationale behind and the rational use of bicarbonate. It will also cover some of the misuse of the agent.

- Discuss why bicarbonate works in tricyclic antidepressant overdose.
- Discuss the current uses for bicarbonate.
- List the situations in which bicarbonate is not indicated or harmful.

TU-78
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Room # N219
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FACULTY

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BICARBONATE USE IN EMERGENCY MEDICINE

AND

ACUTE CARE

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Introduction:

It wasn't that long ago that acid-base management was very simple. If you had a metabolic disturbance, you treated it. Bicarbonate was used for almost any metabolic acidosis, Cardiac arrest, lactic acidosis, and severe DKA were all treated with bicarb--a few amps push and/or some added to the IV bottle. I will try in this handout to review the current status of bicarbonate for use in common acute and emergency care situations.

Bicarbonate may be useful in:

1. Cardiac Arrest
2. Lactic acidosis (including sepsis and hypovolemicihemorrhagic shock)
3. Diabetic ketoacidosis
4. Alcoholic ketoacidosis
5. Hyperkalemia
6. Rhabdomyolysis
7. Tricyclic antidepressant OD
8. Aspirin OD
9. Isoniazid (INH) OD
10. Methanol and Ethylene glycol OD

USEFUL BACKGROUND INFORMATION

Acidemia is a pH below 7.35
Acidosis is a low HCO, (below 20 meq)

Metabolic acidosis is divided into:

1. Wide anion gap
2. Normal anion gap (Also called hyperchloremic metabolic acidosis)

The **Anion Gap =** $Na^+ - (Cl^- + HCO_3^-)$

Normal Anion Gap (AX.) = 10 - 15

Differential Diagnosis of a wide Anion Gap = MUDPILES:

M	Methanol
U	Uremia
D	DKA and AKA (Alcoholic ketoacidosis)
P	Paraldehyde
I	INH and Iron
L	Lactic acidosis
E	Ethylene Glycol
S	Salicylates

Normal gap, or hyperchloremic metabolic acidosis is usually due to either: 1) diarrhea, or 2) renal tubal acidosis (RTA). A helpful pneumonic device is HARDUP:

Differential Diagnosis of a Normal Gap Acidosis = HARDUP

H	Hyperventilation
A	Acids (HCI, Lysine HCl, Ammonium HC 1; Addisons; Carbonic Anlydrace Inhibitors
R	Renal tubular acidosis
D	Diarrhea
U	Uterosigmoidostomy
P	Pancreatic fistula

Facts on Bicarbonate:

- Each ampule of bicarbonate has 44.8 or 50 meq of $NaHCO_3^-$
- pH of Bicarbonate = 8.0
- Osmolarity of an amp is: 1784 mOsm (44.8 meq) or 2000 mOsm (50 meq)
  (2 x Na *(as meq* in 1000 cc)+ GLU/18 + BUN/2.8)
- Each 50 ml amp of bicarb will produce 1250 ml of CO,

****Each 1 meg/kg of bicarb will raise the pH by about 0.1 - 0.15 if given in less than 2-5 minutes**

Relationshio of pH, pCO_2 and HCO_3^- in WIDE GAP ACIDOSIS

$$H^+ = 24 \frac{pH}{HCO_3}$$ *(Too hard to do quickly for most)*

pCO_2 = HCO, *x* 1.5 + *8* ± *2* *(Better)*

* Rule **of 15:** **HCO, + 15 = expected pCO_2**
= expected pH (last 2 digits)

i.e.: If HCO, = 10, then expected pCO_2 = 25 and pH + 7.25

** Becomes inaccurate once HCO_3^- is below IO*

WHY BICARBONATE SHOULD THEORETJCALLY BE USED

Reverses acidosis
Improves cardiac output
Increases fibrillatory threshold
Improves insulin sensitivity
Decreased work of breathing
Decreased length of coma

BUT

Reverses acidosis

but **may cause respiratory acidosis:**

$HCO_3 \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$

Note: ***If*** *ventilation is not increased, hypercarbia becomes dominant effect, as does a paradoxical acidosis. Only if ventilation andperfusion are normal does bicarbonate administration result in raising arterial and venous pH.*

Improves cardiac output

but **only if pH was below 6.8 - 7.0**

Note: This profound acidosis is rarely seen in potentially viable patients. The key is restoring ventilation andperfusion.

Increases fibrillatory threshold

but only **if pH was 6.6 - 6.8**

Note: Respiratory acidosis appears worse than same degree of metabolic acidosis--ventilate, don't bicarbonate.

Improves insulin sensitivity

but **only if pH is 6.6 or lower**

Note: This claim has disappeared in modern DKA therapy, utilizing continuous infusion protocols.

Decreases work of breathing

but **only in pH's incompatible with life using isolated muscle preps or in patients with respiratory acidosis**

Note: Actually increases amount of breathing required because of increased CO_2 load

Decreases length of coma

but *no.*

Note: *Coma based on severity ofacidosis and not on amount of bicarbonate given. Bicarbonate may actually increases length of coma due to huge osmolal load (2000 mOsm)*

WHY BICARBONATE SHOULD NOT BE USED

Intracellular acidosis	**from ↑ pCO_2**
Increased Ca, H^+ , K fluxes	**all pH dependent**
Hypokalemia	**Move K intracellularly**
Tissue hypoxia	**Shifts hemoglobin-oxygen dissociation curve to left**
Hyperosmolarity	*2000* **mOsm**
Hypernatremia	**Na = 50 meq/amp**
Increased CO, generation	**HCO, ⇌ $H_2CO_3^-$ ⇌ CO, + H_2O**
Respiratory acidosis	**Due to CO, generation**
Paradoxical CSF acidosis	**pCO_2 ↑ in CSF**

General conclusions on Bicarbonate

Once the pH approaches 7.1, patients are at risk to become severely acidotic quickly because small falls in HCO_3^- result in big pH changes as pCO_2 cannot fall below 15 - 16.

HCO, 10	pCO_2 25	pH *7.25*
HCO, 5	pco, 15	pH *7.12*
HCO, 2.5	pco, 15	pH *6.88*

For this reason the conservative approach is to begin to replace HCO_3^- when it falls below 10 (pH about 7.2). This should be done via a bicarbonate infusion, not push, at a rate of 0.5-I meq/kg over 10 - 30 minutes depending on the patient's status.

A more anti-bicarbonate approach would be to wait until the pH was below 7.0.

- **The key to correcting acidosis is to correct ventilation and/or perfusion failure.**
- **Bicarbonate rarely is of benefit**
- **It has no value if no ventilation or poor perfusion.**

General References

Adrogue HJ, Madias NE. Management of Life-Threatening Acid-Base Disorders N Engl J Med 1998;338:26-34.

Adrogue HJ, Madias NE. Management of Life-Threatening Acid-Base Disorders. Second of Two Parts. N Engl J Med 1998;338:107-111.

Gluck SL. Acid-Base. Lancet 1998;352:474-479

BICARBONATE'S EFFECTS IN CARDIAC ARREST

Redding and Pearson. So Med J, 1967; 60:926-937.

It was originally felt that bicarb was indicated just before giving epinephrine to reverse the acidosis of cardiac arrest and to increase epinephrine's pressor effects. Work from 1967 onward however, has shown the following:

Bicarbonate did not promote return of adequate circulation;
Bicarbonate did not increase conversion from VF
Bicarbonate did not decrease incidence of VF
Bicarbonate could induce a metabolic alkalosis

Chazen et al. NEJM 1968; 278:360-364.

Severe acidosis is rarely seen
Severe acidosis only in hypercapnic COPD patients.

18 of 22patients in arrest had an acidosis; 10 hadpredominantly a respiratory acidosis, while 8 had a metabolic acidosis. (pH 7.15-7.35)

Bishop and Westfelt. JAMA 1976; 235:506-509.

I meq/kg bicarbonate in well-ventilated/perfused dogs caused pH_a to go from 7.38 to 7.56 and pCO_2 to go from 27 to 49. Osmolarity increased to 349 mOsm.

In acidotic humans during CPR, similar changes noted: 7.23 to 7.48; in esophageally intubatedpatient, pCO_2 went from 194 to 280, and pH fell from 7.08 to 6.90!

Sanders et al. Ann Emerg Med 1984; 13:676-679.

- During first 8 minutes of CPR, well ventilated animals are Alkalotic due to respiratory alkalosis.
- pH changes over next 22 minutes (first half hour of arrest) is mixed respiratory alkalosis and metabolic acidosis.
- Survivors and non-survivors had similar ABGs.

Weil et al. NEJM 1986; 315:153-156.

There are marked differences between arterial and venous blood in arrested patients. Arterial normalcy versus acidotic venous side: the acidosis is due entirely to elevated venous pCO_2

*16 critically illpatients who arrested had average arterial pH of 7.41, but venous pH **of** 7.15; pCO_2 was 32 arterial, vs 74 venous. No significant differences in HCO, on arterial vs venous side.*

Sanders et al. Ann Emerg Med 1988; 17:667-671

No significant acidosis if there has been good CPR and ventilation.
Bicarbonate in well-ventilated, perfused animals may cause marked alkalosis.

2 meq/kg of bicarbonate to well-ventilated/perfused mongrel dogs after 20 minutes of CPR resulted in pH increase from 7.46 to 7.70 arterial, 7.34 venous.

Sanders et al. Ann Emerg Med 1990; 19:1-7.

Bicarbonate plus fluid loading plus rapid CPR improves outcome when compared to normal or rapid CPR without bicarbonate and/or volume.

The acidosis of early cardiac arrest is respiratory;

During the first 10 - 20 minutes a mixed respiratory alkalosis and metabolic acidosis co-exist if ventilation is occurring.

Severe acidosis does NOT exist in ventilated patients.

Sanders et al. Ann Emerg Med 1990; 19:1-7 (Continued).

Bicarbonate increases pCO_2.

Bicarbonate increases osmolarity.

Bicarbonate corrects metabolic acidosis if there is good CPR and ventilation.

NO benefit, however in : 1) Survival 2) Hemodynamics

Compared bicarbonate to carbicarb to dextrose in 21 mongrel dogs, although pH improved, it didn't affect outcome or MAP.

Kette F, et al. JAMA 1991; 266:2121-2126.

Buffer solutions may compromise cardiac resuscitation by reducing coronary perfusion pressure.

Bicarbonate (2.5meq/kg) reduced CPP in CPR by 43-50%; 7/12 animals died vs 9/9 treated with saline lived! (See also supporting editorial by Weisfeldt, JAMA 1991;266:2129-2130, and similar article by Walley KR, et al. J Crit Care 1992;73:114-21.)

Aufdereide TA. Am J Emerg Med 1992; 10:4-7.

Prehospital Bicarbonate use in Cardiac Arrests: A 3 Year Experience

58 pts got no bicarb vs 2 15 pts who got bicarb -- a retrospective review. Bicarb seemed to have some benefit in AS and EMD-PEA though transport times and other variables are confounders.

Buffer therapy during out of hospital CPR
Dybik T, Strand T, Steen PA. Resuscitation 1995;29:89-95.

Randomized clinical trial done in Norway involving 502 patients compared NSS to a special hypertonic buffer mix including bicarbonate. No significant differences in survival though NSS was slightly better 35 vs 24 (14% vs 10%). No significant differences in hospital discharge or ROSC.

An Evidence-Based Evaluation of the use of Sodium bicarbonate during cardiopulmonary resuscitation. Levy MM. Crit Care Clinics 1998;14:457-483.

An excellent review of all available studies including animals and humans. Divides studies up into 5 levels. Makes 7 points and 6 conclusions; In Summary:

Seven Points

1. Successful resuscitation is more dependent on duration of cardiac arrest than on any treatment strategies.

2. Resuscitation outcome is closely related to coronary perfusion pressure and intra-myocardial PCO_2, rather than myocardial hydrogen ion concentration.

3. Hypercarbia prolongs myocyte action potential, independent of hydrogen ion concentration.

4. Venous hypercarbia is produced in response to rapid bolus administration of bicarbonate in the presence of acidosis and circulatory arrest.

5. Bolus administration of bicarbonate induces transient depression of myocardial contractility.

6. Venous hypercarbia is ameliorated rapidly after return of spontaneous circulation of restoration of adequate cardiac output.

7. The time required for buffer equilibration between intravascular and intracellular compartments across cell membranes is much longer for bicarbonate than for carbon dioxide, and may account for the initial decrease and subsequent increase in myocardial contractility after the bolus administration of bicarbonate.

Six Conclusions

1. No human study has demonstrated a beneficial impact on survival.

2. Several human (Grade III-V) studies have demonstrated deleterious effects on physiologic endpoints from the administration of bicarbonate during CPR.

3. Only one prospective RCT (Grade II) has been conducted, and it failed to demonstrate any differences between bicarbonate and control groups.

4. Several animal studies have demonstrated impaired myocardial function in response to bicarbonate administration during CPR.

5. No animal or human studies have demonstrated a beneficial impact on outcomes for the administration of bicarbonate during hypoxic lactic acidosis.

6. Four animal trials have demonstrated survival benefit from the administration of bicarbonate during CPR.

CONCLUSIONS ON ACID-BASE BALANCE DURING CARDIAC ARREST

- Severe metabolic acidosis rare once CPR initiated (arterial pH below 7.2)
- Metabolic acidosis begins relatively late (at least 8 minutes)
- For first 30 minutes of arrest, pH usually above 7.2 (mixed acid-base disturbance)
- Good ventilation and CPR = relatively normal arterial pH (until 20+ minutes into arrest)
- Arterial and venous bloods almost 2 separate systems
- Similarity of arterial vs venous system varies based on both ventilation and perfusion
- Venous hypercarbia and acidosis common during arrest

CONCLUSIONS on BICARBONATE in CARDIAC ARREST

- No proven benefit
- Does not affect epinephrine's effectiveness
- Does not affect incidence of VF or success of defibrillation from VF
- Causes hyperosmolarity and hypercarbia

RECOMMENDATIONS on BICARBONATE DURING CPR

- **Don't use it routinely**
- **Use in CPR only for pre-existing metabolic acidosis (i.e. DKA)**
- **Follow arterial pH for adequacy of ventilation**
- **Follow $ETCO_2$ for adequacy of cardiac output**
- **Use bicarbonate (1 meqikg) if arterial pH is below 7.0 - 7.1**
- **Administer bicarbonate over 30-60 second**

BICARBONATE for ORGANIC ACIDOSIS

There is much controversy on the use of Bicarbonate for organic acidosis-- the lactic acidosis of hemorrhagic, hypovolemia, and endotoxic shock.

LACTIC ACIDOSIS: The Case against Bicarbonate Therapy

Stackpoole PW. Am Int Med 1986; 105:276-278

- The death rate in patients with severe lactic acidosis remains high despite the use of alkali therapy.
- Experimental models of lactic acidosis have failed to show a beneficial effect of sodium bicarbonate therapy when compared to the effects of sodium chloride therapy.
- Bicarbonate therapy for chronic lactic acidosis acutely impairs oxygen delivery to the tissues.
- Administration of bicarbonate results in increased CO, production, which can aggravate acidemia by increasing arterial pCO_2.
- Bicarbonate therapy causes an increase in lactic acid production.

BICARBONATE THERAPY for ORGANIC ACIDOSIS: The Case for its Continued Use

Narins RG, Cohen JJ. Ann Int Med 1987; 106:615-618

- "We have found no basis by which to condemn the use of alkali and believe those who have scorned its use have yet to demonstrate its danger clearly. Until that time, sodium bicarbonate should remain the standard of therapy for this life-threatening condition."
- The poisonous effects of lactic acidosis are lethal; bicarbonate can help buy time until definitive reversal of the underlying pathology. Prior studies have not been well controlled and few are human studies.
- Lactic Acidosis models that have a 100% mortality rate are unfair to use in testing the efficacy of bicarbonate.
- Bicarbonate may not really cause a paradoxical CSF acidosis.
- There is no in vivo data to show bicarbonate adversely affects the Hemoglobin-Oxygen dissociation curve.
- The hypercarbia of bicarbonate infusion can be easily eliminated by increasing ventilation.
- The evidence on the adverse hemodynamic effects of alkali administration is questionable.

STUDIES SUPPORTING BICARBONATE IN SHOCK

J Pcdiatr 1987; 111:817-822

Bicarbonate did not cause a paradoxical intracellular acidosis when studied by ^{31}P spectroscopy in rabbits.

J Crit Care 1988; 3:256-261.

Two meq/kg of bicarb compared to carbicarb (a non CO, generating buffer) in acidotic (7.13) hypotensive and hypoventilated dogs. Found a positive effect; pH rose acutely but only for 3-5 minutes; similar effects on cardiac output--acute rise, then a fall off. Carbicarb was more effective.

STUDIES AGAINST USE OF BICARBONATE IN SHOCK

Science 1985; 227:754-756.

Arterial pH and serum bicarbonate levels decreased with or without a bicarbonate infusion in a hypoxic lactic acidosis dog model. Cardiac output and blood pressure fell only in dogs treated with bicarbonate and not in placebo or saline treated groups.

Crit Care Med 1988; 16:770-782

CO, production increased as did blood lactate levels in bicarbonate treated dogs in hemorrhagic shock. No help in raising BP, cardiac output, arterial or venous pH.

Crit Care Med 1989; 17:1170-1174.

Bicarbonate decreased tissue oxygenation in dogs with hemorrhagic shock; lactate levels higher in bicarbonate group.

Am J Vet Res 1990; 51:1370-1374.

Bicarbonate increased lactate concentrations, and caused hypernatremia, hypokalemia, hyperosmolarity in a pony model of sublethal endotoxic shock.

Ann Int Med 1990; 112:492-498.

Bicarbonate does NOT improve hemodynamics in critically ill patients who have lactic acidosis--a prospective controlled clinical study.

14 patients in ICU on pressors received 2 meq of bicarb over 15 minutes; each also received same volume of saline (served as own control); NO significant difference in pressor response, even in 7 most acidotic patients (pH 6.9-7.2); bicarb did raise average pH from 7.22-7.36 and serum bicarb from 12 to 18.

Crit Care Med 1991; 119:1352-1356.

Bicarbonate did not improve hemodynamic variables nor did it affect tissue oxygenation; it did raise arterial and venous pH.

N Z Med J 1992; 105:6-7.

Bicarbonate administration in acidaemia - is it therapeutic?

An excellent overview editorial on the status of bicarbonate administration in acidosis and shock.

Acad Emerg Med 1995; 2:81-82.

Acidosis in Acute Hemorrhage: Detrimental or Elemental
An editorial of an accompanying article (on blood in shock) which discusses how benign a pH of 7.00 - 7.20 really is.

CONCLUSIONS ON BICARBONATE IN LACTIC ACIDOSIS

- Very controversial
- Use cannot be clearly defined
- May transiently elevate pH in well-ventilated patients
- Does NOT appear to affect outcome

RECOMMENDATIONS ON USE OF BICARBONATE IN LACTIC ACIDOSIS

- Use sparingly, if at all
- Start with 1-2 meq/kg if used
- Infuse over 1 O-l 5 minutes
- Treat underlying problem
- Depend on blood to reverse acidosis in hemorrhagic shock
- Depend on volume in to reverse acidosis in hypovolemic shock
- Reverse sepsis process in septic shock

BICARBONATE IN THE TREATMENT OF DKA

There are 5 major treatment considerations in DKA:

- **Volume**
- **Insulin**
- **Potassium**
- **Bicarbonate**
- **Phosphates**

I will restrict all discusston to bicarbonate.

Bicarbonate was previously used quite aggressively to get pH values rapidly above 7.2. This was done for the usual classic reasons (rapidly reversing acidosis would help the patient, would make insulin work better, etc.)

There have only been five human studies--one prospective and four retrospective. They show the following:

Sodium Bicarbonate Therapy in Severe Diabetic Ketoacidosis
Lever E, Jaspar JB. Am J Med 1983; 75;263-268:

> *95 episodes of DKA: no significant differences in 73 episodes treated with bicarbonate vs 21 treated without.*

Metabolic Effects of Bicarbonate in the Treatment of Diabetic Ketoacidosis
Hale PJ, et al. Brit Med J 1984; 289:1035-1038.

> *16 patients were given bicarbonate compared to 16 who were not. Infusion of 150 meq of bicarbonate: significant fall in blood lactate and total ketone bodies. It did not affect the rate of blood glucose fall.*

Bicarbonate Therapy in Severe Diabetic Ketoacidosis
Morris LR, et al. Annals Int Med 1986; 105:836-840. The only prospective study.

> *21 patients randomized to I) varying doses of bicarbonate based on pH (6.9-7.14) or, 2) no bicarbonate. No significant differences noted in rate of glucose fall, pH changes or bicarbonate levels. Authors conclude with an antibicarbonate message.*

Counterproductive Effects of Sodium Bicarbonate in DKA
Okuda Y et al. J Clin Endo Metab 1996;81:3 **14-370.**

> *7 patients on low dose insulin drips; 3 got bicarbonate at 1 amp/hour x 4 hrs. These bicarbonate treatedpatients took an extra 6 hours to clear all organic acids, Did a repeat with animals and showed increased ketoacidosis with bicarbonate.*

Acid-Base and Electrolyte disturbances in patients with DKA.
Elisaf MS et al. Diab Res Clin Proc 1996;34:23-27.

> *Evaluated 40 pts in DKA; 21 had pure WGMA, 7 also had hyperchloremic MA; 9 had a met alkalosis too: and 3 had a primary resp alkalosis. Dehydratedpts with vomiting got the Met Alk, best hydrated got the hyperchloremic acidosis. Resp Alkalosis.... think sepsis and/or pneumonia.*

Failure of Adjunctive Bicarbonate to Improve **Outcome in Severe Pediatric Diabetic Ketoacidosis**

Green SM et al. Anal Emerg Med 1998;31:41-48.

> *Failure of adjunctive bicarbonate to improve outcome in severe pediatric DKA. Retrospective review of 147 cases in 109 children over 16 years at ORMC. No differences in complications, similar rates of rises in HCO_3 and pH rate of change; the length of hospitalization was however longer by almost I day in those who got bicarbonate.*

Bicarbonate in Diabetic Ketoacidosis has a number of potentially deleterious effects:

- Hyperosmolarity
- Shifting the hemoglobin oxygen dissociation curve
- Causing a paradoxical CSF acidosis. (See p. 17)

Paradoxical CSF Acidosis with Bicarbonate:

Rule 1: **Blood brain barrier (BBB) allows pCO_2 to cross easily**

Rule 2: **The BBB does NOT allow HCO_3^- to cross easily**

Rule 3: **Hyperventilation is determined predominantly by peripheral pH**

1. Normal Patient

Body (Arterial blood)	BBB	Brain (CSF)
pH 7.4		7.4
pco, 40		40
pCO_3 24		24

2. **DKA Patient with protection via BBB**

pH 7.1		7.3
pco, 15		15
pCO_3 5		10

3. **Patient rapidly gets 2-3 ampules (ii-150 meq) of bicarbonate**

pH 7.3		New pH will be determined by new pCO_2 and HCO,
pco, 30		pCO_2 now rises to serum level equilibrates instantly)
HCO, 15		HCO_3 will not cross; stays at original value

4. **Result is CSF acidosis and near WNL serum pH**

pH	7.3	7.05
pCO_2	30	30
$pHCO_3$	15	10

CONCLUSIONS ON BICARBONATE IN DKA

- **Don't use in young, healthy patients unless pH is below 6.9 - 7.0**
- **Use sparingly in sick patients with severe DKA (pH below 7.0 - 7.1, bicarbonate below S-10.)**
- **Use by drip for decompensation in severe DKA**
- **Decompensation in DKA:** **Falling respirations**
  Falling bicarbonate even with insulin and volume
  Worsening CHF
  Worsening AMS

Bicarbonate Drips in DKA: Two amps (88-100 meq) over 10 - 60 minutes

Push bicarbonate ONLY in:

(1) DKA with agonal respirations or pulse
or
(2) DKA and severe hyperkalemia

Additional references:

DKA--the bicarbonate controversy. J Peds 1976; 87:156-159.
(An early easily read discussion)

Cerebral Hypoxia from bicarbonate infusion in DKA. J Peds 1980; 96:968-973.
(argues against bicarbonate due to shift in O_2 saturation curve)

Intracerebral crisis during treatment of DKA. Diabetes Case 1990; 13:22-35.
(CNS crisis unrelated to bicarbonate use or nonuse)

Alkali Therapy in DKA: Biochemical, Physiologic and Clinical perspectives. Diab Metab Rev 1989;8:627-636. (Best recent review on bicarb in DKA, reviews pros and cons of bicarb in DKA; recommends bicarb for severe DKA - enough to raise HCO, - to 10 meg - which will allow pH to rise to 7.15 or greater.)

Riley LJ, Cooper M, Narins RG. Alkali Therapy of Diabetic Ketoacidosis: Biochemical, Physiologic, and Clinical Perspectives. Diabetes Metab Rev 1989;5:627-636.

ALCOHOLIC KETOACIDOSIS (AKA) AND BICARBONATE USE

- AKA is a syndrome which combines (1) dehydration, (2) low glycogen stores, (3) no available carbohydrates with (4) a precipitating event.
- It results in (1) protein and fat breakdown, and (2) rising lactate and beta-hydroxybutrate levels
- Clinically, serum bicarbonates usually are between 5 - 15 meq and pHs usually range from 7.1 - *7.35.*

Treatment of Alcoholic Ketoacidosis

1. Hydrate and give Glucose (D_5NS 200cc/hr)
2. Treat withdrawal (Benzodiazepine, $MgSO_4$, etc.)
3. Thiamine, multivitamins, folate, Niacin
4. Feed the patient
5. Treat underlying cause: (Pancreatitis, CNS events, sepsis, pneumonia, GI bleed, etc.)

Role of Bicarbonate in Alcoholic Ketoacidosis

Treatment of Alcoholic Acidosis
Miller PD et al. Arch Int Med 1978; 138:67-72

Eighteen episodes in 10 patients; stressed the role ofglucose. volume andphosphorous; even with initial HCO_3^- levels of 3-5 in 4patients (pH = 7.05 - 7.15), no bicarbonate required.

Alcoholic Ketoacidosis
Fulop M, et al. Alcoholism 1986; 10:610-615

Twenty-three patients studied biochemically: with only AKA, none required bicarbonate (others with multiple diseases not discussed in depth)

The Syndrome of Alcoholic Ketoacidosis
Wrenn, Slovis. Am J Med 1991;

Largest clinical study of AKA; 74 patients with AKA pH range from 6.95 to 7.45; mixed acid-base disturbances common; no bicarbonate required to reverse process in any patient.

CONCLUSIONS ON BICARBONATE IN AKA

- **NO role in AKA**
- **Failure to correct acidosis with volume and glucose = another process**
- **Beware sepsis, toxin, AMI, DKA**

HYPERKALEMIA

Corey M. Slovis, M.D.

HYPERKALEMIA

Hyperkalemia is the most dangerous acute electrolyte abnormality.

Most K lives inside the cell (ICF = 140-155 meq/L), while a small amount, about 2% total body potassium, is in the extracellular compartment (ECF = 3.5 - 5.0 meq/L).

The potassium difference between the ICF and ECF is the key determinant of the resting membrane potential. As the serum potassium rises, PVCs, VT, a wide complex sine wave, or VF may occur.

There are many causes of hyperkalemia, but two rules must always be followed prior to treating patients:

1) **The number one cause of byperkalemia is hemolysis after (or as) the patient's blood is drawn.**
2) **Treat the patient based on laboratory values and ECG changes, and not just lab values.**

There are 10 "common" causes of hyperkalemia:

- **Spurious** due to hemolysis during or after phlebotomy
  - thrombocytosis
  - leukocytosis
  - abnormal erythrocytes
- **Acidosis**
- **Renal Failure**
- **Iatrogenic** (usually associated with renal failure)
  - intravenous potassium containing medications
  - amino acid infusions
- **Cell death**
  - rhabdomyolysis
  - crush injuries
  - bums
  - tumor lysis syndrome
- **Addison's Disease** (or any low aldosterone state)

- **In vivo hemolysis**
- **Hematologic**
  - WBC > 100,000
  - HCT > 55-65
  - PLTs > 1 ,000,000
  - Tumor lysis syndrome

- **Hyperkalemic Periodic Paralysis**

- **Drugs**
  - Aldactone and K sparing diuretics
  - Captopril and other ACE inhibitors
  - NSAIDS
  - Heparin
  - Succinylcholine
  - Glucagon
  - Beta Blockers
  - Calcium Blockers
  - Digitalis (acute OD)

TREATMENT OF HYPERKALEMIA

There are 3 ECG changes due to hyperkalemia

1. **Tall Peaked T waves** (Seen as K rises above 5.5-6.0)
2. **P - R prolongation** followed by **loss of the P wave** (begins as K rises above 6.0-6.5)
3. **Widening of the QRS** (K usually above 7)

There are three steps to treating hyperkalemia.

Step 1: Reverse the deleterious electrical effects of potassium

a) 5 - 10 cc of 10% CaCl

Step 2: Drive potassium into the cell

a) 2 amps D_{50} over 5 - 10 minutes with 10 units of regular insulin IV push.

b) 2 amps (1 meq/kg) $NaHCO_3$ over 5 - 10 minutes - only if acidotic!

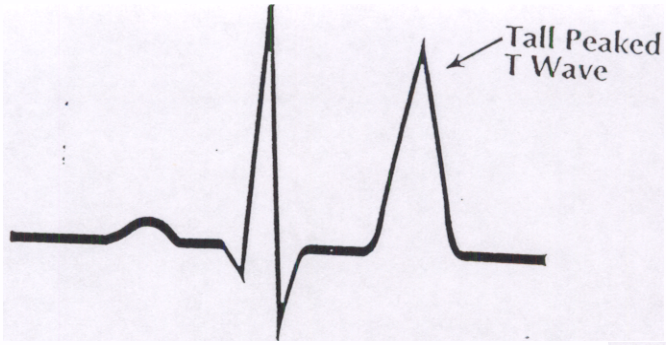
See pages 4-6 for additional methods for moving K into cell
(steps a and b are "standard")

Step 3: Remove potassium from the body

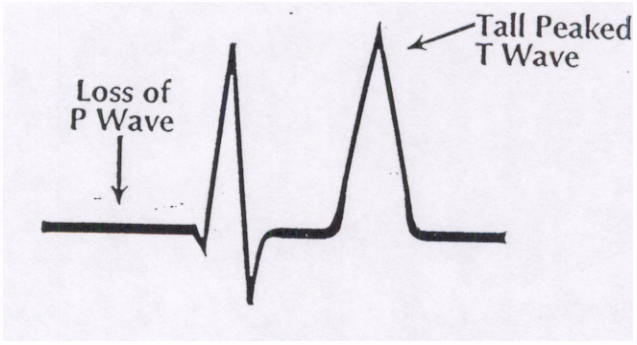
a) NSS at 200 cc/hr and lasix (40 - ? mg) to achieve urine output approaching 150 cc/hr.

b) Kayexalate 50 G in sorbitol PO or by enema

c) Hemodialysis

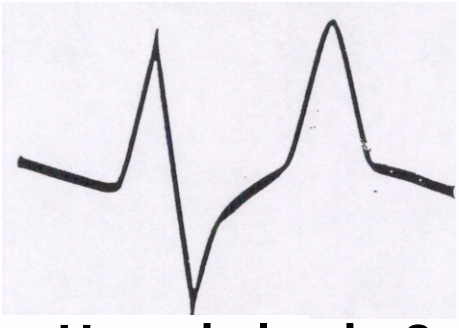


Hyperkalemia 1



Hyperkalemia 2

Widened QRS Merging
With Tall T Wave



Hyperkalemia 3

Comments.

step 1:

Calcium is used only if the QRS is widened. Ifunsure, use 5 cc to start. Use 10 cc in arrest

- Calcium works by "tricking" the cell into thinking there's more of an electrical difference between intracellular and extracellular compartments.
- Ca does not move K intracellularly
- Ca does work for l-30 minutes to restore a more normalized electrical gradient and will temporarily narrow the QRS.

CaCl = 3x Ca gluconate

Approximately 13.6 meq of Ca in 10 cc of CaCl

vs

Approximately 4.6 meq of Ca in 10 cc of Ca gluconate

Calcium is highly sclerosing - try to give it via a large peripheral vein

Dose: In general 10 cc is an appropriate dose. You may want to start with 5 cc over 10 - 20 seconds if unsure; do not give more than 20 cc of CaCl in the first 30 minutes.

Step 2: Moving K Intracellularly

Glucose and Insulin

- Moves K intracellularly by stimulating glucose pump
- Drops K by about 1 .O meq over 20-60 minutes
- Steepest drop is in first 20 minutes
- Use 50 grams of glucose and 10 units insulin
- May give both IV push or over 5-15 minutes

BEWARE HYPOGLYCEMIA 1 HOUR LATER

- **Has no effect in non-acidotic patients**
- Bicarbonate is most useful in patients with serum HCO_3^- levels below 5-10
- Bicarbonate moves K intracellularly in acidotic patients
- Bicarbonate is an adjunct to CaCl, glucose and insulin
- USE bicarbonate in acidotic hyperkalemia patients
- USE 1 meq/kg over IO-20 minutes for most patients
- USE 1 meq/kg IV push in patients with sine wave QRS patterns
- USE IV push for hyperkalemic EMD/PEA

When things were simple, using bicarbonate for hyperkalemia was easy to explain:

For every 0.1 increase in pH, K falls by 0.6 meq.

Unfortunately things are never as simple as in the old days.

Changes in plasma potassium concentration during acute acid-base disturbances.
Androgue HG, Madias NE. Am J Med 1981; 71:456-467.

There are varying effects on serum K when the pH changes and there are different changes with respiratory vs metabolic and in alkalosis and acidosis. Many factors other than just the bicarbonate may be at work. Reviews approximately 30 studies. "Acute acidemia usually results in hyperkalemia and acute alkalemia usually reduces plasma potassium."

Effect of various therapeutic approaches on plasma potassium with major regulating factors in terminal renal failure.
Blumberg A., et al. Am J Med 1988; 85:507-512.

Bicarbonate (2-4 meq/min; total dose 120-240 meq) was ineffective in lowering K values in CRF dialysis patients. Glucose and insulin worked (K from 5.62 to 4.70). Note: pH of patients was 7.37 and went up to 7.51 with bicarbonate.

Bicarbonate in the treatment of severe hyperkalemia (letter).
Spittal. Am J Med 1989; 86:511.

Points out patients of above study had normal pHs and urged bicarbonate use continue in acidotic patients.

Alkalinization Is Ineffective for Severe Hyperkalemia in Nonnephrectomized Dogs.
Acad Emerg Med 1997;4:93-99.
A repeat variation of prior studies. This was a controlled canine study. Hypertonic Saline just as effective as HCO, in lowering K.

Beta Agonists

- cAMP mediated K pump stimulation
- Like epinephrine, stimulates K migration into cell
- Works additively with glucose and insulin
- Usually blocks the hypoglycemia seen with glucose and insulin
- Most studies have used IV albuterol NOT inhaled,
- Dose is usually 0.5 mg diluted in 100 cc given IV over 10-15 min. Lowers K by 0.5 meq - 1 .0 meq over 15-30 min.
- May nebulize in 1 O-20 mg in 4 ml NS over 10 min

STOP BETA AGONISTS IF PVC's DEVELOP

Magnesium

- Stimulates Na-K ATPase pump
- Moves K into cell rapidly
- Works within 5 minutes
- Lowers K by about 0.5 meq
- Dose is l-2 grams over 5-20 minutes
- May cause hypotension in dehydrated patients
- Be careful in patients with CRF
- An excellent antiarrhythmic for K induced ectopy

Volume

- Helps restore cellular Na-K gradient
- Especially good in dehydrated patients
- Especially bad in CHF/CRF
- Beware pulmonary edema

Step 3: Moving K Out of the Body

Saline should be infused more rapidly in hypovolemic patients and slower in patients with CHF.

- Don't use saline and lasix if the patient cannot make urine.
- Each gram of resin binds 0.5 - 1.0 meq of potassium.
- Dialysis is excellent, but usually not readily available in the ED.
  Both HD and PD may be required for massive crush injuries.
  Continuous A-V hemofiltration may also be used.
  HD removes up to 50 meq of potassium/hour.
  PD removes only about 1/5 of that.

Niemann JT, Cairns CB. Hyperkalemia and Ionized Hypocalcemia During Cardiac Arrest and Resuscitation:Possible Culprits for Postcountershock Arrhythmias? Ann Emerg Med 1999:34:1-7.

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Chiu TF, Bullard MJ, Chen JC, et al. Rapid Life-Threatening Hyperkalemia After Addition of Amiloride HCL/Hydrochlorothiazide to Angiotensin-Converting Enzyme Inhibitor Therapy. Ann Emerg Med 1997;30:612-615.

Perazella MA, Mahnensmith RL. Hyperkalemia in the Elderly. J Gen Intern Med 1997;12:646-656.

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Fenton F, Smally AJ, Laut J. Hyperkalemia and Digoxin Toxicity in a Patient with Kidney Failure. Ann Emerg Med 1996;28:440-441.

Sweterlitsch EM, Murphy GW. Acute eletrocardiographic pseudoinfarction pattern in the setting of diabetic ketoacidosis and severe hyperkalemia. Am Heart J 1996; 132: 1086-l 089.

Ho-Jung Him. Combined Effect of Bicarbonate and Insulin with Glucose in Acute Therapy of Hyperkalemia in End-Stage Renal Disease Patients. Nephron 1996;72:476-482.

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Liou HH, Chiang SS, Wu SC, et al. Hypokalemic effects of intravenous infusion or nebulization of salbutamol in patients wtih chronic renal failure: comparative study. Amer J Kidney Dis 1994;23(2):266-271.

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Palevsky PM, Singer I. Disorders of potassium metabolism in endocrine and metabolic emergencies. Wolfson AB, ed. Churchill Livingstone 1990; 17-45.

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BICARBONATE FOR RHABDOMYOLYSIS

There are 5 causes of Rhahdomyolysis:

Toxic metabolic
Ischemic
Intrinsic muscular
Infections
Temperature

Acute Renal Failure (ARF) in rhabdo is caused by multiple factors:

Volume depletion
Shock
Acidosis
Electrolyte abnormalities

The fundamental cause of ARF is probably increased renal vascular resistance resulting in decreased renal blood flow.

Myoglobin is not nephrotoxic, but its metabolite is.

Ferrihemate + Dehydration = low urine flow = Renal Failure

There are a number of treatment options that need to be considered in rhabdomyolysis and in acute renal failure due to rhabdomyolysis.

1. Securement of ABC
2. Aggressive, *early* volume replacement with saline (in field if possible)
3. Maintenance of high urine output
4. Mannitol 10 - 20 g IV
5. Lasix 200 mg IV
6. Alkalinization of urine to pH >6.5 with sodium bicarbonate
7. Hemodynamic monitoring to guide volume replacement and mannitol use
8. Foley catheter to monitor urine output
9. Serial measurements of serum K+, CO,, BUN, creatinine, CPK, Ca, phosphorous, uric acid, albumin, glucose
10. Phosphate binders for elevation of serum phosphorous
11. Early use of ion-exchange resin such as Kayexelate for hyperkalemia
12. Calcium administration only for:
    a) life-threatening cardiotoxicity of hyperkalemia
    b) hypocalcemic symptoms and signs
13. Compartmental pressure monitoring and early fasciotomy for pressures greater than 30-35 mmHg
14. Replacement of clotting factors depleted by DIC

Modified from Wrenn, Slovis. Sorting through rhabdomyolysis: an enigma made manageable. Emerg Med Rpts 1987; 8:161-168

Bicarbonate use in rhabdo is considered controversial by some and absolutely mandatory by others.

The Key to Avoiding ARF in Rhabdomyolysis is Insuring High Urine Flow

Prevention of Acute Renal Failure in Traumatic Rhabdomyolysis

Ron et al. Arch Intern Med 1984; 144:277-280.

Seven patients with crush injuries were treated with average of 568 cc/hr IV fluids with urine output of about 300 cc/hr. Also used mannitol and bicarbonate (685 meq/60 hrs).
NO complications, no ARF.

Early Management of Shock and Prophylaxis

Better OS, Stein JH. NEJM 1990; 322:825-829.

Strongly recommends a forced mannitol-alkaline diuretic to prophylact against hyperkalemia and ARF.
Recommends the equivalent of: D_5½NS
I amp Bicarbonate
10 grams of mannitol (50cc of 20%)

Run at 300-500 cc/hr
Keep urine above 6.5

Other General References

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Better OS, Rubinstein I, Winaver J. Recent insights into the pathogenesis and early management of the crush syndrome. Semin Nephrol 1992; 12:217.

BICARBONATE FOR TRICYCLIC ANTIDEPRESSANT OVERDOSE

The TCAs and related cyclic compounds (CAs--bicyclics, tetracyclics, etc.) are the number one cause of death from OD in patients arriving alive to EDs. It is exceedingly important for emergency medicine and acute care physicians to know how to expertly treat this overdose.

Mechanisms of TCA Toxicity

- Norepinephrine release followed by blocked reuptake
- Alpha blockade
- Anticholinergic effects
- "Membrane stabilization"

Membrane stabilization, or the quinidine effect of TCA's refers to TCA's effects on the action potential of myocardial cells.

The Two Major Cardiac Effects of TCAs

1) **Prolonged reoolarization (phase 2 prolonged)**
   Potassium flux delayed
   Prolonged Q-T interval
   Ventricular ectopy

2) **Slowed depolarization (phase 0 prolonged)**
   Sodium channels blocked **Widened QRS** **Hypotension**

Effects of Sodium and Bicarbonates in TCA Overdose

The cardiotoxic effects of the TCAs resulting in slowed depolarization is predominantly due to TCA-induced blockade of sodium channels. The best way to override sodium channel blockade is by sodium infusion. The other way to decrease TCA's effects is by decreasing the amount of free (or unionized) portion.

TCA's are avidly protein-bound. Approximately 92 - 94% of TCAs are bound at pH 7.4. This goes up to 96 - 98% binding at pH of 7.5 - 7.55.

A pH rise from 7.4 to 7.55 decreases active drug by 50 - 66%

There is some disagreement over whether increasing the protein binding of TCAs works via blocking TCA entry into cells or whether the gradient of active drug out of cells into the alkaline serum (to maintain equilibrium) is more important,

Alkalinize the patient,

NOT the urine or the IV.

Hypertonic Saline vs Bicarbonate in TCA OD

McCabe JL et al. Experimental TCA toxicity: A randomized, controlled comparison of Hypertonic Saline vs Sodium Bicarbonate, and Hyperventilation. Ann Emerg Med 1998; 32:329-333.

29 swine made toxic with elavil (QRS>120 ms and BP<50). Got one of four therapies: (1) placebo vs (2) 10 ml/kg of 7.5% Nacl vs (3) 3 ml/kg HCO_3 vs (4) hyperventilated to pH 7.50 - 7.60.

	Placebo	HTS	HCO,	HV
BP (mm Hg)	57	134	85	60
QRS (msec)	144	80	105	125

Respiratory Alkalosis vs Metabolic Alkalosis

Respiratory alkalosis will not directly override sodium channel blockade as well as saline. Respiratory alkalosis will increase protein binding, however.

Intravenous sodium bicarbonate appears to be superior to hyperventilation.

Beware hyperventilation in a patient with metabolic alkalosis.

Kingston M. Hyperventilation in tricyclic antidepressant poisoning. Crit Care 1979; 7:550.

Sasyniuk BI, et al. Experimental amitriptyline intoxication: Treatment of cardiac toxicity with sodium bicarbonate. Ann Emerg Med 1986; 15: 1036.

Hoffman JR, McElroy CR. Bicarbonate therapy for dysrrhythmia and hypotension in tricyclic antidepressant overdose. West J Med 1981; 134:60.

INDICATIONS TO USE BICARBONATE FOR TCA OVERDOSE

AMS or Lethargy
Seizures
Hypotension
QRS greater than 100 msec
Arrhythmias

ALKALINIZATION IN TCA OD

1 meqikg bicarbonate over 2 - 5 minutes (2 amps over 2 minutes)
Titrate to pH 7.5 - 7.55
Begin drip of ½NS with 1 meq/kg HCO_3^- at 200 cc/hr
Titrate rate and/or add HCO_3^- to maintain pH 7.5 - 7.55
Do not allow patient to hyperventilate also!!

INCREASED TCA TOXICITY

- **Hypoxia**
- **Hypotension**
- **Acidosis**
- **Hypokalemia**
- **Hypomagnesemia**

ALKALINIZE THE PATIENT

NOT the urine or the IV

Additional References

Hedges JR et al. Bicarbonate therapy for the cardiovascular toxicity of amitriptyline in an animal model. J Emerg Med 1985; 3:253.

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Pentel PR, et al. Effect of hypertonic sodium bicarbonate on encainide overdose. Am J Card 1986; 57:578.

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Lovecchio F, Berlin R, Brubacher JR, Sholar JB. Hypertonic Sodium Bicarbonate in an Acute Flecainide Overdose. Am J Emerg Med 1998;16:534-537.

Sharon M, Liebelt EL. Toxicology reviews: Targeted management strategies for cardiovascular toxicity from tricyclic antidepressant overdose: The pivotal role for alkalinization and sodium loading. Discusses HCO_3 and sodium loading in a review article. Ped Emerg Care 1998;14:293-298.

Hoffman JR, Votey SR, Bayer M, Silver L. Effect of Hypertonic Sodium Bicarbonate in the Treatment of Moderate-to-Severe Cyclic Antidepressant Overdose. Am J Emerg Med 1993;11:336-341.

Hoffman JR, et al. Shows “hypertonic bicarbonate” decreases morbidity and mortality in TCA OD. Hypotension corrected in 20/21; QRS shortened in 39/49 and AMS decreased in 40/85. Am J Emerg Med 1993;11:336-341.

BICARBONATE FOR ASPIRIN OVERDOSE

Aspirin's morbidity and mortality is usually due to any number of 5 major toxic effects. Close monitoring is both preventive and therapeutic, A potential sixth effect, non-cardiogenic pulmonary edema, should also be closely monitored.

The Four Phases of Aspirin Overdose

1. Respiratory Alkalosis Phase (hyperventilation due to direct stimulation of central respiratory centers)
2. Mixed Respiratorv Alkalosis Combined with a Metabolic Acidosis (as the ASA dissolves)
3. Metabolic Acidosis (seen in significant OD's as respiratory drive can no longer compensate)
4. Combined Metabolic and Respiratory Acidosis (rare, sudden respiratory failure)

Acute Toxic Effects of Asprin Overdose

‘otential Toxic Effect	Monitor	Therapy
\cidosis	Respiratory rate pH SMA-7	Volume Bicarbonate
Iyperpyrexia	Vital signs Vascular Collapse	Volume Urine output
Iypoglycemia	Finger Stick Glucose SMA-7	Glucose
Hypokalemia	SMA-7 Urinary K EKG (severe cases)	K
Pulmonary and/or Cerebral Edema	O_2 saturation Respiratory rate Mental status	Appropriate Volume

Start D_5 ½ NS + 2 amps of HCO_3 + 40KCL at 200cc/hr

Bicarbonate's use prevents acidosis and dramatically increases ASA excretion via ion trapping

KEY FACTS:

- Bicarbonate is avidly excreted in the urine
- A slow, constant infusion of bicarbonate will alkalinize the urine
- A slow, constant infusion of bicarbonate will NOT alkalinize the serum
- Ionized substances do not cross polar membranes (Le., renal tubule)
- Aspirin has a pKa of 3
- As pH rises, more of aspirin exists as an ion
- Aspirin is normally filtered by glomerulus and then reabsorbed
- In an alkaline urine, aspirin ionizes as it passes through glomerulus
- Ionized aspirin is trapped in urine and is excreted

Maximizing Aspirin Excretion

Dramatic excretion of aspirin occurs once urine is above pH 7.0

Optimal excretion occurs when urine is above 8.0

Forced diuresis is NOT effective and may be dangerous

Maintain urine flow at about l-l.5 cc/kg body weight

Failure to keep normal pH of serum results in aspirin moving across polar membrane of brain and into CSF

Failure to keep elevated pH of serum results in aspirin moving across polar membrane of renal tubule and back into the body

Urinary Alkalinization in Aspirin Overdose

- Add two ampules of bicarbonate to D_5½NS with 40 meq KC1
- Check urine in 1 hour; if urine pH is not above 7.0, add 2 more ampules of bicarb

IMMEDIATELY CORRECT PATIENT'S BICARBONATE DEFICIT:

If patient's serum is acidotic, used 1 meq/kg over 1 O-20 minutes. Recheck pH 5-l 0 minutes after giving bicarbonate.

Beware forced diuresis *(Don't use it: cerebral and pulmonary edema; ineffective)*
Beware acidosis *(ASA into brain, increased reabsorption via kidney)*
Beware hypokalemia *(K lost during therapy due to volume Rx, bicarb, and direct ASA effects)*
Beware pulmonary edema *(From ASA or from high volume therapy)*
Beware missing aspirin toxicity *(Consider ASA in any mixed acid-base disturbance; unexplained AMS or acidosis)*

Best References:

Slovis CM. Aspirin Overdose; in Medicine for the Practicing Physician. Ellenhom and Burceloux. Medical Toxicology 1988 (best text discussion)
Hill. NEJM 1973; 228:1110. Classic OD article Prescott. B Med J 1982;285:1383-1386. (Best alkaline diuresis article)

BICARBONATE FOR ISONIAZID (INH) OD

Severe INH ODs usually present with seizures and acidosis. Seizures are due to INH's effect on GABA, gamma amino butyric acid--the inhibitory neurotransmitter. INH inhibits pyridoxine, the coenzyme required for glutamic acid decarboylase to make GABA from glutamic acid.

INH

glutamate ----I—> GABA

glutamic acid
decarbonate

The profound acidosis of INH is almost completely due to the refractory seizures that occur in ODs approximately 30 - 120 minutes post OD ingestion. There may also be some disruption of the lactate to pyruvate conversion also.

Tox Appl Pharm 1979; 49:377-384.

CONCLUSIONS ON BICARBONATE IN INH ODs

REGENERATING GABA CURES INH ODs

Trying only to correct the acidosis of INH does NOT affect outcome

Use bicarbonate as an adjunct to pyridoxine

Give pyridoxine on a gram per gram ingested INH basis

Yarbrough et al. INH OD treated with high dose pyridoxine.
Ann Emerg Med 1983;12:303-308

Black, Ross. Complete recovery from severe metabolic acidosis with INH poisoning. Ped Emerg Care 1989;5:257-258.

Using bicarbonate once seizures controlled may cause deleterious metabolic alkalosis.

Anesth Anal 1990; 71:554-557.

pH values of 6.6 - 7.0 are common in symptomatic INH OD.
Complete recovery reported even with pH as low as 6.4.

Am J Emerg Med 1987; 5:165-166

RECOMMENDATIONS FOR BICARBONATE IN INH OVERDOSE

- Secure ABCs
- Follow standard toxicologic management protocol (NGT, block absorption, etc.)
- Give pyridoxine gram per gram of INH taken
- Supplement pyridoxine with valium for seizure control
- Give 1 meq/kg bicarbonate over 5 min. for pH below 7.0
- Recheck pH in 5 - 10 minutes
- Titrate bicarbonate only while seizures uncontrolled

NO seizures = NO acidosis = NO bicarbonate

The lactic acidosis of seizures from INH will disappear in 30 - 60 minutes

- Secure the ABCs
- Hydrate
- Avoid rhabdomyolysis

BICARBONATE IN METHANOL AND ETHYLENE GLYCOL ODs

Methanol

- CH, - OH; MW 32; each 3.2 mg% of methanol = 1 mOsm
- Creates metabolic roadblocks in CNS, eye, abdomen
- Diagnosis: Profound acidosis, blindness, retinal edema, pancreatitis
- Alcohol blocks breakdown of methanol to formic acid and formaldehyde
- Methanol is non-toxic; its breakdown products are not
- If congested with ETOH. acidosis and symptoms delayed

Ethylene Glycol

- $HO\text{-}CH_2\text{-}CH_2OH$; MW 62; each 6.2 mg% = 1 mOsm
- An antifreeze agent; a sweetener for wine
- 40 - 60 deaths a year in USA
- Has no odor
- Profound acidosis from oxalic glyoxylic and hippuric acids

THE KEY TO THERAPY OF METHANOL AND ETHYLENE GLYCOL IS THREE-FOLD:

1. **Block metabolism of toxin with ethanol**
2. **Reverse acidosis**
3. **Remove toxin from body**

Loading and Maintenance of Ethanol

A. Give 10% ethanol in D_5W
B. Load with 10cc/kg (about 700 cc--do not load if blood ETOH = 100 mg% or higher)
C. Maintain with 1 - 1.5 cc/kg/hr (70 - 100 cc/hr)
D. Follow ETOH levels hourly X at least first few hours, then Q 2 - 3 hours
E. If dialysis is being used, increase maintenance by 2 - 3X and follow levels
F. continue until toxin level is below 20 - 30 mg%
G. Although not clinically proven, folic acid may help oxidize in Methanol ODs
H. Although not clinically proven, thiamine and pyridoxine may help in ethylene glycol ODs

Bicarbonate Administration

- Patients may present mildly to severely acidotic
- Begin with bicarbonate at 1 meq/kg over 10 - 15 minutes for patients with acidotic pH
- In patients with pH levels below 7.0, 4 - 10 ampules may be required in first 1 - 2 hours
- Move rapidly to hemodialysis in acidotic patients who do not normalize after 1 - 2 meq/kg of bicarbonate

Dialysis

- Dialyze acidotic patients
- Dialyze symptomatic patients
- Dialyze massive overdoses
- Continue dialysis until toxin level is below 20 mg

References

Ekins BR, Rollins DE, et al. Standardized treatment of severe methanol poisoning with ethanol and hemolysis. West J Med 1985; 142:337-340.

Baud FJ, et al. Treatment of ethylene glycol poisoning with intravenous 4-methylpyrazole. N Engl J Med 1988; 319:97-100 (editorial 109-110).

Anderson TJ. Methanol poisoning: factors associated with neurologic complications. Can J Neurol Sci 1989: 16:432-435.

Suit PF, Estes ML. Methanol intoxication: clinical features and differential diagnosis. Cleveland Clinic J of Med. 1990; 57:464-471.

Aabakken L, et al. Osmolal and anion gaps in patients admitted to an emergency medical department. Hum Exp Tox 1994; 13:131-134.

Brent J, McMartin K, Phillips S, Burkhart KK et al. Fomepizole For The Treatment Of Ethylene Glycol Poisoning. N Engl J Med 1999;340:832-838.