Acid Base Disorders

ACOI 2017

Board Review

Case Studies

Disclosures

Nothing to declare

High Anion Gap Acidosis Case 1

40 yo gentleman presenting to ER with coma

labs : pH 7.14/ pCO_2 15; Na 138/ K 6.4/ Cl 100/ HCO_3 5; BS 100/ BUN 18/ S- OSM 340/ ETOH 0/ALB 4.0

funduscopic showed optic neuritis

How do you approach the differential of this acid base disorder ?

Case 1

1. Acidosis or alkalosis - ACIDOSIS
2. Metabolic or respiratory- METABOLIC
3. Compensation appropriate- YES
4. Anion gap – HIGH (138 – 105 =23)
5. Δ gap = Δ HCO3 - YES
6. Osmolar gap – YES (340 – 288 = 52)

Corrected anion gap = 2.5 X (4-albumin)

High Osmolar Gap Acidosis

when there is a high osmolar gap (>20) as well as a high anion gap the differential includes methanol, ethylene glycol, and propylene glycol intoxication

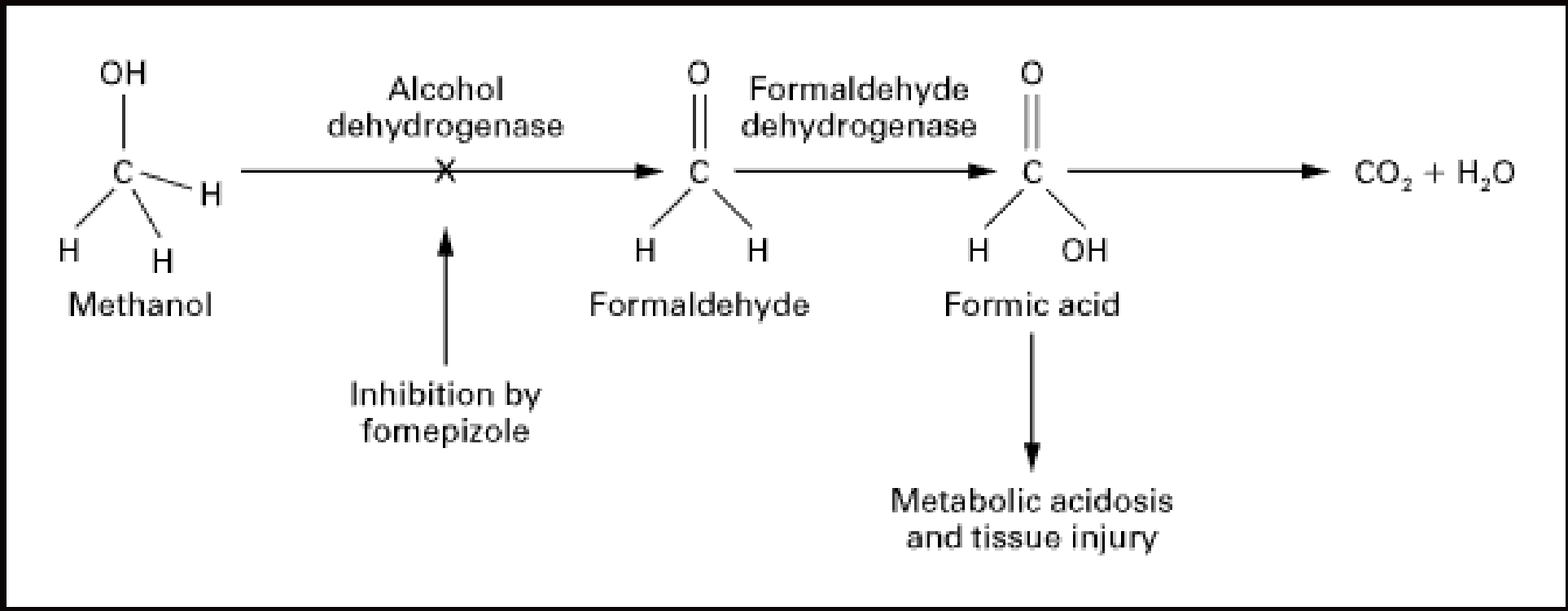
no other gapped acidosis will increase the osmolar gap to this extent

osmolar gap = s-osm (meas) - s-osm (calc)

ABNORMAL > 10 mosm, PATHOLOGIC > 20

High Osmolar Gap Acidosis

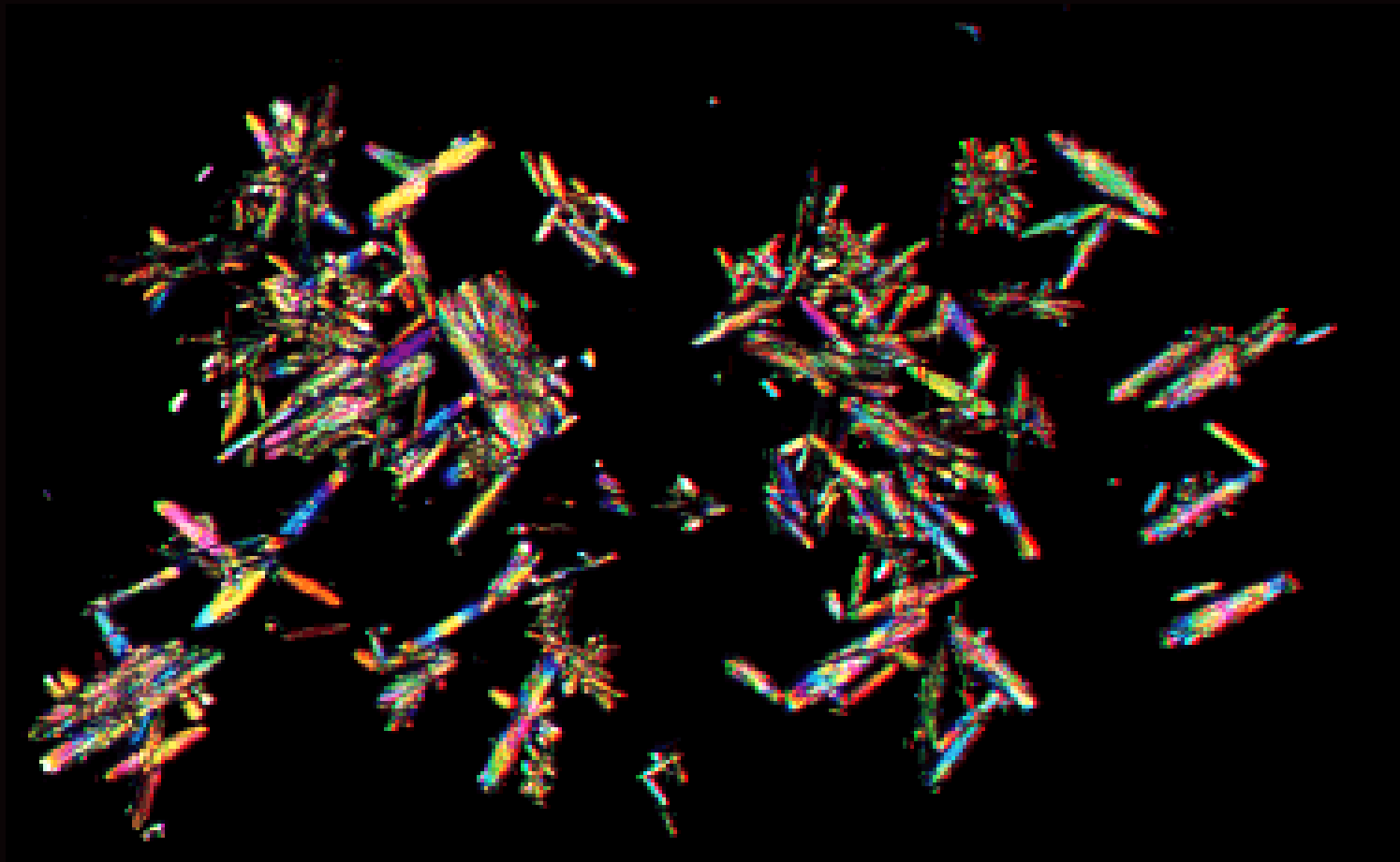
- methanol leads to formic acidosis with CNS and optic toxicity (lethal dose > 15 ml)
- ethylene glycol leads to glycolic and oxalic acidosis with renal and CNS toxicity with needle shaped crystals on UA (lethal dose 1-1.5 ml/kg)
- treatment of both is ETOH or fomepizole to block alcohol dehydrogenase and/or dialysis
- Propylene glycol usually occurs with lorazepam infusion (drug diluent)



Cost $ 3000 dollars/treatment

Major alcohol intoxications[a]

Disorder	Substance(s) Causing Toxicity	Clinical and Laboratory Abnormalities	Comments
Alcoholic (ethanol) ketoacidosis	β-hydroxybutyric acidAcetoacetic acid	Metabolic acidosis	May be most frequent alcohol-related disorder; mortality low relative to other alcohols; rapidly reversible with fluid administration; increase in SOsm inconsistent
Methanol intoxication	Formic acidLactic acidKetones	Metabolic acidosis, hyperosmolality, retinal damage with blindness, putaminal damage with neurologic dysfunction	Less frequent than ethylene glycol; hyperosmolality and high anion gap acidosis can be present alone or together; mortality can be high if not treated quickly
Ethylene glycol intoxication	Glycolic acidCalcium oxalate	Myocardial and cerebral damage and renal failure; metabolic acidosis, hyperosmolality, hypocalcemia	More frequent than methanol intoxication; important cause of intoxications in children; hyperosmolality and high anion gap acidosis can be present alone or together
Diethylene glycol intoxication	2-Hydroxyethoxyacetic acid	Neurological damage, renal failure, metabolic acidosis, hyperosmolality	Very high mortality possibly related to late recognition and treatment; most commonly results from ingestion in contaminated medications or commercial products; hyperosmolality may be less frequent than with other alcohols
Propylene glycol intoxication	Lactic acid	Metabolic acidosis, hyperosmolality	May be most frequent alcohol intoxication in ICU; minimal clinical abnormalities; stopping its administration is sufficient treatment in many cases
Isopropanol intoxication	Isopropanol	Coma, hypotension, hyperosmolality	Hyperosmolality without acidosis; positive nitroprusside reaction



Calcium oxalate monohydrate crystals Urine sediment viewed under polarized light showing coarse, needle-shaped calcium oxalate monohydrate crystals. These crystals have a similar appearance to hippurate crystals. Courtesy of W Merrill Hicks, MD.

High Anion gap without High Osmolar Gap

Uremia - gap 20, GFR < 15ml/min

Salicylates - severe respiratory alkalosis, drug levels should always be checked – lactic acidosis

Lactic acidosis - diagnosis of exclusion A, B and D

Pyroglutamic acidosis – critical illness, females and acetaminophen use. Urine 5-oxyproline

High Anion gap without High Osmolar Gap

Ketoacidosis – abnormal glucagon/insulin ratio

- **diabetic** - acetone positive, BS > 200
- **alcoholic** - during abstinence and BS < 200, acetone may be negative
- **starvation** - diagnosis made by history, acetone may be negative

beta hydroxybutyric acid is the major ketone body in all ketoacidosis

High Anion Gap Acidosis - Treatment

- Treatment of organic acidosis is controversial with physiological data on both sides
- Clinically there is no evidence of improved patient survival
- Therefore, treatment with bicarbonate is reserved for a pH < 7.1 with refractory hypotension or arrhythmia

High Anion Gap Acidosis - Summary

- The presence of a high anion gap as well as a high osmolar gap leads to the diagnosis of intoxication with ethylene glycol or methanol
- The treatment of both are the same (ETOH, fomepizole and dialysis)
- Optic neuritis is seen in methanol intoxication
- Propylene glycol occurs only in inpatients

High Anion Gap Acidosis

Recent reports

Pyroglutamic Acidosis – Acquired Form

- Pyroglutamic acid accumulates during times of glycine deficiency (critical illness, pregnancy and malnutrition) which will deplete glutathione
- Usually occurs in women (urine 5-oxyproline)
- Glutathione is also depleted by acetaminophen use
- Syndrome – unexplained high anion gap acidosis, use of acetaminophen and change in mental status in the setting of critical illness

Propylene Glycol Intoxication

- Propylene glycol (PG) is a solvent used in IV medications (lorazepam)
- Use of lorazepam infusions at > 0.1 mg/kg/hr may cause accumulation of PG leading to a high osmolar high anion gap acidosis (lactic acidosis)
- Treat with fomiperazole

Propafol Infusion Syndrome

- Occurs in critically ill patients
- Myocardial failure, rhabdomyolysis, metabolic acidosis hypertriglyceridemia and renal failure
- Anion gap may be elevated (?? lactic acidosis)
- Risk related to duration (> 48 h) and intensity of infusion
- Infusion > 4mg/kg/hr

Diethylene Glycol

- Substitute for glycerol by disreputable companies selling to developing nations
- Causes CNS and PNS symptoms
- Causes AKI
- Generation of 2-hydroxyethylacetate (HEAA)

Drug induced Lactic Acidosis

Linezolid – usually occurs with prolonged therapy (5-6 weeks)

Metformin – occurs in patients with contraindications given the drug (liver disease, > Stage 3 CKD, CHF, critical illness, peri-operative state, and IV contrast)

HAART HIV – chronic use of many drugs have been implicated (didanosine, stavudinw

Misc – mangosteen, clenbuteral

D-LACTIC ACIDOSIS

- Recent reports of gapped metabolic acidosis in patients with short bowel syndrome
- Occurs after ingesting a large CHO load
- Confusion, gapped metabolic acidosis and negative lactate levels
- Treatment – antibiotics and NPO

Case 2 - Hyperchloremic Metabolic Acidosis

an elderly man present with tachypnea, diarrhea and weakness

labs - pH 7.24/ pCO_2 24; Na 140/ K 6.7/ Cl 120/ HCO_3 10; urine pH 5.0/ U Na 40/ U K 20/ U Cl 50

How do you approach the differential of this acid base disorder?

Case 2

1. Acidosis or alkalosis - ACIDOSIS
2. Metabolic or respiratory- METABOLIC
3. Compensation appropriate - YES
4. Anion gap – NORMAL (10)
5. Δ gap = Δ HCO3 - YES
6. Osmolar gap - NONE

Urine Anion Gap

HCO3 is either resorbed (prox) or regenerated (distal)

To regenerate HCO3 - NH4 is formed distally

In an acidic urine Na+K+NH4 = Cl

NH4 can not be measured therefore

Cl > Na+K if NH4 is present NL DISTAL FX

If Cl < or = Na+K then distal urinary acidification is impaired (UAG abnormal)

Urine Anion Gap

the urine anion gap is useful in distinguishing disorders with normal ammonium excretion from those with abnormal excretion

Normal UAG – Proximal RTA or non renal acidosis (diarrhea etc.) (Cl > Na + K)

Abnormal UAG - CKD (lack of NH4 production), distal RTA Type I and IV or aldosterone deficiency) (Cl ≤ Na + K)

Hyperchloremic Metabolic Acidosis Normal Urine NH4 (Cl > Na + K)

this is due to HCO3 loss with normal distal tubular function

GI - loss of HCO3 due to diarrhea, urinary diversion or pancreatic fistulae

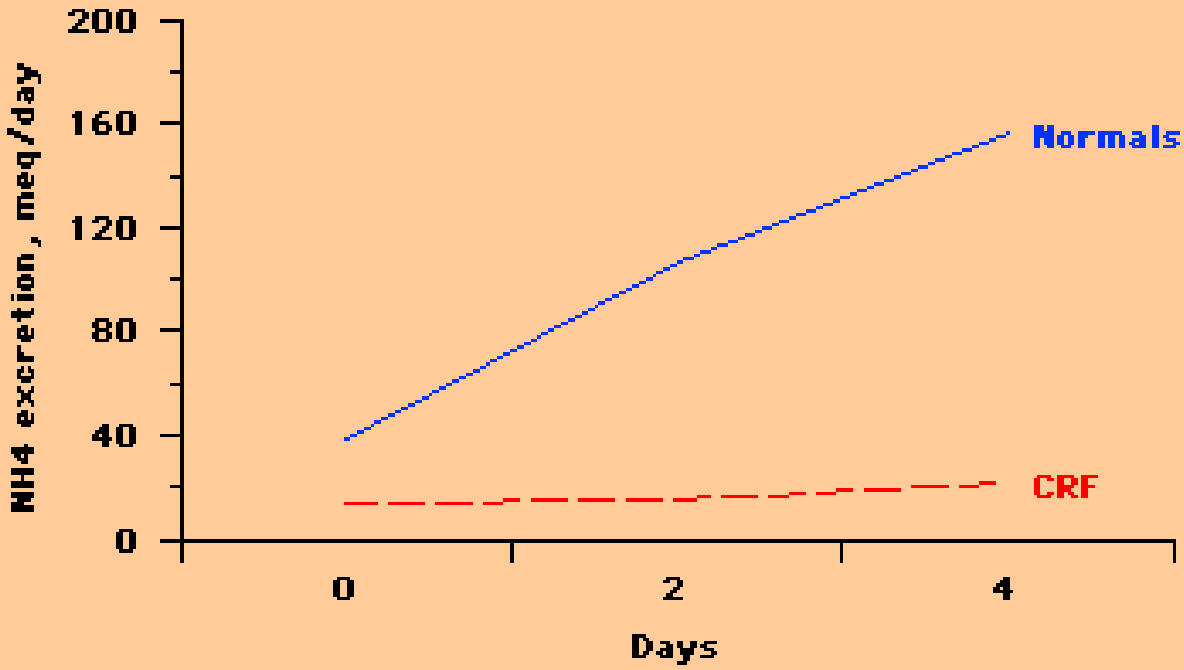
Renal - proximal RTA (type 2) leads to renal HCO3 loss with normal distal regeneration. May be associated with other proximal defects (Fanconi's), hypergammaglobulinemia, drugs (toluene, toperimate, zonisamide, tenofovir, azetazolamide) or multiple myeloma

Hyperchloremic Metabolic Acidosis Abnormal NH4

Classic Distal - a defect in the proton pump leads to a U pH >5.5 and acidosis (**Type 1**) (ampho B, HyperPTH, Sjogren's, medullary sponge kidney

Hyperkalemic Distal - a defect in the aldo sensitive collecting duct leads to acidosis and hyperkalemia with preserved renal acidification (**Type 4**) (obstruction , aldo resistance)

NH3 Defect - CKD leads to abnormal NH3 production with preserved urinary acidification (GFR < 30)



Impaired ammonium excretion in chronic renal failure. Urinary excretion of ammonium (NH4) in normals (solid line) and patients with chronic renal failure (dashed line) at baseline and after an acid load. The plasma bicarbonate concentration fell from 27 to 22 meq/L in normals and from 22 to 14 meq/L in CRF following the acid load. Ammonium excretion rose markedly in normal subjects, but was low at baseline and did not increase in the patients with CRF despite a greater degree of metabolic acidosis. (Data from Welbourne, T, Weber, M, Bank, N, J Clin Invest 1972; 51:1852.)

Defect	U pH	UAG	K (serum)	GFR
Proximal RTA (II)	< 5	Nl	Low	nl
Distal RTA (I)	> 5	Low	Low	Nl
Distal RTA (IV)	< 5	Low	High	Nl to low
CKD	< 5	Low	Nl to high	< 30

Hyperchloremic Metabolic Acidosis Summary

the patient had a hyperchloremic metabolic acidosis with an abnormal urine anion gap - no NH4 excretion despite acidosis

urinary acidification was preserved eliminating Type 1 RTA (U pH < 6.5)

hyperkalemia was consistent with a Type 4 RTA

Figure 4. Correlation between central venous and arterial blood gas values for pH

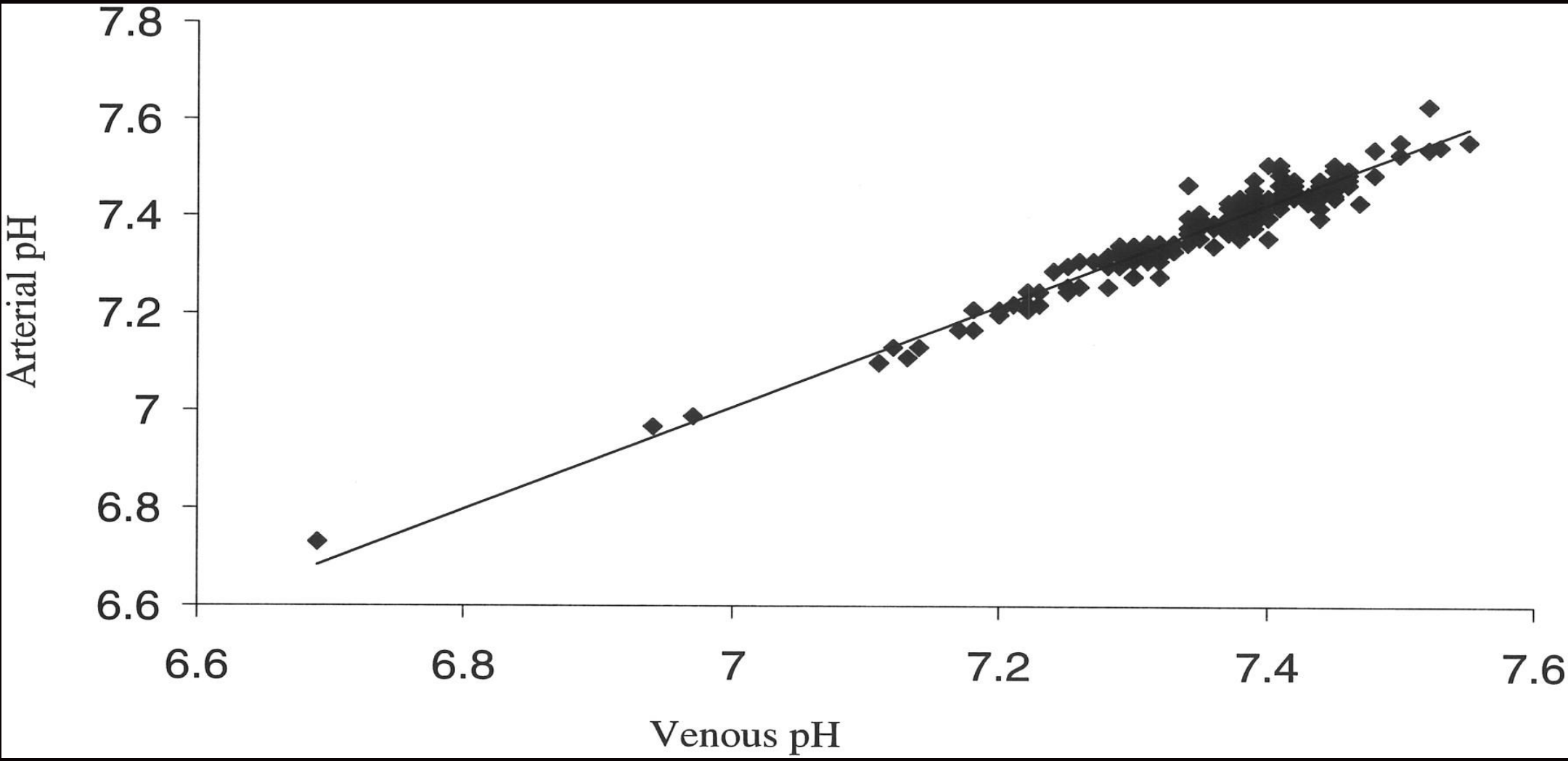


Figure 5. Correlation between central venous and arterial blood gas values for PCO2

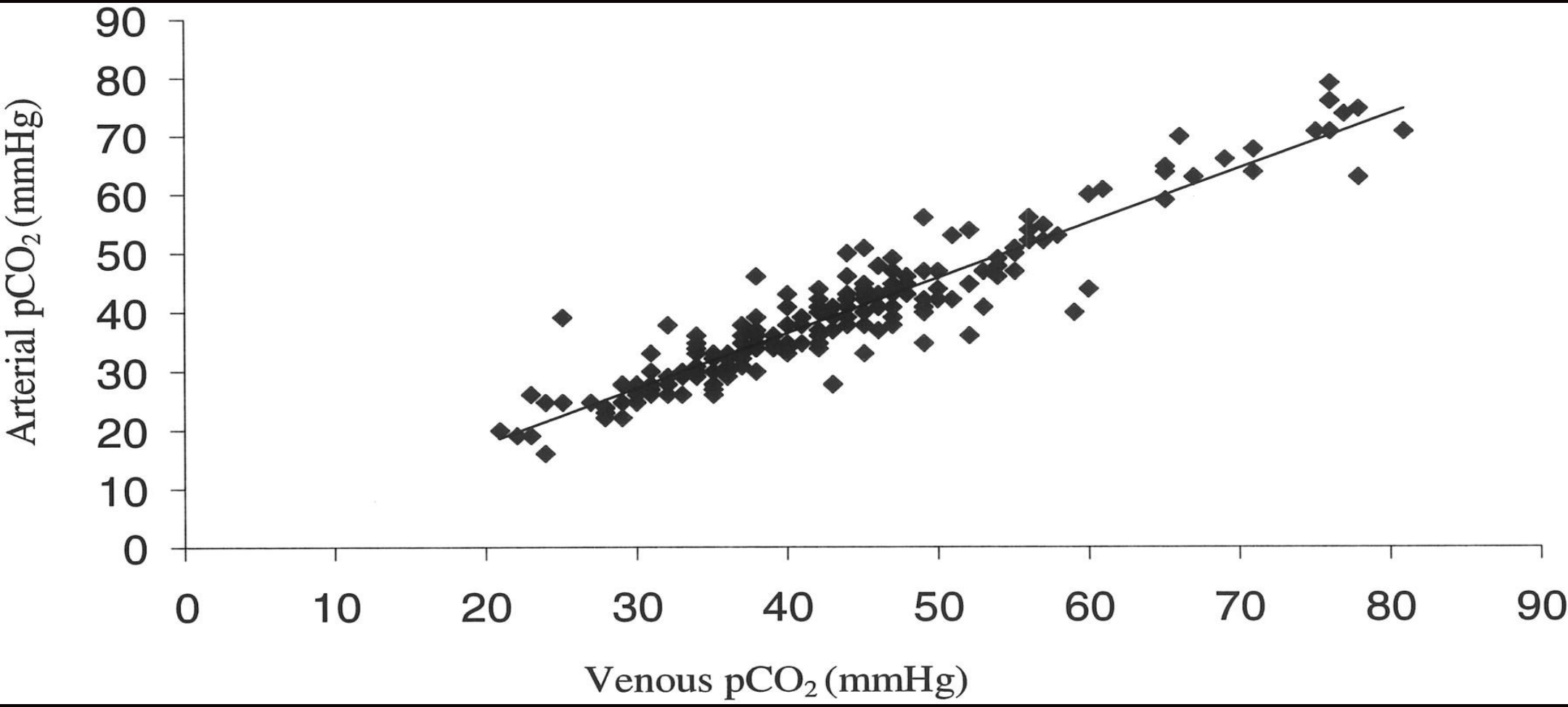
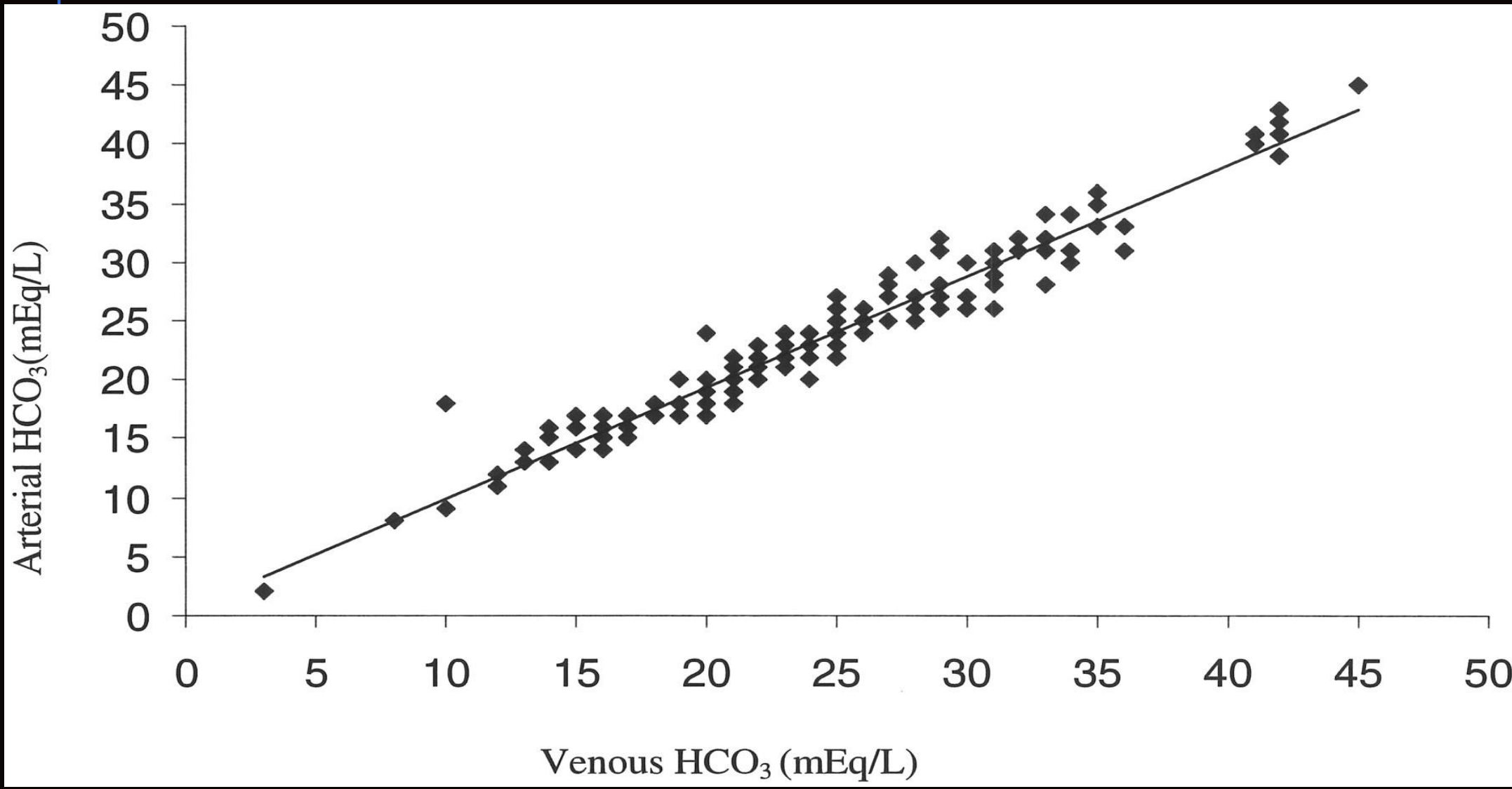


Figure 6. Correlation between central venous and arterial blood gas values for HCO3



Arterial and central venous blood gas values (*n* = 190)

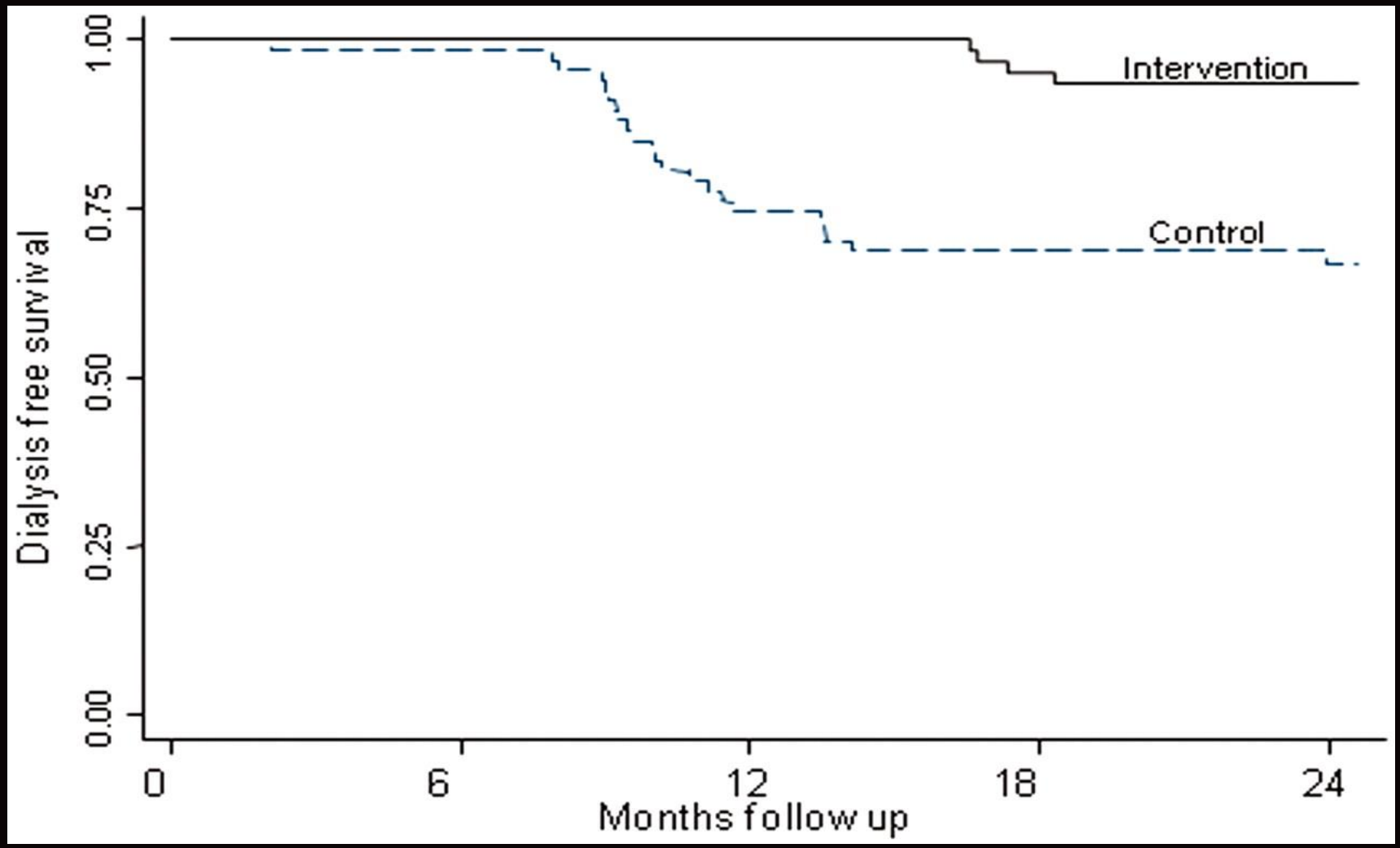
Parameter	Arterial	Venous	Difference
pH	7.37	7.34	.027
pCO2	38.4	42.3	-3.8
HCO3	22.4	23.2	-0.80

Venous Blood Gas

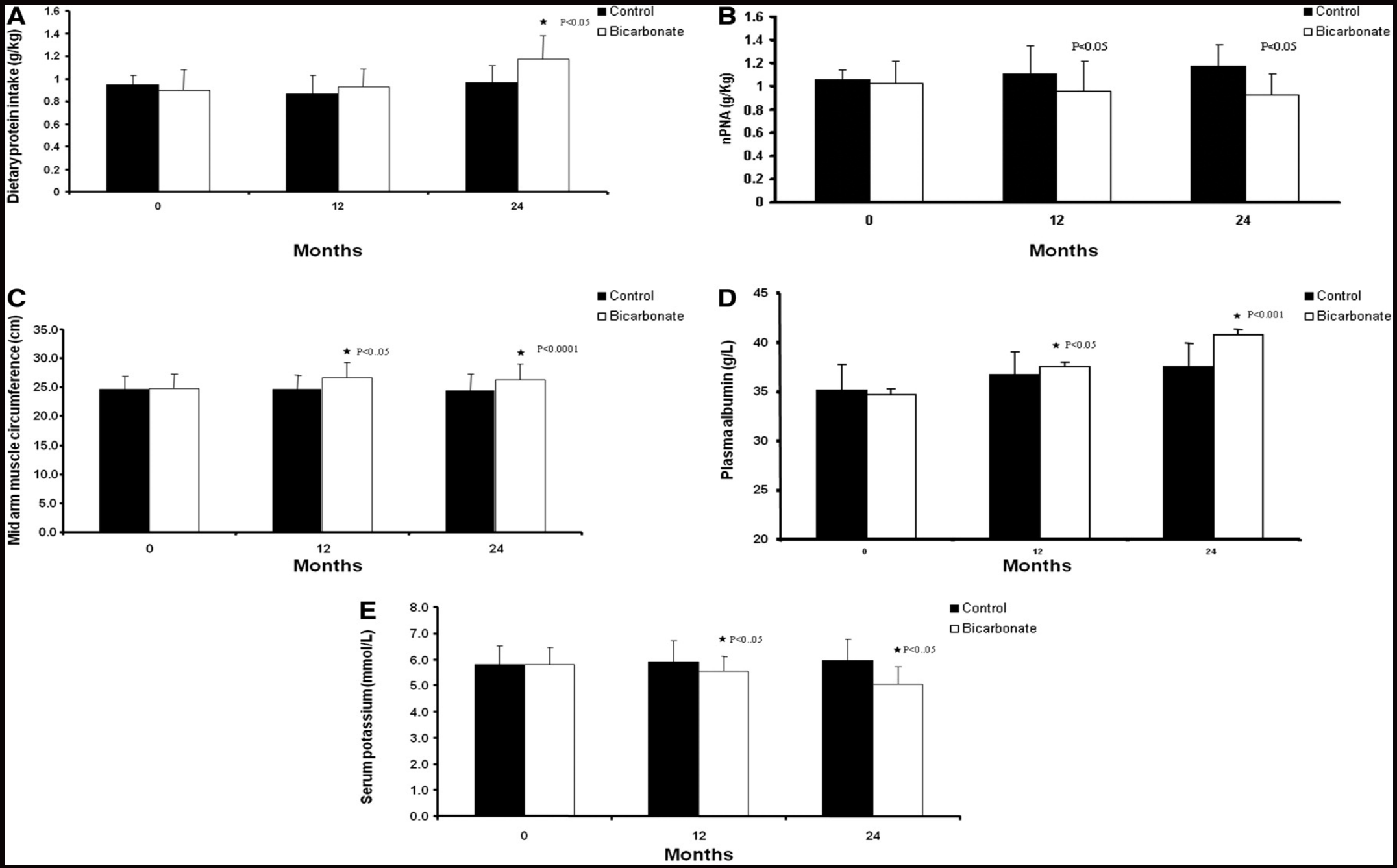
Results in same clinical outcomes as ABGs

Low CO widens the difference

Kaplan-Meier analysis to assess the probability of reaching ESRD for the two groups. Bicarbnate Supplementation Vs. Control



de Brito-Ashurst I et al. JASN 2009;20:2075-2084



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Metabolic Alkalosis

A normotensive ice skater presents with weakness

Labs : pH 7.54/ pCO_2 45; Na 140/ K 2.8/ Cl 95/ HCO_3 38; U Cl 50 U Na 70

Repeat U Cl < 20

How do you approach the differential of this acid base disorder?

Case 3

1. Acidosis or alkalosis - ALKALOSIS
2. Metabolic or respiratory - METABOLIC
3. Compensation appropriate – YES
4. Anion gap – NORMAL (7)
5. Δ gap = Δ HCO3 – YES
6. Osmolar gap - NONE

Metabolic Alkalosis

Generation - loss of HCl from kidneys or GI tract

Maintenance - because of prerenal state, hyperaldosteronism, and hypokalemia the body is unable to excrete HCO3

Cl responsive - when Cl is given it will shut off the maintenance phase and allow the kidney to excrete HCO3 by restoring volume and normalizing aldosterone production

Cl unresponsive - even when Cl is given it will not shut off aldosterone production

Cl Responsive Alkalosis

When NaCl and KCl are given they restore volume and replete K and Cl shutting off aldosterone production

This plus the correction of the prerenal state allow the kidneys to excrete excess HCO3

Treatment - administration of NaCl and KCl

Metabolic Alkalosis Cl Responsive

Diuretic alkalosis - U Cl < 20 after diuretics are stopped

Chloridarrhea - congenital or villous adenoma

Posthypercapnic - usually with chronic respiratory acidosis

Gastric alkalosis - hypokalemia due to renal K wasting

Milk Alkali – hypercalcemia, AKI, and alkalosis

Cystic Fibrosis – skin Cl loss

Milk Alkali Syndrome

- Historically due antacids and large quantities of milk to treat PUD
- Modern –large amount of Ca carbonate and Vit D leading to alkalosis, hypercalcemia and AKI
- Calcium acts like a loop diuretic

Cl Unresponsive Alkalosis

This group of disorders is all have elevated aldosterone or defects in kidney

However, this is not volume (NaCl) responsive but rather volume independent

Administration of NaCl will not inhibit aldo nor will it correct the prerenal state

Treatment - diamox, HCl, spironolactone

Metabolic Alkalosis Cl Unresponsive

Primary aldo excess - pharmacologic or primary aldosteronism

Secondary aldo excess - CHF, cirrhosis, RAS, ?Barter's, hypomagnesemia

Primary renal Cl loss - Barter's syndrome (furosemide pump), Gitelman's syndrome (thiazide pump), Liddle's syndrome and diuretics

Metabolic Alkalosis - Summary

- Patient had a metabolic alkalosis with high urine Cl initially due to diuretic abuse
- Stopping the diuretic stopped the loss of urinary Cl
- She had an eating disorder – Diuretic abuse

Metabolic Alkalosis Update

- Permissive hypercapneic ventilation – current recommendations for ventilation in the setting of acute lung injury. Use of HCO_3 for pH < 7.2. This may lead to posthypercapneic alkalosis
- Performance enhancement – use of $NaHCO_3$ pre exercise will enhance performance

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