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PATTERN OF BICARBONATE IN PATIENTS ON MAINTENANCE HEMODIALYSIS

Anchana Raj[1]*, E. Sam Jeevakumar[2], Anusree VS[3], Gokul Krishna[3], Padmesh PR[3]

[1]Doctor of Pharmacy Student, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram.

[2]Head of Department, Department of Pharmacy Practice, Sree Krishna College of Pharmacy and Research Center, Thiruvananthapuram.

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***Corresponding Author**
Anchana Raj
Doctor of Pharmacy Student, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram.

ABSTRACT

Chronic metabolic acidosis is common in dialysis patients. Acid base balance in chronic kidney disease patients with metabolic acidosis can the corrected by supplementing bicarbonate via the dialysate. Serum bicarbonate level in dialysis patients is determined by several factors that includes dietary protein intake, nutritional status and dialysis prescription etc… Metabolic acidosis occurs when there is accumulation of plasma anions in excess of cations reduces plasma pH concentration. Replacement of sodium bicarbonate to patients can be done when sodium bicarbonate loss due to diarrhea or renal proximal tubular acidosis.[1] Serum bicarbonate level in individuals with normal renal function is 24-28mEq/l and the acid base values with pH of 7.38–7.42 and pCO2 is 38–42 mmHg. In patients on maintenance hemodialysis (MHD), the bicarbonate level is highest for post dialysis and lowest for predialysis. The average predialysis serum bicarbonate ranges from 20 to 24 mEq/l at the beginning of the week with the dialysate bicarbonate set at 35 mEq/L.[2] The current kidney dialysis outcomes quality initiative guidelines recommend predialysis serum bicarbonate >22mEq/l. Normally functioning kidneys maintain acid base homeostasis by excreting hydrogen ions (as ammonium) and regenerating bicarbonate. In End stage renal disease (ESRD), alkali supplementation through dialysis helps to prevent accumulation of acid and maintain the pH in the physiological range. Metabolic acidosis is a common consequence for the progressive loss of kidney function. The progressive chronic kidney disease (CKD) and poor survival of these patients is because of low serum bicarbonate level.[3]

KEYWORDS: Dalysate bicarbonate, Hemodialysis, Metabolic acidosis.

INTRODUCTION

Kidneys are the major organ responsible for maintaining normal acid-base homeostasis in human body. Conditions with impaired kidney function, including chronic kidney disease(CKD) are associated with the development of metabolic acidosis which may cause progressive loss of kidney function. Metabolic acidosis is a common consequence of CKD patients and correction of the same is the treatment strategy for the patients care who is having chronic kidney disease. Its main causes are reduced tubular bicarbonate re-absorption, impaired ammonia excretion and insufficient production of renal bicarbonate in accordance with the amount of acid secreted by the body and ingested with food. Metabolic acidosis develops when GFR is decreased to 20-30 ml/min.[4]

Persistent metabolic acidosis may cause certain adverse effects in patients with CKD including protein energy wasting, inflammation, bone disease and disturbance in endocrine function. Chronic kidney disease have results in the irreversible decrease in glomerular filtration rate(GFR) and the decrease in blood Ph is one of the major complications of this disorder. Chronic metabolic acidosis increases the catabolism of protein and thus may results in the development of some inflammatory process like malnutrition-inflammation atherosclerosis (MIA) syndrome. Metabolic acidosis may develop the risk of osteoporosis in CKD patients. Metabolic acidosis may also contribute to beta 2 micro-globulin amyloidosis by increasing the concentration of beta 2 micro globulin. In patients with hyper tri-glyceridemia, the triglycerides concentration can be reduced by administration of serum bicarbonate. In CKD patients, metabolic acidosis impairs the conversion of thyroxine to triiodothyronine which results in serum triiodothyronine concentration.[5]

Hemodialysis (HD) and peritoneal dialysis (PD) are the two forms of renal replacement therapy (RRT). Hemodialysis is the most important method for the correction of metabolic acidosis in ESRD patients. Both methods use a base in the dialysate to correct metabolic acidosis by replenishing serum bicarbonate. KDOQI (Kidney disease quality of life) guidelines recommend serum bicarbonate levels ≥22mEq/l in patients on dialysis. Concentration of bicarbonate in venous blood should be measured in all CKD patients to check for metabolic acidosis. Metabolic acidosis is diagnosed when the venous bicarbonate concentration is <22 mmol/l. ESRD patients on hemodialysis are affected by predialysis acidosis.[2]

DIALYSATE BUFFER

Dialysate buffers are the buffers which are found in the form of bicarbonate or certain precursors like lactate, citrate or acetate buffers. The main dialysate buffer used for hemodialysis is sodium bicarbonate. Acetate is not a buffer as it is metabolized to bicarbonate. Acetate is cheaper than producing bicarbonate based dialysate. Use of acetate as the main buffer in high efficiency hemodialysis may results in some complications such as arterial hypotension, high incidence of nausea, vomiting and headache, worsened metabolic acidemia, and hypoxemia in some individuals. The cause of such morbidity is due to accumulation of acetate and its toxicity results in stimulation of interleukin production from monocytes, slow metabolism of acetate to bicarbonate, and bicarbonate removal from the blood space due to acute metabolic acidemia. Final dialysate PH can be maintained using Acid concentrate contains acetic acid, citric acid or sodium diacetate. Consumption of organic acids and bicarbonate from acid concentrate and bicarbonate concentration leading to gain of sodium acetate in the final dialysate solution. Acetate, after entry into the bloodstream, will be metabolized to bicarbonate via the citric acid cycle.[6]

HEMODIALYSIS

Hemodialysis is the dialysis which was performed for 4 hours as twice or thrice weekly. Reverse osmosis treated water were used with individual rationing dialysis machine. Volumetric ultra filtration control was also accessible in all the machines. Polysulfone hollow fiber dialyzers having a co-efficient with mass transfer area of 500-600 ml/min and ultrafiltration co-efficient 5.5 ml/mmHg were used. Dialysate flow rate was 500 ml/min and blood flow rates were choose as according to the patient needs. Dialyzer can be reuse by using automated methods. The adequancy of dialysis were determined using the single pool Kt/V.[7] Kt/V is a number which is used to quantify the adequancy of hemodialysis and peritoneal dialysis. K is dialysis clearance of urea, t is dialysis time, and V is the volume of distribution of urea which is approximately equal to the patients total body water.[8]

When bicarbonate correction is done rapidly and increases in the blood pH results in rapid shift of potassium ions from the compartment of which could lead to a sudden decrease in potassium levels (hypokalemia) with certain cardiovascular consequences such as cardiac arrhythmia (deviation from normal rhythm of heart) or cardiac arrest. Extracellular fluids to intracellular fluids with a rapid shift of potassium from the extracellular to the intracellular compartment, which could lead to a sudden hypokalemic status with cardiovascular

consequences such as arrhythmias, left ventricular hypertrophy or cardiac arrest due to decline in kidney function. In a thrice weekly dialysis schedule on using high bicarbonate buffer inadequately could be responsible for increased mortality during post dialysis.[9]

Serum bicarbonate levels may get increased in patients receiving hemodialysis. Bicarbonate is the main source of dialysate buffer for the correction of metabolic acidosis in chronic kidney failure patients. High efficacy membrane and higher blood flows have been increase the delivery of bicarbonate. The associated level of serum bicarbonate was found to be 20-22.5mEq/l.[1] The National Kidney Foundation Kidney Disease Outcomes Quality Initiative(KDOQI) recommended at a level of serum bicarbonate of ≥22 mEq/l during predialysis.[2] Patients whose bicarbonate level is high during predialysis may had the worst markers of dietary protein intake, nutritional status such as both albumin and prealbumin or markers of body composition. Serum bicarbonate levels is lower than the 20–22 mmol/l in predialysis recommending that a bicarbonate based dialysate is not the correct solution for hemodialysis patients. Using a thrice-weekly dialysis schedule with adequate protein intake, the current bicarbonate load was found to be insufficient to compensate for a 2 days acid load.

Mild metabolic alkalosis may cause frequent hypotensive episodes and high bicarbonate concentrations of dialysate greater than 38mmol/l is associated with high frequency of hypotensive symptoms. When the dialysate bicarbonate concentration exceeds 38mmol/l, cardiac index of the patient is decreased.[10]

Bicarbonate Levels In Pre and Post Dialysis and Mortality In Patients Receiving Hemodialysis

The dialysate flow rate was 500ml/min for all individuals and the dialysis duration schedule was for 4 hours. Bicarbonate was the buffer mainly used for dialysis and it's level measured in the dialysate bath was found to be 34mEq/l. If the urine output of patients is >100 ml/day shows significant residual renal function. Most of the kidney failure patients are anemic due to lack of production of erythropoietin (It is a hormone which is secreted by kidney). The patients who were anemic being treated with erythropoietin and iron which stimulates the production and maintenance of red blood cells in response to cellular hypoxia.

The mean predialysis serum bicarbonate level was 19.95 mEq/l and the mean postdialysis serum bicarbonate level was 23.45mEq/l. Patients who is on hemodialysis had acidemia as

well as metabolic acidosis with pH <7.35 and serum bicarbonate level of <22mEq/l. Most of the patients with chronic kidney disease have wasting of muscles progressively due to abnormalities in the vitamins D metabolism or in serum calcium concentration, acidosis, prolonged inactivity and malnutrition. Metabolic acidosis is the major causes of malnutrition before initiation of dialysis. The correction of metabolic acidosis improve serum albumin levels in hemodialysis patients. The mean blood flow rate was 219ml/min in patients who had predialysis bicarbonate levels <22mEq/l during hemodialysis.[11]

Mortality is a major factor elevated in patients on chronic kidney disease (CKD) on hemodialysis. CKD patients on stage 4 and 5 has been shown a rate of three to six fold higher mortality risk than patients with glomerular filtration rate >60 ml/min/1.73m2. Both low and high serum bicarbonate levels have been associated with high risk of death in patients receiving hemodialysis. The mortality associated with low serum bicarbonate is after comorbidity, inflammation and after adjustment for markers of nutrition where as for mortality associated with high bicarbonate level is markedly attenuated. This says that high serum bicarbonate levels during predialysis is a indicator for patients with ongoing inflammation, poor nutrition and a high rate of morbidity. Hence serum bicarbonate, protein catabolic rate, serum albumin and serum phosphate levels are linked inversely in patients with end stage renal disease (ESRD). Serum bicarbonate level is approximately 1mEq/l lower after the long interdialytic interval.[12]

Medication like revlamer hydrochloride reduces serum bicarbonate level during hemodialysis with the serum dialystae bicarbonate level and inversely relates to the predialysis level. The death occur in CkD patients is mainly due to sepsis, dicontinuation of hemodialysis, advanced malignancies, polytrauma following accident, intracranial bleed and ischemic heart disease. Increased dialysis dose provide a survival advantage to the patients along with increased frequency of dialysis and serum albumin level. The survival outcomes among hemodialysis patients can be increased by minimizing infectious complications, preventing cardiovascular events and by improving nutrition. Moreover pneumonia was also the most common causes of deaths related to certain infections followed by cellulitis, catheter related infections, pyogenic discitis and disseminated varicella. Among all these causes, sepsis is the major event mainly occur in CKD patients. The most common causes of sepsis are due to vascular access related infections such as abscess of the arterio venous fistula(AVF), catheter related bacteremia and also urinary tract infection.[7]

Acid Base Therapy in ESRD

Kidneys remove acid from the body through urine and maintain bicarbonate level in the blood appropriately. But in CKD patients, kidneys can't remove enough acids which can lead to a condition called metabolic acidosis. Patients with chronic kidney disease (CKD) and end-stage kidney failure (ESRD) cause metabolic derangements such as acid base and electrolyte imbalances such as metabolic acidosis, hyperkalemia and alterations in sodium and water balance.[2] ESRD patients on hemodialysis (HD) are affected by varying degrees of pre-dialysis acidosis, post-dialysis alkalosis, dyskalemia and large solute and shifting of fluids.

Acid-base and electrolyte imbalances are commonly occur in chronic kidney disease (CKD) and end-stage kidney failure (ESRD) patients. The changes become more crucial as CKD progresses to ESRD, leading to morbidity and mortality. Bicarbonate is the major buffer used for correcting acid base balance in patients on hemodialysis. The different side effects associated with hemodialysis treatment are nausea, vomiting, headache, muscle cramps, dry skin, itchy skin and hemodyanamic instability.

The recommended level of serum bicarbonate level was ≥ 22mEq/l in patients with chronic kidney disease (CKD) and the predialysis serum bicarbonate level was at 20-22mEq/l. The predialysis level of serum bicarbonate in patient receiving hemodialysis makes retention of acid during interdialytic interval. The average level of serum bicarbonate can be the difference between both pre and post dialysis bicarbonate level. Predialysis Ph were the major marker to define a patients acid bade status. Predialysis pH should be changed before changing the concentration of dialysate bicarbonate or oral alkali in patients with congestive heart failure(CHF), chronic obstructive pulmonary disease (COPD) and cirrhosis.[13]

METABOLIC ACIDOSIS IN CKD

Metabolic acidosis is defined as a reduction in serum bicarbonate concentration with a reduction in blood pH in kidney failure patients. It occur due to inability of the kidney to synthesize ammonia [ammoniagenesis] and excrete hydrogen ions (H+) ions. The tubular secretion of ammonia by kidney is stimulated by intracellular acidosis. Metabolic acidosis leads to decreased metabolism on protein, muscle, bone with negative nitrogen balance, attenuated albumin synthesis and increased protein degradation leading to weakness of muscles, loss of body mass and protein energy malnutrition. It can also affect the bone due to bicarbonate (buffer) effect for excess acid in the kidney. This results in abnormal vitamin D

metabolism may causes osteomalasia and renal osteodytrophy in chronic kidney failure patients.[14]

Metabolic acidosis is the major consequences among CKD patients. The major mechanism involved in development of metabolic acidosis is due to the reduced reabsorption of the filtered bicarbonate associated with impaired synthesis of sufficient bicarbonate. The mortality rate is increased in those patients are due to their bicarbonate concentration in blood falls below 23mmol/l. This indicates that the target concentration of bicarbonate in blood of CKD patients should be above 22-23mmol/l. The severity of metabolic acidosis in CKD patients progressively rises when glomerular filtration rate (GFR) falls below 40ml/min/1.73 m2. Serum bicarbonate level decreases as age progresses, that is mainly after 60 years. Low bicarbonate levels are common in patients with low GFR rate. The patients with stage 4 and 5 of CKD have a serum bicarbonate level of 22 mmol/l. Death is increased as bicarbonate level is <22mmol/l.

Metabolic acidosis can be corrected by supplementing oral bicarbonate for CKD patients and for dialysis patients by increasing the concentration of bicarbonate in dialysis solution.[15]

CONSEQUENCES OF METABOLIC ACIDOSIS

a. Exacerbation of bone disease

Metabolic acidosis can be a major factor for the exacerbation of bone disease in both adults and children (cause impair growth in children) with or without CKD. In kidney failure patients, parathyroid hormones (PTH) levels are increased and have deficiency of vitamin D. This is because of metabolic acidosis can stimulate parathyroid hromone synthesis and reduce vitamin D levels. Increase in parathyroid hormone can cause osteoporosis in CKD patients. Metabolic acidosis also decrease the cellular response to parathyroid hormone (PTH). The progression of bone disease on CKD patients are common due to decrease in parathyroid hormone levels and vitamin D levels.[16] Prolonged metabolic acidosis can stimulate osteoclast related bone resorption and inhibit osteoblast related bone formation. In hemodialysis patients, PTH levels are increased in patients with higher serum chloride concentration during hemodialysis.

PTH levels in CKD patients can be decreased by dialysate base concentration. This can also able to reduce bone resorption and improve bone formation. PTH levels can also be suppressed by correcting metabolic acidosis.[17]

b. Increased muscle wasting

Skeletal muscle wasting is also a major consequence occur in CKD patients characterized by loss of muscle mass, strength and function. It is occur not only due to nutritional deprivation but also due to metabolic acidosis.Metabolic acidosis lowers the intracellular pH in muscle to trigger muscle protein catabolism. The loss of lean body mass results from an increase in the rate of muscle protein degradation.[16]

c. Reduced albumin synthesis

Hypoalbuminemia is the major indicator of protein energy wasting in dialysis patients may increase morbidity and mortality. Hypoalbuminemia is associated with recurrent cardiac failure in hemodialysis patients. Increased breakdown of proteins, increased amino acid concentration and reduced protein synthesis are the contributing factors for reduced albumin concentration with metabolic acidosis.[16]

Cardiovascular Effects of Metabolic Acidosis

Cardiovascular disease is the major cause of mortality in patients with CKD. Inflammatory conditions like metabolic acidosis plays a major role in the progression of atherosclerotic heart disease. So it is evident that metabolic acidosis could be related to increased severity of cardiovascular disease often associated with attenuated catecholamine efficacy, myocardial depression and cardiac arrhythmia.

Cardiac output and cardiac contractility of heart is decreased when the PH falls below 7.1. The impairment in the cardiac output seems to be PH dependent when PH is reduced from 7.4 to 7.2.[17] Metabolic acidosis could also reduce cardiac contractility by changing intercellular calcium disposition. Hence patients with diabetic ketoacidosis were not associated with depressed cardiac function when PH decreased to 6.8.

Metabolic acidosis may affect endothelial cells and vascular smooth muscle cells. Metabolic acidosis can alter calcium disposition intracellular and reduces the adreno receptors on the cell surface. It can relax vascular smooth muscles by opening the ATP-mediated potassium channels. Metabolic acidosis can produce a direct vasodilator effect by up regulate the nitric oxide synthase in the endothelial and vascular smooth muscle cells.[18]

Cardiac arrhythmias is mainly occur in CKD patients due to metabolic acidosis. The changes or decrease in the pH results changes in the rhythm of heart. This may result in the abnormal

depolarization and repolarization in the purkinje fibres of heart and depolarization of ventricular fibres. Therefore, ventricular arrhythmia can lead to sudden cardiac death.[19]

CORRECTION OF METABOLIC ACIDOSIS WITH BICARBONATE THERAPY

Alkali therapy

Alkali therapy has been the major treatment to reduce the progression of CKD in patients with reduced GFR not in dialysis treatment. Stage 3 and stage 4 CKD patients kidney function have been preserved by supplementing alkali which increases the bicarbonate levels to 25-26 mEq/l.[20] Sodium bicarbonate is the most frequently used buffer. It is mainly used to prevent the metabolic acidemia. The plasma bicarbonate therapy must be increased to 8mmol/L for effective bicarbonate therapy.[21]

Diet

Increasing intake of fruit and vegetable may decrease accumulation of acid in the body in the body. The reason is fruits and vegetables can increase alkali production where as foods such as cheese, cereals, eggs and meats make the acid in the body.[22]

COMPLICATIONS OF BICARBONATE THERAPY

Bicarbonate therapy may have some compilations like hypernatremia and hyperosmolality. However, these adverse effects can be prevent by addition of sodium chloride and 5% dextrose. Overload of extracellular fluid volume is another consequence of bicarbonate therapy and risk is somewhat higher in patients with congestive heart failure and renal failure patients. Extracellular fluid volume can be prevented by furosemide is a loop diuretic. If the patient condition is worst, hemodialysis may be needed.[23]

CONCLUSION

Metabolic acidosis is a common acid-base disorder. Serum bicarbonate levels is increased in CKD patients due to poor protein intake and poor appetite. So Serum bicarbonate should be checked periodically in patients on maintenance hemodialysis with metabolic acidosis as it may increase cardiovascular risk.[24] Sodium bicarbonate administration usually a necessitate therapeutic intervention to corrects the acidosis in order to achieve a serum bicarbonate level of at least 22 mEq/l and it also maintain the PH in ESRD patients. So Serum bicarbonate level <24mEq/l should be corrected in CKD or ESRD patients on dialysis as low serum bicarbonate level may results in poor survival. Hence serum bicarbonate level is lower before dialysis and higher after dialysis.[25]

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