

STUDY OF ACID-BASE BALANCE IN PATIENTS
WITH HEPATO-CELLULAR FAILURE

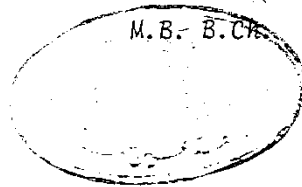
THESIS

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CONTENTS

	Page
I - Introduction & aim of the work	1
II - Review of the literature	3
- Acid-base Homeostasis	3
- Acid-base disorders	17
- Acid-base balance & electrolyte abnormalities in hepato-cellular failure	40
- Parameters of acid-base balance	49
III - Material and methods	56
IV - Results	61
V - Discussion	78
VI - Summary & conclusion	86
VII - References	89
VIII - Arabic summary	106

INTRODUCTION
and
AIM OF THE WORK

INTRODUCTION & AIM OF THE WORK

Hepato-cellular failure can complicate almost all forms of liver diseases such as hepatitis or cirrhosis which are common in our country.

Disturbance in acid-base balance may be present in patients with hepatocellular failure. They may have respiratory alkalosis due to stimulation of respiratory center, metabolic alkalosis due to hypokalemia (Sherlock, S., 1981) or metabolic acidosis due to accumulation of lactate, pyruvate and other organic acids. Also mixed respiratory and metabolic alkalosis can be present. (Zeive, L. 1982).

Recently, the liver is proved to have an essential role in acid-base homeostasis (Häussinger, D., 1985).

Alkalosis increases ammonia toxicity and so might exacerbate the neurological state in patients with hepato-cellular failure, because the transfer of ionized ammonia across the cell membranes and hence into the brain increases in the presence of extracellular

alkalosis (Sherlock, S., 1981).

The aim of this study is to evaluate the acid-base balance in patients with hepato-cellular failure which can help in the prediction of the prognosis and in the management of these patients.

REVIEW

CHAPTER I

ACID-BASE HOMEOSTASIS

INTRODUCTION :

Acid-base homeostasis in man is accomplished by the maintenance of systemic arterial pH within a narrow range despite acid and alkaline loads originating from the daily intake and degradation of foods.

As illustrated by Henderson-Hasselbalch equation,

$$\text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{\text{Pco}_2}$$

The arterial pH is determined by the level of bicarbonate and dissolved carbon dioxide, or the metabolic and respiratory components of acid-base balance respectively.

In normal individuals, arterial pH is maintained between 7.35 to 7.45. This impressive homeostatic process is the result of protection of body pH by many lines of defense (Thomas, D. 1983) :

- 1- The body buffers (extracellular and intracellular) which provide chemical buffering of acid or alkali entering the plasma.

- 2- Pulmonary regulation of P_{CO_2} , a process which allows carbonic acid (H_2CO_3) to be eliminated by the lung as CO_2 .
- 3- Renal reabsorption and excretion of bicarbonate and excretion of acids (phosphoric acid, sulfuric acid and ammonium).
- 4- The liver which shares in pH homeostasis via urea and intercellular glutamine cycles (Häussinger, D. et al 1985).

These regulatory mechanisms cooperate to dispose of the normal daily load of CO_2 and non volatile acid as well as the occasional addition of alkali to extracellular fluid. The important concept is that the final pH, or H^+ concentration is determined by the ratio of HCO_3^- and P_{CO_2} not by the absolute amount of either (Melvin, E., 1983).

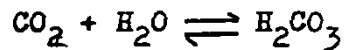
Body Buffer Systems :

Whether acid is added as CO_2 or as a metabolic acid the addition of appreciable amounts of protons to body water would result in significant changes in pH if there were not significant amount of buffers available. A buffer is a substance that has ability to bind or release H^+ in solution, thus keeping the pH of the solution relatively constant despite the addition of considerable quantities of acid or base.

buffers can be divided into three major components :
bicarbonate / carbonic acid, proteins, ~~phosphate and~~
buffering by ionic shifts (Roos, A., 1981).

Bicarbonate, Carbonic Acid & Carbon Dioxide :

It is one of the most effective buffers because H_2CO_3 level in plasma is in equilibrium with dissolved CO_2 and the amount of dissolved CO_2 is controlled by respiration. In addition, the plasma concentration of HCO_3^- is regulated by the kidney. The reaction :



is catalyzed by the carbonic anhydrase and it is one of the fastest reaction in metabolism (Genong, W. F., 1983).

The level of carbonic acid is the function of the partial pressure of CO_2 (P_{CO_2}). Changes in P_{CO_2} will change carbonic acid concentration. The relationship between P_{CO_2} and H_2CO_3 in body fluids is such that :

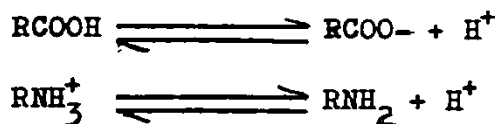
$$H_2CO_3 = 0.03 \times P_{CO_2} \quad (\text{ in mmHg }).$$

The equilibrium between CO_2 and H_2CO_3 is important

because CO_2 is highly permeable throughout the body and no significant cellular barriers to CO_2 are known to exist. Thus, change in Pco_2 induced by respiratory variations are reflected simultaneously by changes in the intracellular systems (Moren, T. 1967).

Proteins Buffers :

Plasma proteins are effective buffers because both their free carboxyl and amino groups dissociate :



Another important protein buffer is provided by the dissociation of imidazole groups of histidine residues of hemoglobin in blood. It has 6 times the buffering capacity of the plasma proteins. In addition, the action of hemoglobin is unique because the imidazole groups of deoxygenated hemoglobin dissociate less than those of oxyhemoglobin, making Hb a weaker acid and therefore a better buffer than HbO_2 (Genong, W. F. 1983).

Phosphates Buffers :



The phosphate pool is comprised of intracellular and extracellular phosphate, and is regulated by vitamin D. and parathyroid hormone acting on bone, kidney and gut. The phosphate pool includes serum inorganic phosphate (3.5 to 5.0 mg / dl), intracellular phosphate, and calcium phosphate in bone. While the middle pK of phosphate (6.8) is ideal for buffering in the physiologic range, its low concentration limits its importance as a buffer in the extracellular fluid, but organophosphorus compounds and phosphate are very important as intracellular buffers (Sutton, R., 1981).

Buffering by Ionic Shifts :

The intracellular and extracellular compartments are linked by several systems. Two major ion exchange systems are important. The first of these is the proton-cations (Na^+ or K^+) exchanger which allows an excess or deficit of protons in either compartment.

to be partially transferred to the other compartment for buffering there in. The chloride-bicarbonate exchange is the other major ion-exchange pathway used in buffering (Melvin, E. 1983).

Renal & Respiratory Response :

The kidney is responsible for recovery of bicarbonate and excretion of acids with generation of new bicarbonate. This generation occurs by formation of protons and bicarbonate from water and carbon dioxide in reactions catalyzed by carbonic anhydrase in the distal tubules.

The kidneys have more than enough capacity to deal with normal levels of acid arising from ingestion or metabolism. Also if the normal kidney were confronted by an excess bicarbonate load (attributable to any cause) bicarbonaturia would result (Cogan, M. G., et al 1983).

Metabolism produces 15,000 to 20,000 mmol of carbon dioxide daily in adults. The respiratory system excretes ~~an~~ equal amount in order to maintain the total body content of CO_2 at a constant level reflected by the sea level arterial Pco_2 of approximately 40 mmHg (Kaehny, W. D. 1983).

.. In the presence of normal pulmonary function and normal control of that function, CO_2 generated by metabolism does not alter acid-base status (Cohen, J. J. & Kassirer, J. P. 1982).