



Serum Ammonia Levels as a Prognostic Predictor in Hepatic Encephalopathy.

Medicine

**DR. ANUSHKA
K. WAIKAR**

ASSOCIATE PROFESSOR, DEPARTMENT OF MEDICINE, RAJARSHREE CHATRAPATI SHAHU MAHARAJ GOVERNMENT MEDICAL COLLEGE, KOLHAPUR.

**DR. KAUSTHUBH
WAIKAR**

**DR. ANITA
PARITEKAR**

ABSTRACT

Aim - To study the serial changes in serum ammonia level in a patient of liver disease with neuropsychiatric manifestation and prognostic predictor in hepatic encephalopathy.

Material and Methods :- 59 diagnosed cases of liver cell dysfunction admitted to medical college at Kolhapur were studied with prospective study. Clinical features, lab parameter mainly serum ammonia levels and outcome were evaluated in all patients with hepatic encephalopathy.

Results :- Among 59 cases of hepatic encephalopathy 11% were hyperacute, 48% were acute, 24% were subacute and 15% chronic cases. And in these cases serum ammonia levels were seen higher in hyperacute and acute stages whereas in subacute and chronic cases it goes on reducing.

Conclusion:- Levels of serum ammonia level below 87 $\mu\text{mol/lit}$ is the prognostic indicator and high chances of improvement. Levels above 115 $\mu\text{mol/lit}$ have irreversible prognosis and mostly found in comatose state.

KEYWORDS:

serum ammonia, encephalopathy, liver diseases.

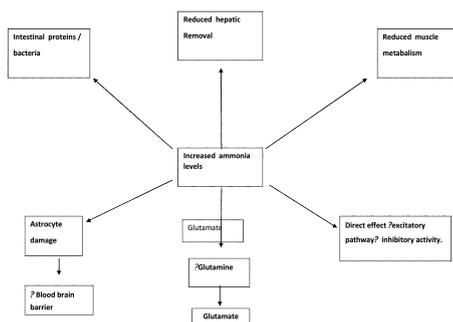
Introduction

Hepatic encephalopathy is the term applied to wide range of neuropsychiatry changes in patients with significant liver dysfunction. Dysfunction of liver may be

- 1) Acute / fulminant
- 2) Major portosystemic bypass of liver.
- 3) Chronic liver disease / cirrhosis.
- 4) Clinical picture of hepatic encephalopathy is complex and affects all parts of brain. There are neurological and psychiatric components. Variability between patients is a marked feature.

Most ammonia levels in the body forms when protein is broken down by bacteria in the intestines.(9) The liver normally converts ammonia into urea, which is then eliminated in urine. Ammonia levels in the blood rise when the liver is not able to convert ammonia to urea. This may be caused by cirrhosis or severe hepatitis(1). The implication of ammonia in the pathogenesis of hepatic encephalopathy is based on four sets of observation.

- 1) Blood ammonia levels are elevated in patients with hepatic encephalopathy.
- 2) Precipitating factors of hepatic encephalopathy results in hyperammonemia.
- 3) Induction of hypothesis in animal studies.
- 4) Treatments to lower serum ammonia improves stages of encephalopathy. Glutamate



In acute and chronic liver disease increased ammonia levels are seen. In fulminant hepatic failure, elevated arterial levels above 200 microgram/dl have been associated with an increased risk of Cerebral herniation(4). Normal value of 11 micromol/dl to 35 are reported for enzymatic procedure.

Hepatic encephalopathy has been graded by West Haven criteria(2) as

Grade 0- No abnormality, no flapping tremor.

Grade 1- Lack of awareness, altered sleep pattern, shortened attention span, asterixis may be.

Grade 2- Lethargy, disorientation, inappropriate behavior, slurred speech and obvious asterixis(3).

Grade 3- Gross disorientation, bizarre behaviour, stupor, absent asterixis.

Grade 4- Coma

In this study serum ammonia levels help in early diagnosis and prognosis of hepatic encephalopathy. High levels of ammonia in the blood may be caused by liver disease, such as cirrhosis or hepatitis, Reye Syndrome, heart failure causing congestion of liver, kidney failure, severe bleeding from the stomach or intestines.(5,6,7)

Material and Methods:

After informed consent from patients attendant and ethical clearance from ethical committee a prospective observational study was conducted on 59 patients of hepatic cell failure. All patients were diagnosed with detailed history and laboratory testing including serial levels of serum ammonia levels on 1st day, 3rd day and 5th day of diagnosis. Both arterial and venous sample can be used for estimation of serum ammonia levels. The major interference for the assay of serum ammonia estimation is from contamination by ammonia in air and water. Also temperature of air can change values. So it is strictly collected in cold temperature and cold chain is maintained. Sample of blood immediately analyzed to prevent error in estimation of ammonia value. Analytical and physiological

variables including drug –patients on neomycin(12), lactulose lowering ammonia excluded and other substances which influence ammonia concentrations have been considered. (young et al). All data recorded and analyzed for morality and mortality. All data recorded and analysed and compared with standard results.

Result:

Among 59 patients of diagnosed hepatic encephalopathy patients are graded according to west heaven criteria and serial serum ammonia levels. Ammonia is formed to be the predominant causative agent for hepatic encephalopathy. It is helpful for diagnosis and as a guide to treatment. Normal levels are below 35 micromol/dl. Elevated level above this are used as an indicator to institute therapy for hepatic encephalopathy.

We found strong co-relation between ammonia level and the severity of hepatic encephalopathy. Ammonia measurement was performed using newer and more reliable enzymatic method and grading of encephalopathy was bonded to the ammonia measurements. Under these conditions ammonia levels co-related strongly with severity.

In this study 34% cases seen in grade 1, 16% in grade 2, 12% in grade 3 and 38% in grade 4. Lowest values such as 20 micromol/dl is seen in grade 1 and all reading are below 126 micromol/dl suggesting good prognostic values. But in cases of grade 3 and grade 4 the serum ammonia values are maximum above 160 micromol/dl which indicates poor prognostic indicator such finding also confirmed by STAHL J.(20)

In this study we also found that serial levels of ammonia levels during the treatment of hepatic encephalopathy shown decrease in levels of ammonia. Nevertheless, there remains substantial overlap in ammonia levels by grades of hepatic encephalopathy which may be explained by variability in ammonia levels through the day, a possible lay between elevation in ammonia levels and hepatic encephalopathy in some patients, or the possibility that compounds other than ammonia are also involved in the pathogenesis of hepatic encephalopathy. Janus Pona and anjana Agrawal(2003) also found the similar observation in their study.(15)

Conclusion :-

Levels of serum ammonia level below 87 micromol/ lit is the prognostic indicator and high chances of improvement. Levels above 115 micromol / lit have irreversible prognosis and mostly found in comatose state. Serum ammonia levels are strongly co-relating with severity and grades of hepatic encephalopathy and a diagnostic indicator in case of hepatic encephalopathy. Thus serum ammonia levels are used for prognosis of hepatic encephalopathy. It cannot be used as diagnostic criteria as many factors such as protein diet, use of medicines such as- acetazolamides, valproate, furosemide, strenuous exercise can affect levels.

References:

1. Anand A. C., Medicine update- Hepatic encephalopathy. 1994;51-60
2. Andres T, Blei, Juan Cardoba (West Heaven Criteria) Hepatic encephalopathy Vol-96, No 7, 2001.
3. Butterworth R F, The neurobiology of hepatic encephalopathy. Semin liver dis 1996;16:235-244.
4. Caesar J., Levels of glutamin and ammonia and the pH of cerebrospinal fluid and plasma in patient with liver disease. Clinical Science 1962;22,23-41
5. Conn H. O., Current diagnosis and treatment of hepatic coma. Hospital practice 1973;8,65-72
6. Corria J B., Areias, Mantura, Gannel, and Mendez F, Livercirrhosis; clinical experience with 274 selected cases. Digestion 1981;4L:233.
7. Crofton A C. Hepatic insufficiency: its causes, recognition, significance and treatment. Med Rec 1906;69:653-656.
8. Dudley E J., Schever D. J. and Sherlock s., Natural history of hepatitis association australia antigen positive chronic liver disease. The Lancet 1972L: 11-1388.
9. Ehrlich, Plum and duffy; Blood and brain ammonia concentrations after loading. Journal of neurochemistry 980;34,1538-1542.
10. Erikson, Parson and Whren, Branched chain amino acids in the s23,801-6.
11. Fericha F. T., A clinical trial on disease of liver. New Sydenham soc. London 1860.
12. Fisher C J, Faion W W; Blood ammonia levels in hepatic cirrhosis, their control by the oral neomycin. New England Journal Medicine 1957;257:1030-1077.
13. Harrison's Principles Of Internal Medicine, 16th edition. Hepatic Encephalopathy p.1867-1869.
14. James J H, Zipparo V, Jeppson B, Fischer J E., Hyperammonemia, plasma amino acid

imbalance and blood brain amino acid transport: a unified theory of portal-systemic encephalopathy. Lancet 1979;2:772-775.

15. Janus P Ong, Anjana Agarwal, Derk Krieger- Correlation between ammonia levels and the severity of hepatic encephalopathy. American Journal Of Medicine Vol-114, 188-193, 2003.
16. Najarian J S, Harper H A, A clinical study of arginine on blood ammonia. A M J Med 1956;21:832-842
17. O; Grady J. G., Alexander Gjm, Hayllar K. M., Williams R. Early indicators of prognosis in fulminant hepatic failure. Gastroenterology 1988;94,1186-92.
18. Phear, Sherlock S and Summer Skill- Blood ammonia levels in liver disease and hepatic coma. Lancet 1955: 836-840.
19. Sherlock s & James Dooley; Diseases of liver & hepatobiliary system, 10th Edition, p.75-101.
20. Stahl J; Studies of blood ammonia in liver disease. Its diagnostic, prognostic and therapeutic significance. Ann of Int. Med. 1963;58, 1-24.s
21. Young D S. Effect of preanalytical variables on clinical, laboratorial tests, first edition, AACC Press Washington, D. C., 3-20,3-21, 1993.
22. Zieve L, Doizaki, WM, Zieve FJ.- Synergism between mercaptans and ammonia in the production of coma. J Lab Clin Med 1974;83:16-28.