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Clinical Management of Severe Acute Hepatic Failure with Special Reference to Liv.52 Therapy

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Acute hepatic failure is a clinical syndrome characterised by severe impairment of liver function and mental changes of various grades. Fulminant hepatic failure surveillance study maintains that the syndrome must occur within 8 weeks of the onset of illness in patients in whom previous liver function is presumed to be normal, and the patients must have mental changes in addition to manifestations of disordered hepatic function.

Though the syndrome is recognised clinically, in spite of tremendous strides in the field of hepatology, definite treatment of acute hepatic failure still remains a problem.

In spite of a significantly high mortality, acute hepato-cellular failure is considered to be potentially reversible, and recovery and survival are being reported. It is obvious therefore that all efforts should be made to save the life of the patient.

Corticosteroids, exchange transfusions, hyperbaric oxygen, co-enzymes and lately levodopa have all been reported to be useful in the management of such cases with variable degrees of recovery and survival rates.

Since the original reports on the utility of corticosteroids by Cucci and Katz (1952), they have been used extensively in the treatment of hepatic failure. Ducci and Katz reported a 66% survival rate which actually consisted of 2 survivors out of 3 patients. Subsequently Katz *et al.* (1962) reported a 39% survival rate (9 out of 23 patients).

However, later studies revealed no significant difference in the recovery rate between the patients who had received these agents, and those who had not. Burnell and his co-workers (1967) found only one survivor in 26. At the Royal Free Hospital, 2 out of 4 patients with fulminant hepatitis survived after prednisolone, while 3 out of 24 lived without this medication. It is stated that there is neither theoretical nor experimental support for the use of corticosteroids in acute hepatic failure. Furthermore their use entails serious complications by way of infections, gastric erosions and haemorrhage, and pancreatitis which frequently prove fatal.

Utility of corticosteroids is, therefore, controversial and complications may outweigh any advantage which they may confer.

In the present knowledge it is held that the treatment of acute severe hepatic failure consists mainly of symptomatic and supportive therapy until hepatic recovery and regeneration has taken place. In addition to good supportive care, further objectives are to prevent liver damage and to promote liver cell regeneration.

Liv.52 has been claimed to be one such indigenous drug which prevents further liver damage and promotes liver cell generation. Clinical and experimental studies indicate that Liv.52:
(1) prevents hepatic damage,
(2) promotes hepatocellular repair and regeneration.

Each ml. of Liv.52* (A product of The Himalaya Drug Co.) drops consists of Exts.:

Capparis spinosa	17 mg
Cichorium intybus	17 mg
Solanum nigrum	8 mg
Cassia occidentalis	4 mg
Terminalia arjuna	8 mg
Achillea millefolium	4 mg
Tamarix gallica	4 mg

Prepared in the juices and decoctions of various hepatic stimulants.

Considerable evidence is available on the utility of Liv.52 in infective hepatitis. The present study was designed to find out its efficacy in cases with acute hepatic failure, and its relative utility vis-à-vis corticosteroid therapy.

MATERIAL AND METHODS

Cases of acute hepatic failure presumably due to viral hepatitis were studied over a thirteeen-month period. In addition to clinical signs of hepatic failure (progressive jaundice, fever, fetor hepaticus, flapping tremors, changes in liver dullness), mental changes of varying severity formed the criteria for clinical selection of such cases.

Severity of the disease was categorised on the basis of grades of mental changes.

Grade I:	In confused state with altered mood/behaviour by way of euphoria or depression.
Grade II:	In drowsy condition with inappropriate behaviour.
Grade III:	In stuporous condition most of the time but arousable.
Grade IV:	In coma but responsive to painful stimuli.
Grade V:	In deep coma with no response to painful stimuli.

For the sake of uniformity of assessment, patients with Grade IV coma only have been included in the present study.

Duration of coma before initiation of therapy was also enquired in each case.

Children under 14 years of age and pregnant women were excluded from this study since they were likely to influence the prognosis and vitiate the assessment of results.

In addition to routine haemogram, stool examination and urinalysis, serum bilirubin, S.G.O.T., thymol turbidity, thymol flocculation, Van den Bergh reaction, alkaline phosphatase, prothrombin time, blood urea, serum electrolytes, serum albumin, blood glucose, and blood grouping and matching were done in every case.

Serum bilirubin was measured as a base line and to check progress.

In addition the usual measures of nursing, all dietary proteins were stopped and calories were given as glucose by intragastric or parenteral route. Fluid and electrolyte balance was maintained. Colonic cleansing was achieved with regular bowel wash. Sedatives were avoided. Neomycin was given orally (1 g four times daily). Ampicillin or penicillin were given only when patients showed

evidence of some definite infection. Patients were put at random on corticosteroids or Liv.52 therapy.

Corticosteroid preparation used was prednisolone 30-40 mg per day. Liv.52 therapy consisted of Liv.52 drops, 20 drops four times daily. Liv.52 drops provide higher concentration and ease of administration.

OBSERVATIONS AND RESULTS

Sixteen patients with acute hepatic failure were studied. There were 10 males and 6 females.

The following Table shows the age incidence:

Table 1		
Sl. No.	Age Groups	No. of cases in each group
1.	15 – 25	4
2.	26 – 35	6
3.	36 – 45	4
4.	46	2

Therapeutic categorisation was made into 2 groups. Patients in group 'A' (9 patients) in addition to general symptomatic and supportive treatment received prednisolone in usual dosage. Patients in group `B' (7 patients) in addition to routine therapy received Liv.52 as concentrated drops. All the patients were of Grade IV coma.

Duration of coma before the initiation of therapy could not be definitely established because of indefinite replies in majority of the cases.

Serum bilirubin levels could not be used as indices for severity of encephalopathy since there had been no correlation between the level of serum bilirubin and the extent of mental aberration.

Table 2: Showing serum bilirubin levels and severity of encephalopathy			
Group 'A' (9 cases)		Group 'B' (7 cases)	
Coma grade	Serum Bilirubin levels in mg%	Coma grade	Serum Bilirubin levels in mg%
4	6.2	4	18.0
4	8.8	4	7.5
4	4.6	4	13.0
4	19.6	4	6.4
4	16.0	4	5.2
4	7.0	4	18.0
4	6.9	4	14.4
4	13.0		
4	23.0		

Results of therapy are shown in Table 3.

Table 3: Showing the results of therapy (Total number of cases 16)			
Therapeutic grouping	No. of cases in each group	No. of cases who recovered	%
A (on Corticosteroids)	9	3	33%
B (On Liv.52)	7	3	43%

It is seen from Table 4 that the recovery from coma was earlier in cases on Liv.52 therapy. Average duration of the coma period with Liv.52 was 5.2 days as against 6 days with corticosteroids.

Table 4: Duration of coma in cases who recovered (Total number of cases who recovered, 6)

Therapeutic grouping	No. of cases in each group	No. of cases who recovered in each group	Duration of coma in days (Average)
A (on Corticosteroids)	9	3	6 days
B (On Liv.52)	7	3	5.2 days

DISCUSSION

Survival of patients with acute hepatic failure is variably reported in literature. In grade IV or V coma, it is of the order of 12.20%. However, since acute hepatic failure is potentially reversible, adequate therapy to prevent further liver damage and to promote liver cell regeneration will enhance the recovery rate in such cases. Liv.52 was used in this study to achieve these objectives. Its therapeutic efficacy was also compared with corticosteroid administration.

Overall recovery rate in the study (both groups together) was about 37%. In the group treated with corticosteroids it was about 33% while in Group B treated with Liv.52 it was about 43%. Though there is not much significant difference in the recovery rate in the two groups, nevertheless it has been observed that the duration of coma after initiation of therapy in cases who survived was less in patients treated with Liv.52 than in those treated with corticosteroids. Thus, in patients who ultimately survived, recovery seemed to commence relatively earlier with Liv.52. Though, at present it is difficult to determine the value of this type of therapy from such a limited study, nevertheless it indicates the relative utility of Liv.52 in promoting early recovery. However, further controlled study on a larger group of patients with different grades of coma is needed before any definite conclusions can be drawn.

In those who recovered on Liv.52 no side effects were noted.

SUMMARY AND CONCLUSIONS

Sixteen cases of hepatic coma of grade IV severity have been studied from the view point of therapy with corticosteroids and Liv.52.

Nine cases received corticosteroids while Liv.52 was given to 7 cases.

Three out of 9 cases (33%) on corticosteroid therapy recovered; while 3 out of 7 (43%) receiving Liv.52 recovered.

Average duration of coma was 5.2 days in those recovering in Liv.52 group while it was observed to be 6 days in the corticosteroid group. Thus, this pilot study indicates the value of Liv.52 in promoting early recovery.

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