

Viral Hepatitis in Children

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ABSTRACT

One hundred and twenty cases of viral hepatitis were randomised into four equal groups, viz., A, B, C and D. Group A received Liv.52 alone; Group B received prednisone alone; Group C received a combination of Liv.52 and prednisone and Group D received only supportive therapy without either Liv.52 or steroids. Liver biopsies were performed before commencement of therapy and repeated during and after treatment along with other relevant biochemical investigations. Though all cases recovered completely, recovery was earliest in Liv.52 treated cases. Addition of steroids to Liv.52 did not show any extra advantage. Cases treated with steroids alone took longer time for histopathological recovery than those treated with Liv.52 alone. The mean recovery period for Liv.52 treated cases with or without prednisone was 5 weeks, while cases receiving prednisone alone recovered in a mean period of 10 weeks. Those with only supportive treatment took about 14 weeks for complete recovery.

INTRODUCTION

Viral hepatitis is one of the commonest causes of jaundice in children and is one of the diseases still unconquered even in the West. In children, its course is usually mild but can lead to post-hepatic cirrhosis, chronic cholestasis, subacute necrosis and hepatic failure. The chances of such complications are great, particularly in our country, where malnutrition is extremely rampant¹. There is no specific therapy for viral hepatitis, and therefore a drug, which can restore liver function quickly without producing harmful effects, and is reasonably inexpensive, is most welcome. Of late, there have been a number of reports about the efficacy of Liv.52 in this disease^{2,3}.

The purpose of this paper is to review our experiences with 120 cases of viral hepatitis on whom controlled studies have been made, with special reference to therapy with Liv.52 and steroids.

MATERIAL AND METHODS

One hundred and twenty cases of viral hepatitis admitted to the Paediatric Wards of the Institute of Child Health, Niloufer Hospital, during the 2½ year period from January 1972 to August 1974, consecutively, were randomised into four groups, 30 in each group and designated as Groups A, B, C and D. A proforma was designed for the purpose of study which included a detailed history and physical examination and routine investigations, such as complete blood picture, urinalysis for bile salts, bile pigments and urobilinogen and liver function tests, which included serum bilirubin, Vanden Bergh, thymol turbidity, thymol flocculation, total serum proteins, albumin/globulin ratio, serum transaminase, etc. Liver biopsy was done on admission and repeated during and after treatment at intervals varying from 3 to 12 weeks. Treatment for Group A cases consisted of Liv.52 alone, for Group B, prednisone alone, while Group C received a combination of Liv.52 and prednisone and Group D received only placebo with supportive treatment (Table 1). The results of treatment were analysed at the end of the study.

OBSERVATIONS

Infective hepatitis accounted for 1.4 per cent of total hospital admissions, with a slight preponderance for males, the male-female ratio being 65:55. Peak incidence was observed during the late summer and winter months, although cases were encountered throughout the year.

Age in years	Group A	Group B	Group C	Group D
Upto 20 years	Liv.52, 2 teaspoons, twice a day	Prednisone, 2 mg/kg for 2 weeks	Liv.52	Placebo
2-10 years	Liv.52, 2 teaspoons, thrice a day	Prednisone 1 mg/kg for 1 week	Prednisone	
10-12 years	Liv.52, 2 tablets, thrice a day	Prednisone, ½ mg/kg for one week		

Age: The ages of these children ranged from 4 months to 12 years, highest incidence being in the age group 3-5 years (Table 2).

Socio-economic status: Seventy two per cent belonged to the poor socio-economic group, 15 per cent to the middle-income group and the rest to the high income group.

Duration of jaundice: Jaundice lasted for less than 10 days prior to admission in the majority of cases (60 per cent). It was detected after admission in 3 per cent (Table 3).

Age	No. of cases	Percentage
Below 1 year	12	10
1 - 3 years	24	20
3 - 5 years	48	40
5 - 8 years	20	16.7
8 - 12 years	16	13.3

Duration	No. of cases	Percentage
Less than 10 days	72	60
10 - 20 days	24	20
20 - 30 days	12	10
30 - 36 days	8	7
(Jaundice after admission)	4	3

Symptoms: Lack of appetite of sudden onset was the most frequent complaint, and jaundice was noticed by mothers in 70 per cent cases, the time of appearance of jaundice varying from 2-8 days after the loss of appetite. Fever was present in 88 per cent and yellow urine was noticed by the mother in 86 per cent cases. Clay coloured stools were present in 55 per cent. Intense pruritus was the presenting symptom in 6 per cent cases, in whom enlarged tender liver and jaundice were detected by the examining doctor in the outdoor department. Four per cent cases presented with fever with chills and rigors and were mistaken for malaria on admission. In 3 per cent, jaundice appeared after admission. None of the cases presented with hepatic coma, although altered sensorium was noticed in 2 cases (Table 4).

Signs: Seventy three per cent had mild jaundice, while 21 per cent had what could be called moderate jaundice. Rest 6 per cent had very severe jaundice and presented with severe pruritus. Liver was enlarged in 98 per cent, the hepatomegaly ranging from 1-6 cm below the costal margin in the midclavicular line. Tenderness was discernible in 68 per cent, although it was difficult to appreciate tenderness in infants below 1 year. There was no hepatomegaly but only discomfort on pressing the subcostal region in 2 per cent. Lymph nodes were enlarged in 34 per cent. Ascites was seen in 2 per cent and bradycardia was detected in 2 per cent. These children had oedema of legs also. Electrocardiogram showed only sinus bradycardia.

Laboratory investigations: The serum bilirubin levels ranged from 2-15 mg% and alkaline phosphatase levels from 10-25 King Armstrong units. Thymol turbidity ranged from 1-10 units.

Elevated levels of serum glutamic oxalo acetic and pyruvic transaminase (SGOT and SGPT) were found in 87 per cent cases.

The histopathologic changes in liver included vacuolation of hepatocytes in varying degrees with scanty and granular cytoplasm. The portal tracts were infiltrated with mononuclear cells and segmented leucocytes. Focal areas of necrosis were noticed in 48 per cent and there was destruction of limiting plate in 32 per cent. Cholestasis with bile pigment in hepatocytes and biliary canaliculi was found in only 5 per cent. The glycogen content of the liver cells was found to be reduced in sections stained with Periodic acid Schiff. The reticulin framework was found to be disturbed in all cases.

Complaint	No. of cases	Percentage
Lack of appetite	120	100
Fever	106	88
Yellow urine	103	86
Jaundice	84	70
Clay coloured stools	66	55
Nausea or vomiting	60	50
Pain in abdomen	36	30
Pruritus	7	6
Insomnia	7	6
Chills and rigors	5	4
Altered sensorium	2	1.7
Bleeding tendencies	2	1.7

Results of treatment: Table 5 shows the comparison of the four groups with respect to age, sex, duration of symptoms and mean serum bilirubin level, and Table 6 shows the results of treatment in these groups.

Groups	Mean age	Sex ratio Male/female	Duration of symptoms, mean period in days	Mean serum bilirubin mg/100 ml
A	4 years	18/12	10	8
B	3 years 10 months	16/14	11	7
C	4 years 2 months	15/15	9	7.4
D	3½ years	16/14	12	11.2

Groups		Group A	Group B	Group C	Group D	
1.	Return of appetite	4	10	5	14	
2.	Liver size reduction	10	18	14	28	
3.	Clearance of jaundice	12	17	11	14	
4.	Normalisation of	Serum bilirubin	10	18	12	26
		Thymol turbidity	14	21	13	30
		SGOT & SGPT	18	26	21	34
		Alkaline phosphatase	16	23	16	30
5.	Histopathologic recovery	35	70	36	98	

The clinical, biochemical and histopathologic recovery was earliest in Group A. Appetite returned to normal earliest in Group A (mean period - 4 days), followed by Group C (mean period - 5 days). A general sense of well being was present in Groups A and C. Jaundice disappeared clinically in a mean period of 12 days in Group A, while in Groups B and D, the mean period for disappearance of jaundice was 17 and 14 days, respectively. The cases in Group C took 11 days for clearance of

jaundice. Biochemical remission in terms of serum bilirubin, thymol turbidity, SGOT and SGPT values was also earliest in Groups A and C.

Histopathologic recovery, in terms of complete regeneration of liver cells decrease or disappearance of mononuclear infiltration of portal tracts, absence of vacuolation of hepatocytes and normalisation of their glycogen content in sections stained with Periodic acid Schiff, etc., was noticed in all groups. However, complete histopathologic recovery was seen in a mean period of 5 weeks in Groups A and C. Groups B and D took 10 and 14 weeks, respectively, for completing histopathologic recovery.

Side effects of prednisone therapy, such as mooning of face, etc., were seen in all cases of Groups B and C.

DISCUSSION

Viral hepatitis is often a self-limiting disease, but can have high mortality and morbidity during epidemics⁴, particularly where malnutrition is endemic. Therapy with inexpensive and efficient drugs is, therefore, welcome.

Peak incidence was in pre-school age group, an observation made by other workers⁵ also. The higher frequency noted in our study during the summer months also agrees with the observations of other workers⁶. Lack of appetite with irritability and fever should alert the physician for the development of jaundice, in a few days, and urine examination for bile salts, bile pigments and urobilinogen should be a routine in such cases. Early detection is of importance, to avoid administration of hepatotoxic drugs, such as chlorpromazine, etc., for vomiting or drugs, such as cyproheptadine hydrochloride for appetite.

Abdominal pain was noticed in 30 per cent, which is in agreement with the observations of Sule *et al.*⁷. It is attributed to perihepatitis, distension of Glisson's capsule, phlegmonous enteritis or sudden shrinkage of liver in acute hepatic necrosis⁸.

Majority of our cases belonged to the poor socio-economic group, and obvious signs of malnutrition were found in 28 per cent cases. Seventeen per cent were clearly malnourished in another study⁹.

Corticosteroids did produce clinical and biochemical remission as observed by Duccy¹⁰ although Sule *et al.*⁷ did not find much change in the histologic lesions. In our study, Group B experienced clinical remission much later than the Groups A and C and the histopathologic improvement also took much longer time than Groups A and C. Our study has also revealed that addition of corticosteroids to Liv.52 does not seem to have any extra advantage in treatment and routine management of cases. All cases on corticosteroids developed mooning of the face and oedema of feet as observed by Libov¹¹.

The efficacy of Liv.52 was observed by several other workers^{2,3,5,7,8,9}. The drug is a herbal preparation with anabolic, aperient, diuretic, stomachic and protective and has regenerative action on the liver. It is also relatively inexpensive and has no toxic side effects. Patients in our study (Groups A and C) experienced improvement in symptomatology earliest, and this is also corroborated by the biochemical and histopathologic improvement. The absence of untoward side effects with even prolonged administration makes this drug safe and effective in the management of viral hepatitis.

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