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Role of Various Types of Treatment in Infectious Hepatitis

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INTRODUCTION

Infectious Hepatitis is a systemic illness with world-wide distribution. It is caused by a virus IH (A) of which three serologically different types have been isolated.

The disease was first described by Hippocrates in 460-377 BC. Since then it has been reported upon by countless authors. Whenever there is a massive gathering of human population, as in wars, the disease is likely to occur in epidemic form. At other times, the disease shows itself by sporadic cases and occasional epidemics. Thus a remarkable epidemic of 35,000 cases occurred in Delhi in 1955. This followed floods and the diversion of a river so that the city water supply was heavily contaminated with sewage. Although the disease essentially follows a self-limited course, with a mortality of less than 0.5% and chronic symptoms less than 5% of the disease it is important from the military point of view because it reduces the man-power by rendering the patient ineffective for 6-14 weeks (including the sick leave).

As yet there is no specific treatment available for this disease. Prevention of this disease is therefore the sheet anchor for its eradication. However, a physician can get good results if he concentrates upon minimising the damage to hepatic parenchyma, encourages its regeneration and keeps the patient alive till the disease process terminates by itself. Various types of treatment have been in vogue from time to time. It is difficult to assess their relative therapeutic value because of the varied manifestations of the disease, its self-limited course, low mortality and lack of critical controlled studies. Moreover, a susceptible animal has not yet been found. Tissue culture methods may yield promising results.

In view of the above author presents here a study of 676 cases of Infectious Hepatitis with special reference to the role of "Liv.52" (The Himalaya Drug Co.) and corticosteroids in its treatment.

MATERIAL AND METHODS

An epidemic of Infectious Hepatitis broke out in Siliguri area in Apr. 66. Six hundred and seventy six cases occurring amongst soldiers and other defence employees were admitted in a General Hospital from May to August 66 comprised the material for this study. A careful history including history of alcohol consumption, past history of jaundice, amoebiasis, ingestion of any hepatotoxic drugs and details of injections transfusions received, if any, during the proceeding one year was taken. A thorough clinical examination was carried out in each case. The investigations, included: urine for bile salts, bile pigments, urobilinogen and routine examination; Blood for HB%, TLC, DLC and ESR; Stool for ova and cysts; liver function tests, including Vandenbergh test, serum bilirubin, total serum protein, serum albumin, serum globulin, A:G:Ratio and flocculation tests; SGPT and alkaline phosphatase were estimated only in selected cases. Liver biopsy was not done in any of the cases.

Diagnosis was based on typical history, characteristic clinical picture, course and laboratory findings. All cases of other types of jaundice and other hepatic disorders were excluded from this study.

The case were grouped as follows:-

Group I: On admission all except 50 cases mentioned below were given the following treatment:

(a) Bed-rest was enforced in all cases till they started showing satisfactory improvement at which stage they were allowed up and about in the ward and then in the hospital area, before being finally sent on sick leave,

(b) Diet: Majority of patients could be coaxed to take 'O' diet (non vegetarian/vegetarian) inspite of slight anorexia. Those who had marked nausea and anorexia, were either given boiled 'O' diet or put on 'N' diet with extras to provide menu to their taste. Plenty of sweet drink were given to every patient. As soon as their appetite improved they were also switched on to 'O' diet. Those who had coexisting anaemia or failed to gain weight satisfactorily were given 'C' diet. If any case showed any evidence of impending coma proteins were immediately deleted from the diet and then gradually re-added as the improvement occurred,

(c) Tablet Vit. B complex 1 tab. thrice a day and Vit. C, 100 mg thrice a day for 10 to 14 days.

Group II: Fifty cases on admission selected at random were treated with Liv.52 tabs thrice a day for 14 days in addition to treatment at I above.

Group III: Those cases of group I and group II who after 10 days of treatment did not show expected clinical improvement and in whom serum bilirubin level rose to above 12.0 mg% were given in addition oral prednisolone.

Group IV: Patients of fulminant hepatitis were treated as follows: (a) absolute bed-rest with usual care of comatosed patients, (b) Parental glucose (20%) 2 litres in 24 hours, (c) I.V. hydrocortisone hemisuccinate 10 mg 6 hourly.

Oral prednisolone was substituted as soon as possible in doses of 80 mg daily and then gradually tapered off in three to four weeks time. (d) Tetracycline orally 500 mg 6 hourly (e) Complete stoppage of proteins (f) Daily bowel wash (g) supportive therapy with injection Vit. B complex, injection Vit. C, Injection Vit.K and vasopressor drugs.

Disposal of Cases: The patient was considered fit for discharge when (a) he became asymptomatic, regained his normal appetite and picked up weight, (b) Liver was either not palpable or just palpable but not tender, (c) urine was free from bile pigments and urobilinogen reappeared and (d) serum bilirubin was 0.6 mg% or less.

After discharge from hospital the patients were sent on 4 to 8 weeks sick leave and to be reviewed at the end of that period. They were advised to avoid alcohol at least for one year.

OBSERVATIONS AND FINDINGS

The main symptoms noted were feeling weakness (59.4%), abdominal pain/discomfort special in right hypochondrium (43.3%), loss of appetite (37.2%) nausea (21.7%), vomiting (12%), fever (11.2%) and pruritis (2.8%). All cases at the time of admission had jaundice, tenderness of right hypochondrium was present in 98.1%, palpable liver in 93% cases and palpable spleen in 5% cases; urine for bile pigments was positive in all cases and bile salts were detected in 83%of cases; serum bilirubin was raised in all patients. Total and differential blood counts were within normal limits.

Out of 626 cases of Group I, 6 cases developed fulminant hepatitis and 111 cases required additional prednisolone after 10 days. 509 cases made an uneventful recovery. Their appetite

improved on an average in 5 days and feeling of well-being returned in 7 days. On an average the urine started clearing on the 7th day and serum bilirubin showed a fall of 1 to 3 mg on every 4th day.

Out of 50 cases of Group II only one case required corticosteroids at a later stage as compared to 111 cases in Group I. No case developed fulminant hepatitis. Forty nine cases made smooth recovery. Their appetite and feeling of well-being returned in 3 and 5 days respectively. Thus it was quicker than in Group I. Similarly nausea, vomiting and abdominal discomfort subsided 24-48 hours earlier than in Group I. The urine also started changing colour earlier i.e. on fifth day and serum bilirubin registered a fall of 2 to 4 mg every fourth day. Their hospital stay on an average was less by 4 to 7 days as compared to Group I.

One hundred and eleven cases of Group I and one case of Group II were started on oral prednisolone on 11th day as follows:-

30 mg for five days, 20 mg for five days, 15 mg for five days, 10 mg for five days and 5 mg for five days. In majority of the cases this 25 days treatment was sufficient but this treatment had to be prolonged with proper modification of doses for 35 days in 13 cases and for 50 days in 5 cases because serum bilirubin had not fallen below 1 mg% in 25 days.

Six cases of Group I were started on corticosteroid therapy with other treatment already mentioned earlier than 10 days because they showed evidence of hepatic precoma. The main symptoms noticed were disturbed consciousness, irritability and mental confusion. Typical flapping tremor was seen in only one case. Another case who went into hepatic coma, developed simultaneously acute renal failure. Patient developed oilguria and blood urea went up to 380 mg%. There was no history of any surgical operation and nothing suggestive of Weil's disease. TLC, DLC were within normal limits. The patient was given usual conservative treatment for acute renal failure in addition to the Group IV treatment. Patient regained consciousness after 42 hours, gradually kidneys started functioning and patient made good recovery.

DISCUSSION

Out of 626 cases of Infectious Hepatitis in Group I, 509 cases made an uneventful recovery on conservative treatment alone with adequate rest and appropriate diet without any corticosteroid therapy. This suggests that in majority of the patients this treatment is sufficient. Chalmers *et al.* (1955) found in American soldiers, during Korean War, that less rigid bed-rest reduced the period of Hospitalisation, Infectious Hepatitis is an unpredictable disease. It is therefore, difficult to say which case may take an unfavourable turn. It is hence, wise to insist upon bed-rest in every case, till the disease process shows signs of regression. The diet regime followed in cases in this series was found to be both practical and satisfactory. The practice, of putting every cases of Infectious Hepatitis on 'C' diet is to be deprecated. Similarly a rigid fat-free diet is required only in very few cases and has no merit to qualify its routine use. On the other hand it has been shown by Hoagland *et al.* (1946) that patients receiving higher fat diet regained their weight more rapidly and bromsulphalein tests reverted to normal sooner.

In the Group II cases who were given Liv.52 in addition to above treatment, appetite and a feeling of well-being returned more quickly, nausea, vomiting and abdominal discomfort disappeared at a more rapid rate; jaundice cleared earlier and serum bilirubin level dropped more rapidly. This finding is in agreement with other Workers. Menon and Ravindran (1966) noticed similar effects in 29 patients of Infectious Hepatitis treated with conservative treatment and Liv.52. Sule *et al.* (1968) found significantly better results in cases of Infectious Hepatitis treated with Liv.52 as compared to control group. Athavale (1966) studied the effect of Liv.52 in children in whom the presenting complaint was anorexia. He noticed that out of 263 patients treated with Liv.52, 167 showed

marked increase in appetite and after treatment the children showed gain in weight, a sense of well-being and improved bowel action while in the control group only 32 children showed increase in appetite. Patel *et al.* (1963) and Joglekar *et al.* (1963) have demonstrated liver protective action of Liv.52 in rats and mice.

The exact mode of action of Liv.52 is still not fully understood. It stimulates hepatic function possibly by reducing intra hepatic congestion thereby relieving cholestasis. It is also likely that it helps in quicker regeneration of hepatic parenchyma. Its hepatostimulant, anabolic, stomachic, choleretic and diuretic actions are in all likelihood due to different components of Liv.52. Thus it brings about its definite although non-specific protective action on liver in more than one way.

Inspite of the fact, that corticosteroids have been widely used in the treatment of Infectious Hepatitis and that the steroid 'Whitewash' improves the morale of both patient and physician, there is no satisfactory, controlled evidence to show that corticosteroids materially affect the underlying liver pathology. Vakil *et al.* (1965) could not find any difference in liver biopsy study in patients treated with steroids and those not treated. The exact mode of action of corticosteroids is not known. It may be that they act by exerting anti-inflammatory effect on liver, reducing intra-hepatic oedema and cellular infiltration. Thus corticosteroids cause rapid symptomatic, drop in serum bilirubin and alkaline phosphatase level and more rapid reversion to normal of the transaminase and flocculation tests. In a disease such as viral hepatitis which tends towards spontaneous recovery, this benefit is not sufficient to justify the routine use of a costly drug like corticosteroid. The recovery of 81.3% of cases without any corticosteroid treatment in Group I and 98% cases in Group II in the present series, confirms the impression that this treatment is not required in an average case.

It is further likely that 112 cases of Group I and one case of Group II who were put on corticosteriods on 11th day after they failed to show the expected improvement, might have, if given more time, also shown satisfactory improvement. However with addition of corticosteroids their clinical condition definitely improved within 3 days, in that felt subjectively better, appetite improved and jaundice cleared rapidly and serum bilirubin level dropped quicker. Thus, although corticosteroid treatment is not required in an average case, it has a useful role to play if the patient does not show subjective and objective improvement in about 10 days time, malaise and anorexia persist, jaundice persists on deepening and liver function tests show progressive deterioration.

Six patients were started on corticosteroid treatment because they developed evidence hepatic coma. The role of corticosteroids in such cases (Shah and Singh 1967, Vakil *et al.* 1965, Katz *et al.* 1962). Results are better if this treatment is started at precoma rather than coma stage and in every case other treatment as mentioned for Group IV patient must also be instituted. The treatment once started must be carried well into convalescence because premature withdrawal causes relapse (Sherlock, 1963). All the 6 cases in this series recovered, presumably, because, they came from comparatively healthy stock, were hospitalised early where under day-to-day clinical observation and therapeutic measures for hepatic coma were started at the earliest indication.

SUMMARY AND CONCLUSIONS

Six hundred and seventy six cases of Infectious Hepatitis was treated and comparative value of various therapeutic measures was studied. An average case of Infectious Hepatitis will recover with the conservative treatment alone. It is wise to insist upon bed-rest in every case of Infectious Hepatitis till the patient starts showing improvement. Rigid fat-free diet or 'C' diet is not considered necessary.

Patient's appetite and his clinical condition should constitute the guide lines. In majority of the patients 'O' diet with plenty of sweet drinks would fill the bill. A few patients would require 'N' diet with extras.

The inclusion of Liv.52 in the conservative regime adds materially to the patient's comfort and accelerates the recovery. There is therefore sufficient justification to include it in the routine treatment of Infectious Hepatitis.

While corticosteroids are not required in an average case of Infectious Hepatitis they are useful in patients who do not show clinical improvement with conservative treatment, have prolonged deep jaundice and are likely to go into a stage of sub-acute or fulminant Hepatitis. The treatment of course should be started early, rather than late, should be carried will into convalescence.

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