THE EFFECT OF PREDNISOLONE ON THE CLINICAL COURSE OF ACUTE VIRAL HEPATITIS

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At present, there is no evidence that known agents directly attack the causal virus, (viral hepatitis) once the virus has affected the liver. The role of corticosteroids and its derivatives in the treatment of acute viral hepatitis has been discussed. The mortality of the epidemic hepatitis is low but the morbidity is high, a few cases may become very severe and even fatal. Although the use of corticosteroids and its derivatives often resulted in a dramatic subjective improvement and a rapid decline in serum bilirubin level, a recent report by using double statistical analysis by student t' and X^2 tests of Person disproved the aforementioned result. (De Ritis *et al.* 1964).

The purpose of this report is to study the effects of prednisolone on the clinical course of acute viral hepatitis with particular reference to the durations of abnormal serum bilirubin level in the control and treated patients.

MATERIALS AND METHODS

Cases in this series were studied from those who were admitted to the Department of Medicine, Siriraj Hospital. Eighty-nine patients, 49 males and 40 females with ages ranging from 13 to 46 years were selected (Table 1). They were divided into two groups: Group I were those who were admitted during November 1962-December 1963 and were given conventional therapy. Group II were those who were admitted during January 1963-November 1963 and were given conventional therapy plus prednisolone.

Table 1
Showing Distribution of Cases by Age and Sex

Age	Group I (Control)		Group II (Prednisolone)	
	Male	Female	Male	Female
13-20	11	6	7	3
21-30	14	12	8	11
31-40	2	5	4	2
41-50	2	-	1	1
Total	29	23	20	17

The purpose of the authors is to study relatively mild cases; therefore the diagnosis and selection of the patients were based on the following:—

1. The disease was benign; those who had clinical manifestations of fever in the icteric period, stupor and prolonged jaundice with elevation of serum alkaline phosphatase of more than 15 Bodansky units, were excluded.
2. There were laboratory evidence and history of ascending jaundice after prodromal symptoms, which were mild, that is, no parenteral fluid and antiemetics were required.
3. There was elevation of serum glutamic pyruvic and serum glutamic oxaloacetic transaminases.

In this series, the serum transaminases in all but 9 cases (or 10 per cent, 6 in Group I and 3 in Group II) rose more than 300 units, and the ratio between SGOT and SGPT was less than 0.8 in all but 14 cases (or 16 per cent, 6 in Group I and 8 in Group II). Thirty-two out of 52 cases in Group I (62 per cent)

had serum level of GPT over 500 units and 11 cases (21 per cent) had the serum level of over 1000 units. There were 20 out of 32 cases (63 per cent) in Group II in which the serum transaminase rose above 500 units and in 10 cases the serum transaminase was above 1,000 units.

Table 2
Showing the Mean Values and Standard Deviations of SGPT and Bilirubin Levels from the Onset of Illness to the Time when the Values Returned to Normal

	Group I (Control)		Group II (Prednisolone)	
	Mean	S.D.	Mean	S.D.
SGPT	31.1	10.3	34.7	13.0
Bilirubin	31.8	10.4	35.1	14.6

Principal treatment consisted of bed rest 'ad libitum', high caloric and high vitamin diet. Patients in Group II were given prednisolone additionally. Daily dosage of 40 mg. per day was given initially for a period of 7 days or until definite signs of subjective improvement were obtained and was gradually tailed-off over a period of 4 to 6 weeks. Liver function tests including serum protein, seroflocculation tests and alkaline phosphatase were performed twice a week and serum bilirubin and serum glutamic oxaloacetic and pyruvic transaminase were carried out every other day.

RESULTS

1. *Subjective symptoms.* There was a dramatic disappearance of toxemic symptoms such as anorexia, vomiting, myalgia and weakness in the treated group in comparison to the control one. This response, including the sense of well-being occurred within 24 to 72 hours after administration of prednisolone in all except 2 cases in this group. In the control group, such symptoms lasted from one to nine days but they disappeared gradually in contrast to those in the treated group.

2. *Liver Function Tests.*

a) *Transaminases:* Regardless of the initial levels, the rate of fall of transaminases in both groups as illustrated in the figures were similar. Fig. 1 and Fig. 2, showed the serum

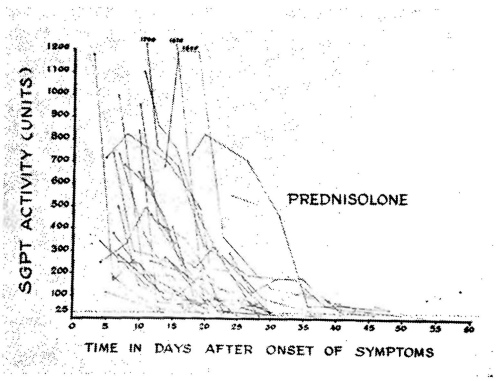

Fig. 1—Showing SGPT activity in the "Control" Group I.

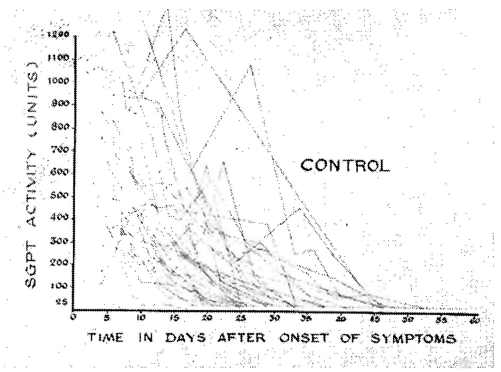

Fig. 2—Showing SGPT activity in the "treated" Group II.

glutamic pyruvic transaminase level in 44 patients of the control group and in 30 patients of the treated group. The serum glutamic oxaloacetic transaminase, which was not shown, presented a similar pattern. From the figures, there were two phases reflecting the fall of transaminases, which were similar in both groups. The first phase was shown by the more vertical lines, representing the rapid fall in serum transaminases levels, and turning abruptly into the second

phase in which the line is more horizontal, presenting the gradual fall in the serum levels. The duration, from the onset of symptoms to the time when the values returned to normal in the control group varied from 17 to 60 days and in the treated group from 15 to 69 days. The means were 37.1 and 34.7 days and standard deviations 10.3 and 13.0 respectively. The difference among these figures are of no statistical significance. Both transaminases returning to normal levels in the same week was found in 86.7 per cent of all cases in this series.

b) *Bilirubin:* The durations from the onset of the symptoms to the time when the serum bilirubin level returned to normal (total bilirubin of less than 1.0 mg. per cent) in the control group varied from 17 to 60 days and in the treated group from 11 to 67 days. The means were 31.8 and 35.1 days and standard deviations 10.4 and 14.6 respectively. There were also no statistically significant difference between the two groups.

Regardless of the initial level,the rate of fall of serum bilirubin, determined on the fourth day after reaching the maximal level in the control group and on the fourth day after prednisolone adminstration showed no significant difference. The difference between the two values of serum bilirubin in the control group varied from 1.8 to 7.0 mg. per cent and in the treated group from 1.7 to 6.5 mg. per cent.

c) Other liver function tests including cephalin cholesterol flocculation, thymol turbidity, zinc turbidity and alkaline phosphatase did not show any significant difference between the two groups. There were two cases in which the serum alkaline phosphatase decreased remarkably, that is, from 13.6 to 6.7 and from 11.1 to 5.5 Bodansky units, four days after prednisolone administration.

3. *Complications and side-effects.* There were no serious complications in this series. The only side- effects found were acne in 5 cases and a slight moon face in one case.

4. *Follow-up Study.* Three years follow-up was possible in 41 cases in Group I and 30 cases in Group II. There were two cases, one in Group I and one in Group II who developed recurrent attacks of hepatitis. These attacks, occurring four and six months thereafter, had symptoms and laboratory findings closely similar to the previous one but the durations were shorter. Bromsulfalein retention test was done regularly in every patient. There were two patients in group II who had persistent retention between 9 to 13 per cent but without any deterioration of health.

DISCUSSION

No evidence has yet been available that steroids decrease the liver necrosis in typical viral hepatitis. There was moreover, increase in the incidence of relapses after treatment with steroids, (Evans *et al*, I and II, 1953). There were many reports stating that steroids administration results in a more rapid decrease in transaminase and bilirubin level in the serum (Schiff, 1969). De Ritis *et al*, (1964) could not demonstrate a significant difference in the rate of decline of bilirubin, transaminase and adolase, although in the group treated with prednisolone the differences were slightly smaller in all indices.

In our study, there was somewhat definite statistical evidence that the rate of decline of serum bilirubin among the two groups of patients, the control and the group receiving prednisolone, were not different. Moreover, the mean values and standard deviations of serum glutamic pyruvic transaminase and bilirubin levels from the onset of illness to the time when the value returned to normal in the two groups, were not different· Our results were similar to those of De Ritis and associates. Mode of action of prednisolone

inducing immediate and rapid fall in serum bilirubin in patients with acute viral hepatitis has not been clarified. William and Billing (1961) could demonstrate that increase in biliary excretion of bile pigment could not be accounted for because there was no increase in fecal urobilinogen and urinary urobilirubinogen at the same time. There was also lack of increasing urinary excretion of bilirubin or decrease in red blood cell breakdown. They suggested the most probable explanation was that the bile pigments are excreted via another metabolic and colourless pathway.

Decrease in serum bilirubin level immediately after prednisolone or ACTH administration, formerly known as ACTH test (Summerskill *et al.* 1961) could not be proved to be useful in this series. According to the authors experience sometime after serum bilirubin has reached the peak it could drop rapidly, as much as 7 mg. per cent in the course of 4 days. The time when prednisolone was administered has to be taken into consideration before the interpretation of the result. If it was given early in the course, when serum bilirubin was rising, i. e. before it has reached its peak, serum bilirubin might not drop at all. When prednisolone was given late in the course, when serum bilirubin was decreasing, i. e. after it has reached its peak, serum bilirubin could drop more than 50 per cent of the former level.

We agree with many authors (Schiff, 1969) that steroid therapy is not indicated in typical acute viral hepatitis. It should be tried when the disease is unusually severe, cholestatic type of hepatitis or in cases with recurrences.

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