

B.S.P. Test in the Evaluation of Therapy in Hepatic Cirrhosis by an Indigenous Drug – Liv.52

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There are several types of liver function tests employed clinically to determine various cellular functions and excretory capacity of hepatocytes. Bromsulphalein test is one of the most sensitive liver function tests used for detection of even minute hepatocellular damage in the absence of jaundice. Out of several thousand tests with this dye, untoward reaction is only reported to be produced amongst 14 cases (Astin, 1965). This test, therefore, could be used with safety and accuracy for estimation of the severity of liver damage and hence to assess prognosis and evaluate therapy in diseases like hepatic cirrhosis.

The disorder of liver cirrhosis is still a disease of unknown aetiology and has a bad prognostic outlook. There occurs destruction of hepatic cells with disorganisation of hepatic architecture, fibrosis with regeneration nodule formation. The clinical severity of the disease is related ultimately to the degree of underlying hepatocellular damage as had been shown from time to time by Ricketts *et al* (1948), Popper *et al* (1950), Jingran (1965) and Dasgupta and Mukerjee (1970). Management of this disorder is mainly supportive (Ellis, 1962). An indigenous drug Liv.52, has got reported evidence of powerful effect in preventing hepatotoxic effect of noxious agents like carbon tetrachloride, etc. (Northover, 1960; Joglekar *et al* 1963; Patel *et al* 1963; Karandikar *et al* 1963; Sule *et al* 1956; Murkibhavi and Sheth, 1957; and Captain *et al* 1966). Recently in a U.S. laboratory it has been shown that this drug causes rapid regeneration of liver cells following liver injury as determine by tests with H³ labelled thymidine with autoradiographic technique of recording the results (Joglekar and Leevy, 1970). Clinical reports pointing towards successful results in therapy by using this drug in various hepatic disorders like hepatic cirrhosis, viral hepatitis, etc., have also been reported in literature by Mathur (1957), Patrao (1957), Sheth *et al* (1960, 1963), Vyas *et al* (1963), Menon *et al* (1966), Arora (1969) and Mukerjee and Dasgupta (1970(a)).

A clinical application of the drug 'Liv.52', therefore, was thought of for trial in cases of hepatic cirrhosis and assessment of the result of therapy, with main emphasis on change of hepatocellular damage following the use of the drug, was to be done by noting changes in pre-and post-treatment standard bromsulphalein (B.S.P.) retention test.

MATERIAL AND METHODS

A total of 42 cases of needle biopsy confirmed hepatic cirrhosis of varying age and sex were selected for the study. The highest age of the patients noted was 68 years and the lowest being 22. The cases were treated with 'Liv.52' tablets (2 tablets thrice daily) or with placebo (2 tablets thrice daily), for varying duration of 3, 6 and 9 months in different groups divided and titled as Group A, B and C respectively. The placebo treated cases served as controls. The total number of cases treated in each group with either placebo or 'Liv.52' are shown in Table I. 'Liv.52' will be mentioned hereafter as the drug in this paper. No other supportive treatment with vitamins, etc., was done except in a few cases where diuretics were used as an additional helping agent.

Table I: Distribution of cases treated and their duration of therapy				
Therapy	No. of cases	No. of cases	No. of cases	Total
	Group A (treated for 3 months)	Group B (treated for 6 months)	Group C (treated for 9 months)	
Drug	9	4	14	27
Placebo	6	3	6	15

B.S.P. test was performed in each case before and after the end of therapy. A 5% solution of the dye was injected intravenously, in empty stomach, in a dose of 5 mgm./kg. body weight and a venous sample was taken from the opposite hand after 45 minutes of the injection. The estimation of dye retained was then detected by alkalinising the serum with development of a purple colour which is measured photometrically and compared with a standard curve by following the methods mentioned by Mateer *et al* (1942).

This standard B.S.P. test was also carried out in 20 normal controls of varying age and sex without any clinical evidence of liver disease and the data thus obtained served as our control data of B.S.P. results (45 minutes value) in our own laboratory.

The pre-treatment results of B.S.P. test in each case and in each group of observation were compared with post-treatment values and changes noted were assessed by statistical tests for evaluating the significance of the results obtained.

Detailed clinical analysis of pre- and post-treatment alterations were also noted and so also the results of various routine liver function tests like serum albumin, globulin, alkaline phosphatase, etc., but their results are not presented and discussed here.

RESULTS

Clinically the cases treated with placebo did not show much improvement, whereas those treated with drug showed better response. The details are discussed in a separate paper (Mukerjee and Dasgupta, 1970 (b)). The results of the B.S.P. tests are described as follows:

- I. *B.S.P. results in normal controls:* Of the 20 observations made in normal persons the lowest retention was noted to be 0.0% and the highest 5.0%. The details are shown in Fig. 1. Average result in control was $2.45\% \pm 0.86$ (S.D.).
- II. *B.S.P. results in placebo treated cases:* The different results with details in each case and group of cases are shown in Fig. 2. The result shows majority of figures were much in excess of our own control figures, lowest being 12%. The response to treatment as revealed from post-treatment values is definitely bad in majority of the cases, in all the groups. In fact deterioration of B.S.P. values has occurred in majority of the cases. Statistical analysis of the same as shown in Table II also confirms that the result of therapy is insignificant by placebo treatment.

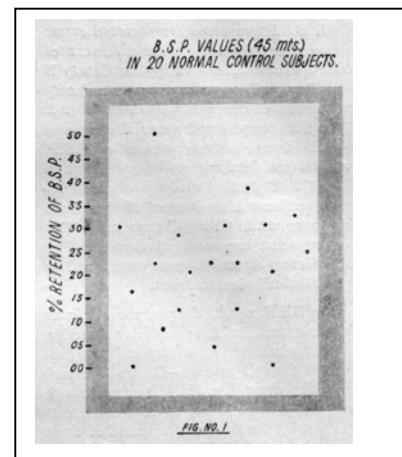
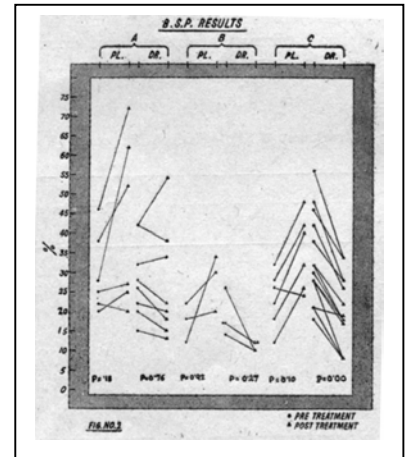


Table II: Statistical results of change in pre- and post-treatment of B.S.P. values in 42 cases of cirrhosis				
Therapy	Statistical values			Remarks
	SD	T	P	
<i>Placebo</i>				
Group A	10.04	-1.6	0.186	Insignificant
Group B	16.55	-0.11	0.922	Insignificant
Group C	7.45	-1.96	0.108	Insignificant
<i>Drugs</i>				
Group A	6.00	0.32	0.76	Insignificant
Group B	5.69	1.32	0.278	Highly significant
Group C	3.74	3.60	0.0026	Highly significant

III. *B.S.P. results in drug-treated cases:* There occurred overall improvement of B.S.P. values after therapy in Group B and Group C cases, mainly in majority of Group C cases, as shown in Fig. 2. Group A drug-treated case also showed a little degree of improvement of B.S.P. values (the detailed results are shown in Fig. 2). Statistical analysis of these results confirms high degrees of significant improvement in Group C cases only. But the apparent improvement in Group A and B cases was found to be statistically insignificant.



The B.S.P. results thereby show definite improvement in hepatocellular function among cirrhotics when treated for prolonged time (9 months – Group C cases) with the drug ‘Liv.52’. Treatment with placebo is ineffective, so also the treatment with the drug for a period of three and six months. No toxic effect due to drug treatment was noted in any case.

DISCUSSION

The dye bromsulphalein is entirely handled by the liver like bilirubin and high values of its retention are obvious in a disease like hepatic cirrhosis. Though there are several factors like age, blood flow to the liver, etc., the average B.S.P. retention in 45 minutes in Indian cirrhotics has been reported to be 19.3 (± 9.7) in one of the research publications of Indian Council of Medical Research (1969). Our control values are much less than this but the individual values in patients were actually close to it or at times exceeded the average value mentioned above. This is a pointer to the degree of associated liver cell damage which is always associated with clinical cirrhosis as could be guessed by B.S.P. tests.

Statistical evaluation of the results of B.S.P. test obtained in the study clearly shows that long-term treatment with the indigenous drug ‘Liv.52’ certainly produces improvement in hepatic cell damage associated with cirrhosis. Natural tendency of the disease leads to progressive deterioration of the liver functions as is also confirmed from the results of placebo treatment. Achievement by drug treatment in cirrhosis is remarkable in this study. Though modern management is only concerned with supportive treatment of the disease, no good therapeutic agent has so far been dealt with to bring definite improvement of hepatocellular destruction in cirrhosis, which this indigenous drug has successfully done. Treatment with newer diuretics or operative management of portal hypertension might have opened new hope for the cirrhotic patients but both the procedures are ineffective and useless in the presence of advanced hepatocellular damage (Sherlock, 1968, Ellis, 1962) when associated with this disease. Supportive treatment still therefore holds good and the results of this study proved that for supportive treatment the drug ‘Liv.52’ would improve definitely the hepatocellular damage and bring new hope to the cirrhotics, if treated for a long time.

SUMMARY

Standard B.S.P. test was done in 42 needle biopsy confirmed cases of hepatic cirrhosis before and after treatment with an indigenous drug 'Liv.52'. Out of 42 cases 27 were treated with the drug and 15 with placebo for a period of 3, 6 and 9 months.

Statistical evaluation of result of therapy based on B.S.P. values showed significant improvement of hepatocellular function in the group of cases treated for 9 months with 'Liv.52'. Treatment with the drug for 3 and 6 months and placebo treatment of all duration had insignificant results.

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