(***Probe*** (1973): (XIII), 1, 1-8)

Clinical Evaluation of Liv.52 Therapy in Malnutrition During Infancy and Childhood

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Millions of children in India are suffering from malnutrition. The problem of malnutrition is most marked during the rapidly growing period of infancy and early childhood, as the child is exposed to many infections, negative food habits and social customs governing its upbringing. Various regimes have been tried in the management of malnutrition, like various preparations of food substances, anabolic steroids, antihistaminics, tetracyclines, etc. It is claimed that Liv.52 assists weight gain and hence we undertook this trial.

Anorexia is a common feature of malnutrition and to overcome it is, many a time, certainly difficult. Liv.52 is claimed to have choleretic and stimulating action on the liver, which brings to the optimal level the complicated functional mechanism of the liver and revives lost appetite. It promotes nitrogen retention thereby increasing growth. Similar properties have also been claimed for anabolic steroids but they cannot be used for long periods without any untoward effect on the growing child.

COMPOSITION, ACTIVE PRINCIPLES AND PROPERTIES OF LIV.52

Properties of the drugs enumerated here are according to the Indian Materia Medica by Nadkarni (1954) and Chopra (1958) and are as follows:

1. *Capparis spinosa* (Hindi: Kabra)
Active principles are glucoside and rutin. It is used in loss of appetite and scurvy.

2. *Cassia occidentalis* (Hindi: Kasondi)
Active principles are achrosine, tannic acid, fatty matters, sugar etc. It is used to relieve spasm and is also useful in relieving the flatulence of the dyspeptics.

3. *Cichorium intybus* (Hindi: Kasni)
Active principles are glucoside, cichorin, bitter principle lactucin. It is useful in obstructions or torpor of liver and in checking bilious enlargement of spleen with general dropsy. Flowers made into sherbat are given in liver disorders.

4. *Solanum nigrum* (Hindi: Makoi)
Active principles are alkaloids, solanine and solanidine. It is useful in inflammatory swellings and chronic cirrhosis of the liver and affections of the spleen.

5. *Terminalia arjuna* (Hindi: Arjuna)
Active principles are sodium carbonate, calcium carbonate and alkaline chlorides.

6. *Tamarix gallica* (Hindi: Jhau)

Active principle is tannic acid. It is a mild laxative as it causes soft motions without irritation to bowels. It has a sweet taste and so is suitable for children.

7. *Achillea millefolium*
Active principles are glucoside and achillein.

8. Mandur bhasma
Active principle is ferroso-ferric oxide. It is a haematinic.

MATERIAL AND METHODS
The present trial on Liv.52 has been carried out in 30 cases of malnutrition while 10 cases served as a control. The patients for the present study were selected from the Children Medical Out-patient Department and Children Medical Ward, J.A. Group of Hospitals, attached to G.R. Medical College, Gwalior. The selected cases were from various age groups and of either sex.

A detailed history of each case was taken regarding infectious diseases in the past, socio-economic status of the family, environmental contact, dietetic status, milestones and family illness. A thorough physical and clinical examination was done in each case. Laboratory tests included haemoglobin estimation, total red blood corpuscles count, total and differential white blood corpuscles count, routine and microscopic examination of urine and stool.

Special attention was given, in each case, to the presence of minor ailments, e.g. diarrhoea, worm infestations and infection, so that the results would not be vitiated. They were treated promptly and patients were included in the series only when cured.

40 cases, included in the present series, were divided into two groups.

1. Group A — 30 cases — Liv.52 was given in addition to routine dietetic therapy.
2. Group B — 10 cases — Routine dietetic therapy without Liv.52 served as control.

Liv.52 was given in the following schedule:

	Drops	Syrup	Tablets
Infants	5 drops t.i.d.	1 cc. t.i.d.	—
Children			
Below 3 years	10 drops t.i.d	2.5 cc. b.d.	—
Above 3 years	—	1 t.s.f. t.i.d.	1 tab. b.d.

All the patients of group A and B in the series, were given the proper amount of proteins and calories in the form of a balanced diet containing milk, eggs, banana and other additional carbohydrate foods to make up calories and other essential vitamins and minerals for the age. The child's capacity to digest the diet was taken into consideration in increasing the daily requirements under proper supervision. Steady weight gain was taken as the primary indication to assume the adequacy of proteins and calories in a particular case for which bi-weekly thorough check-up was done.

Most of the children of both the groups were followed up for 45 days after being included in the series. Improvement in symptoms, in all cases, specially anorexia, swelling of the limbs, skin changes, irritability, were recorded weekly, a record of weight gain was maintained bi-weekly while estimation of haemoglobin was repeated after every week.

OBSERVATIONS

The following observations were recorded.

Table 1: Showing sex incidence in malnutrition				
Sex	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
Male	19	63.33	6	60
Female	11	36.66	4	40
Total	30	100	10	100

Table 2: Showing age incidence in malnutrition				
Age	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
0 – 1 years	11	36.66	2	20
1 – 2 years	9	30.00	3	30
2 – 3 years	4	13.33	5	50
3 – 4 years	4	13.33	–	–
4 – 5 years	2	6.66	–	–
Total	30	100%	10	100%

Table 3: Showing per capita monthly income of affected families				
Range in Rs.	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
0 – 15	3	10.00	1	10
16 – 25	17	56.67	4	40
25 – 50	8	26.66	5	50
50 – 75	2	6.66	–	–
Total	30	100%	10	100%

Table 4: Showing symptomatology in malnutrition				
Symptoms	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
Anorexia	25	83.34	9	90
Diarrhoea	24	80.00	7	70
Failure to grow	21	70.00	7	70
Irritability	19	63.33	8	80
Swelling over lower limbs	13	43.33	4	40
Skin changes	13	43.33	4	40
Fever	11	36.66	2	20
Cough	8	26.66	2	20
Vomiting	6	20.00	3	30
Ulcers over tongue	4	13.33	2	20

Table 5: Showing physical signs in malnutrition				
Signs	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
Underweight	30	100	10	100
Loss of subcutaneous fat	28	93.33	6	60
Hair changes	24	80.00	9	90
Anaemia	23	76.66	10	100
Hepatomegaly	21	70.00	7	70
Wrinkling of skin	16	53.33	5	50
Oedema	14	46.66	4	40
Below normal height	12	40.00	5	50
Hypovitaminosis	8	26.66	4	40
Dermatosis	6	20.00	3	30
Stomatitis	4	13.33	2	20
Evidences of scurvy	1	3.33	—	—
Ascites	1	3.33	—	—

Table 6: Showing percentage of expected weight for the age				
Range	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
25 – 50%	21	70.00	6	60
51 – 65%	7	23.33	3	30
66 – 90%	2	6.66	1	10
Total	30	100%	10	100%

Table 7: Showing degree of malnutrition				
Degree	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
Ist Degree	21	70.00	6	60
IInd Degree	7	23.33	3	30
IIIrd Degree	2	6.66	1	10
Total	30	100%	10	100%

Table 8: Showing type of malnutrition				
Type of malnutrition	Group A (Treated)		Group B (Control)	
	No. of cases	%	No. of cases	%
Marasmic Malnutrition	20	66.67	6	60
Kwashiorkor	3	10.00	2	20
Oedematous Malnutrition	3	10.0	–	–
Marasmic Kwashiorkor	4	13.33	2	20
Total	30	100%	10	100%

Table 9: Showing improvement in symptomatology in patients in group A and B after starting the therapy		
Symptoms	Group A in days	Group B in days
Anorexia	6	13
Diarrhoea	3	5
Irritability	6	10
Swelling over lower limbs	9	14
Skin changes	15	21
Fever	3	4
Vomiting	2	3
Ulcers over tongue	5	7

Table 10: Showing mean weight gain after 7th, 15th, 30th and 45th day of starting treatment					
	Grade of malnutrition	7th day	15th day	30th day	45th day
Group A (treated)	I	0.3 kg	0.5 kg	0.62 kg	0.8 kg
	II	0.4 kg	1.2 kg	1.55 kg	2.0 kg
	III	0.5 kg	1.5 kg	1.8 kg	2.2 kg
Group B (control)	I	0.2 kg	0.3 kg	0.4 kg	0.8 kg
	II	0.25 kg	0.5 kg	0.75 kg	1.1 kg
	III	0.4 kg	0.8 kg	1.1 kg	1.3 kg

DISCUSSION

Sheth *et al* (1963) reported that Liv.52 has a salutary effect in cases of anorexia of varied aetiology. Athavale (1966) noticed marked improvement in appetite with Liv.52 therapy. Kale *et al* (1966) tried Liv.52 on 54 female albino rats of similar age and weight and found that there was a significant gain in weight as compared to the control group. Srinivasan *et al* (1968) reported the increased rate of gain in weight and spontaneous food consumption as compared to the controls, in freshly weaned guinea-pigs when Liv.52 was administered.

Mukherjee (1969) administered Liv.52 in those children who did not show any improvement in appetite with haematinics and vitamins in their convalescent period, and found a definite improvement in appetite and well-being. Prasad *et al* (1969) tried Liv.52 in 12 cases of malnutrition and found a good response in 66.7% and fair response in 33.3%. the most significant feature of adding Liv.52 to the therapy was the immense increase in appetite and power to assimilate without bowel disturbances in all cases of malnutrition. This was in a much shorter time than in the control group. Indira Bai (1970) reported the early return of appetite and regain of body weight after administering Liv.52. Dayal *et al* (1970), in a study of 31 cases of malnutrition with Liv.52 therapy, reported that there was a distinct improvement in general condition, return of appetite and weight gain.

Kulkarni *et al* (1970) reported that Liv.52, like anabolic steroids, can promote growth even in the presence of a catabolic agent. Prasad *et al* (1971) tried Liv.52 as an adjunct to medical treatment in marasmic malnutrition and found all increased in weight in the course of 3 weeks treatment. Saxena (1971) reported that Liv.52 has a definite and well established place in the therapy of anorexia. Shesha Chari (1971) reported a distinct improvement in appetite within 10 days of treatment with the drug. Kulkarni *et al* (1971) concluded that Liv.52 by its anabolic activity counteracts the catabolic activity of prednisolone as efficiently as the anabolic steroids. Tirumala Rao *et al* (1972) found that Liv.52 has similar actions in producing a positive nitrogen balance as the anabolic steroids, usually given to promote better growth and development in marasmic children. Kulkarni *et al* (1972) studied the effect of Liv.52 on nitrogen balance and androgenic activity and reported that Liv.52 has anabolic activity without any overt androgenic activity in rats; especially when they are in negative nitrogen balance.

The present study of 40 infants and children comprised 25 males and 15 females. Majority of cases (34 cases) were below 3 years of age, which reflects, to some extent, a higher incidence of malnutrition in younger children (Table 1 and 2).

Anorexia, diarrhoea, failure to grow, swelling over limbs and skin changes were the most frequent symptoms in children having malnutrition in the present series (Table 4). Underweight, loss of subcutaneous fat, hair changes, anaemia, hepatomegaly, oedema were the commonly elicited signs in infants and children included in the present series (Table 5).

Almost two-thirds of cases (65%) in the present series were suffering from marasmic malnutrition, 15% from marasmic kwashiorkor, 12.5% from kwashiorkor while 7.5% of cases from oedematous malnutrition (Table 8).

As is evident from Table 9 the improvement in symptoms was recorded earlier in cases of group A than in group B. This observation of improvement in group A in the present series may be, because of an indirect effect of Liv.52, as it has got hepatic stimulant and choleretic actions.

In 85% of cases in the present series, anorexia was found to be the commonest problem for which parents have consulted the paediatrician. It has been observed that anorexia has improved, to the extent, comparable to normal appetite, significantly earlier in group A cases (average 6 days) than in control cases (average 13 days) (Table 9).

The mean increase in gain in weight in group A, in grade I malnutrition was recorded 0.8 kg in contrast to 0.6 kg in control cases, in grade II malnutrition 2 kg in comparison to 1.1 kg and IIIrd grade of malnutrition 2.2 kg in comparison to 1.3 kg. In both the group of cases, it was observed that the maximum gain in weight occurred in the first 15 days of the therapy and was in proportion to the severity of malnutrition (Table 10).

In the present series, children of group A and group B, were selected from similar age groups, suffering from a comparable severity of malnutrition and similar type of food was provided to both of them – the only difference being that in group A cases, Liv.52 therapy was administered in addition to diet therapy while in group B cases, Liv.52 was not administered. We have seen that in group A cases, the return of appetite was earlier, improvement in symptoms quicker and rate of gain in weight was much more rapid than in group B cases. Though we could not evaluate any definite mechanism of action of Liv.52 in cases of malnutrition from the present study, we observed that the drug has some action which brings about a marked improvement in appetite, a feeling of well-being, gain in weight and nitrogen retention. The property concerning nitrogen retention of Liv.52, from this study, appears to be like that of anabolic steroids.

CONCLUSION

The exact mode of action of Liv.52 as far as gain in weight is concerned, is not fully understood, but it appears that as Liv.52 is a powerful hepatic stimulant and choleretic it markedly increases the functional efficiency of the liver, and by its multifaceted action of promoting various enzymatic activities, stimulates the complex mechanism of appetite. Thus Liv.52 has a definite role in getting over the initial anorexia as evidenced by the improvement in the clinical signs. The study has shown that Liv.52 has a similar action in improving nitrogen balance as the anabolic steroids.

Liv.52 has a definite place in the therapy to promote a better nutritional balance in the paediatric age group, which is generally affected by various degrees of malnutritions.

SUMMARY

A clinical trial of Liv.52 in children with various degrees of malnutrition was undertaken in 30 cases, while 10 cases served as control. The recovery was assessed by physical and clinical examinations. The therapeutic results have been compared with control cases.

The drug is safe, non-toxic and it has multiple actions i.e. hepatic stimulant, choleretic, stomachic, anabolic, aetiotropic and encourages normal growth in children. From the present study it appears that Liv.52 has a definite and well-established place in the therapy of anorexia and malnutrition.

ACKNOWLEDGEMENT
We are thankful to Professor I.P. Agrawal, Dean G.R. Medical College, and Dr. Hissamuddin, Joint Director and Superintendent, J.A. Group of Hospitals, Gwalior, for permission to publish the article. We thank M/s Himalaya Drug Co. Private Ltd., for the liberal supply of Liv.52 used in these clinical trials.

REFERENCES

1. Athavale, V.B., 'Mechanism of anorexia and effect of Liv.52 on food intake'; *Probe* (1966): 6, 12.
2. Chopra, R.N., Chopra, I.C., Handa, K.L., Kapur, L.D., (1958) *Chopra's Indigenous drugs of India*, 2nd Ed.
3. Dayal, R.S., Kalra, K., Rajvanshi, V.S. and Baheti, P.C., 'A clinico-pathological study of hepatomegaly with special reference to Liv.52 therapy', *Journal of the Indian Medical Profession* (1970): 9, 7768.
4. Indira Bai, K., Mallikarjuna Rao, V.P.R. and Subba Rao, K.V., "Therapy of anorexia with Liv.52', *The Antiseptic* (1970): 8, 615.
5. Kale, A.K., Kulkarni, (Mrs.) S.D., Joglekar, G.V. and Balwani, J.H., 'Effect of Liv.52 on growth and alcohol induced hepatic dysfunction in rats', *Current Medical Practice* (1966): 10, 240.
6. Kulkarni, S.D. and Joglekar, G.V., 'Effect of Liv.52 on growing rats under the influence of corticosteroids', *Indian Practitioner* (1970): 5, 299.
7. Kulkarni, S.D., Kulkarni, D.S., Vasantgadkar, P.S. and Joglekar, G.V. "Study on Liv.52 – an indigenous anabolic compound', *Indian Practitioner* (1971): 2, 145.
8. Mukherji, J.P., 'Treatment of anorexia by Liv.52', *Probe* (1969): 1, 25.
9. Nadkarni, A.K. (1954) Dr. K.M. Nadkarni's *Indian Materia Medica*, 3rd Ed. The Popular Book Depot, Bombay-7 and Dhootpapeshwar Prakashan Ltd., Panvel.
10. Prasad, L.S. and Tripathi, D., 'Studies with Liv.52', *Probe* (1969): 1,1.
11. Prasad, L.S. and Prasad, K., 'Some observations on Liv.52 in the treatment of infective hepatitis and cirrhosis of the liver', *Probe* (1971): 3, 114.
12. Saxena, S., 'Liv.52 in anorexia in paediatric practice', *Current Medical Practice* (1971): 1, 580.
13. Sesha Chari, K.R., *Bharat Medical Journal* (1971): 2, 181.
14. Sheth, S.C., Tibrewala, N.S., Warerker, U.R. and Karande, V.S., 'Therapy of anorexia with Liv.52', *Probe* (1963): 4, 137.
15. Shrinivasan, S. and Balwani, J.H. 'Effect of Liv.52 on the growth and food consumption of Laboratory animals', *Indian Veterinary Journal* (1968): 45, 773.
16. Tirumala Rao, P., Khan, A.M. and Anjaiah, K., 'The effect of Liv.52 on the pattern of weight gain in children with marasmus and other degrees of malnutrition as compared with that of non-virilising androgens', *Probe* (1973): 2, 78.