

THE TREATMENT OF POSTOPERATIVE HYPOPROTEINEMIA IN PATIENTS WITH CANCER OF THE COLON AND RECTUM*

GEORGE E. BINKLEY, M. B. (Tor.), JULES C. ABELS, M.D.,†

AND

C. P. RHOADS, M.D.

NEW YORK, N. Y.

FROM THE COLON AND RECTUM SERVICE OF MEMORIAL HOSPITAL, NEW YORK, N. Y.

THE PHYSIOLOGIC DERANGEMENT of patients with cancer of the colon and the rectum deserves careful consideration when surgery is contemplated. The ability of these patients to maintain normal levels of serum protein and a satisfactory status of liver function before and after operation are important factors in the successful treatment of their disease. There is considerable evidence to show that a persistent hypoproteinemia may result in tissue edema, ascites, altered motility of the gastro-intestinal tract, wound disruptions, and an increased susceptibility to infection.¹ The many complications that may follow major surgery in patients with liver disease is common clinical knowledge. These range from febrile reaction to sudden death from so-called liver shock.² Experience in our clinic has proven that many of these complications can be avoided when the patient maintains a satisfactory level of serum protein. Moreover, we feel that during the past few years, since this factor of hypoproteinemia has been given careful attention, the postoperative mortality and morbidity have been decreased (Table I).

TABLE I
OPERATIONS WITH OPERATIVE MORTALITY ON THE COLON AND RECTUM SERVICE—YEAR 1942

Type of Operation	Number of Patients	Deaths
<i>Rectum:</i>		
Abdomino-perineal (one stage)	55	0
Perineal Resection:		
With abdominal colostomy	8	
With perineal colostomy	2	0
Colostomies	54	6
<i>Colon:</i>		
Iliotransversecolostomy	4	0
Resection of right colon	3	0
Resection of left colon (Mikulicz)	8	0
Resection of transverse colon (Mikulicz)	1	0
Exploratory for carcinomatosis	2	1
Cecostomy	1	1

Previous investigations in this hospital of a group of patients with cancer of the esophagus, stomach, colon and rectum revealed that 58 per cent in this group were hypoproteinemic.³ Also, in a study of 100 patients with gastric cancer, hypoproteinemia was found preoperatively in 67 per cent.⁴ In the

* This investigation was undertaken with the aid of a grant from the National Cancer Institute.

† Finney-Howell Fellow.

latter group the hypoproteinemia was due chiefly to an inability of the livers of these individuals to fabricate albumins rather than to a deficiency of protein in the diet or to an increased protein catabolism.⁵

In the present communication an analysis of a group of patients with malignant neoplasms of the colon and the rectum is presented. An effort was made to determine in these patients the frequency and degree of hypoproteinemia before and after they were subjected to operation, and to suggest a type of treatment which was found to be satisfactory for this disorder.

In all, 65 patients were studied. These were selected from 100 consecutive admissions to the Rectum and Colon Service. The remaining 35 were discarded because of inadequate studies and reports. The diagnosis was proven in all instances. The tumors were located as follows: Ten in the right colon, 14 in the left colon, and 41 in the rectum or rectosigmoid. All patients were submitted to and survived operation. The procedure consisted of radical resection of the tumor in the patients considered operable, and a short-circuiting, palliative procedure in those who had reached the inoperable stage.

Determination of the serum protein was made by the falling-drop method of Weech, *et al.*⁶ Levels below 6.5 grams per cent were considered abnormal.^{4, 7}

In the 65 patients, hypoproteinemia was noted preoperatively in 23, or 36 per cent. This figure is lower than that found in the patients with gastrointestinal cancer³ and also lower than that in patients with gastric cancer.⁴ Apparently, the incidence and severity of the hypoproteinemia in these individuals could not be correlated with their ingestion of protein. Sixty of the 65 patients were considered to have ingested normal diets until the time of admission (Table II).

TABLE II
THE PREOPERATIVE LEVELS OF SERUM PROTEIN IN PATIENTS WITH CANCER OF THE RECTUM AND COLON

Serum Protein, Gm. per 100 Ml.	No. of Patients Preoperatively	No. of Patients on Adequate Diets	No. of Patients on Inadequate Diets or who Suffered from Diarrhea
4.6—5.0	0	0	0
5.1—5.5	3	2	1
5.6—6.0	3	3	0
6.1—6.5	17	14	3
6.6—7.0	21	18	3
7.1—7.5	18	15	3
7.6—8.0	3	3	0

It is very important to note that after operation almost all the patients with cancer of the rectum and colon became hypoproteinemic. In the first postoperative week 56 of the 65 patients (86 per cent) had abnormally low levels. Preoperative, none of these patients had concentrations of less than 5.1 grams per cent, but after operation four had these very low levels. Likewise, only three had preoperatively concentrations of from 5.1 to 5.5 grams per cent, but after operation 21 had levels in this range (Table III).

TABLE III

THE PRE- AND POSTOPERATIVE LEVELS OF SERUM PROTEIN IN PATIENTS WITH CANCER OF THE RECTUM AND COLON

Serum Protein, Gm. per 100 Ml.	No. of Patients Preoperatively	No. of Patients Postoperatively
4.6—5.0	0	4
5.1—5.5	3	21
5.6—6.0	3	21
6.1—6.5	17	10
6.6—7.0	21	6
7.1—7.5	18	2
7.6—8.0	3	1

Fifty-two of the 65 patients studied received parenteral protein therapy. Apparently, a normal level of protein cannot always be obtained and maintained by dietary nitrogen nor even by the intravenous administration of from 20 to 60 grams of amino-acids (Table IV). It has been found necessary for this purpose to use blood, plasma, and a high protein-carbohydrate diet. Whole blood was employed in most instances, since its administration

TABLE IV

THE LEVELS OF SERUM PROTEIN IN PATIENTS WITH CANCER OF THE RECTUM AND COLON, WHO RECEIVED NO PARENTERAL PROTEIN POSTOPERATIVELY

Patient	Serum Protein, Gm. per 100 Ml.		Amount and Source of Nitrogen Postoperatively	Days of Nitrogen Source Administration	Serum Protein Level after Nitrogen Administration Gm. per 100 Ml.	Surgical Complication
	Preoperatively	1st Day Postoperatively				
F.G.....	6.2	5.4	Intravenous amino-acids, 15-60 Gm., q.d.	10	5.5	Ileus
A.E.....	6.4	6.0	Oral protein, 40 Gm., q.d.	5	5.5	
L.G.....	6.7	6.2	Oral protein,	8	5.9	
E.K.....	6.5	5.9	Intravenous amino-acids, 15-40 Gm., q.d.	7	6.0	
K.D.....	6.4	5.3	Oral protein, 45-70 Gm., q.d.	10	5.4	Marked abdominal distention
I.C.....	—	5.4	Intravenous amino-acids, 30-75 Gm., q.d.	12	5.6	Wound disruption
B.C.....	6.4	5.9	Oral protein, 40 Gm., q.d.	14	5.9	
K.P.....	6.6	—	Oral protein, 30-60 Gm., q.d. 45 Gm., q.d.	18	5.7	Wound disruption

not only increases the level of serum protein but also the red count and the hemoglobin content. Infusions of blood plasma were given to those patients who had hypoproteinemia unassociated with anemia. As soon as the patients could tolerate food after operation, high protein diets were used in all instances. Milk protein was given from the third or fourth postoperative day and the amount increased until the patients received about 100 grams daily. Thirty-two patients received only blood transfusions, while 20 received both whole blood and plasma. By these measures it was possible

POSTOPERATIVE HYPOPROTEINEMIA

to raise the concentrations of serum protein in 46 of the 52 patients. These increases ranged from 0.2 to 2.1 grams per cent, and the average increase was 1.6 grams per cent. All the levels finally were above 5.0 grams per cent (Table V). Fifty of the 52 patients (96 per cent) were hypoproteinemic after operation, but after the treatment described only 24, or 46 per cent, had serum protein levels below normal.

TABLE V
THE SERUM PROTEIN LEVELS IN PATIENTS WITH CANCER OF THE RECTUM AND COLON, PREOPERATIVELY, POSTOPERATIVELY, AND AFTER THERAPY

Serum Protein, Gm. per 100 Ml.	Number of Patients		After Therapy
	Preoperatively	Postoperatively	
4.6—5.0	0	4	0
5.1—5.5	2	20	3
5.6—6.0	3	17	5
6.1—6.5	13	9	16
6.6—7.0	19	2	20
7.1—7.5	13	0	6
7.6—8.0	1	0	2

Although it is essential to combat immediately the hypoproteinemia in patients subjected to surgery by the repeated administration of blood or plasma, it would not be possible to continue such procedures indefinitely. However, if the hypoproteinemia which developed after surgical manipulation was only a transitory affair, then the temporary replacement of serum protein by infusion would be feasible until that time when the patient would fabricate sufficient protein from dietary nitrogen. In order to ascertain whether or not patients with cancer of the colon and rectum eventually could depend only upon dietary nitrogen to maintain their preoperative or normal concentrations of serum protein, determinations of that substance were made in a group of 14 patients at variable periods after they had received their last infusion of blood or plasma (Table VI). With but one exception, it was found that the serum protein levels of these individuals,

TABLE VI
THE ABILITY OF PATIENTS WITH CANCER OF THE RECTUM AND COLON TO FABRICATE PROTEIN AFTER OPERATION

Patient	Serum Protein, Gm. per 100 Ml.			
	Preoperative Level	Level During First Week Postoperative	Days After Last Infusion	Level At That Time
A.W.....	6.8	5.7	60	7.5
H.R.....	7.8	6.4	20	6.8
J.C.....	6.6	5.2	34	7.5
A.R.....	6.6	5.7	150	7.0
J.F.....	7.6	5.4	100	6.6
C.C.....	5.3	4.8	30	6.3
J.D.....	7.1	6.6	84	6.3
J.R.....	6.7	5.0	23	6.6
K.D.....	6.4	5.0	30	6.4
E.S.....	7.0	6.2	55	6.4
A.E.....	6.4	5.5	20	6.8
L.C.....	7.5	5.7	22	7.1
C.D.....	7.1	5.3	20	7.0
A.M.....	6.8	6.1	31	6.9

from 20 to 150 days after they received their last parenteral protein, were significantly higher than the levels during the first postoperative week. Of the 14 patients, one had hypoproteinemia preoperatively; during the first postoperative week this abnormality was noted in 13; and, finally, considerably after the last parenteral protein, only four still had mild reductions of their serum protein concentrations. These observations would indicate, therefore, that the chief purpose of the measures taken in this investigation to combat postoperative hypoproteinemia was to supply enough protein during that short period when the surgical procedure might have increased protein catabolism or impaired protein fabrication.

The ability to counteract hypoproteinemia was greatly handicapped by the presence of acute infections. Of the 52 patients studied, in which the above form of treatment was instituted, six failed to obtain any increase in the serum protein level; and four of these six suffered with an acute infection. In these instances, the refractory hypoproteinemia might have been due to the effects of the infection on the liver or to additional protein catabolism. Other workers⁸ have demonstrated the presence of impaired hepatic function during pneumonia, sepsis, and acute rheumatic fever.

Eighteen of the 52 patients studied had infections of the genito-urinary tract for which sulphone drugs were employed. It was noted that the amount of blood and plasma required to combat the hypoproteinemia of these individuals was greater than that needed for the patients without infections. The former group received from 500 to 3150 ml. of blood, the average being 1800 ml., while the average amount of blood required for the latter group with hypoproteinemia ranged from 250 to 2700 ml. and averaged 950 ml. The average amount of plasma was 1200 ml. for the patients with infections, and 740 ml. for those who did not develop infections. Of the 18 patients with bladder infections, four, or 23 per cent, failed to show any rise in their levels of serum protein during the first 14 days of treatment. In ten other instances, or 55 per cent, an increase of the serum protein level was noted only after the 14th day of treatment (Table VII).

TABLE VII
THE ABILITY OF INFECTION TO IMPAIR THE EFFECTS OF HIGH PROTEIN THERAPY

	Patients without Infection of the Bladder	Patients with Infection of the Bladder
Number.....	34	18
No serum protein rise after therapy in.....	6%	23%
Delayed serum protein rise (14 days or more) in....	29%	55%

These findings strongly suggest that the treatment of hypoproteinemia is made much more difficult by the presence of infection, which seems to set up a vicious circle in that it induces a fall in the serum protein level, and the presence of hypoproteinemia decreases the patient's resistance.¹ In certain of these individuals with infection it may be difficult or impossible to maintain a satisfactory serum protein concentration; nevertheless, the administration of blood or plasma in these instances probably avoids the

development of dangerously low serum protein levels and consequent grave surgical complications.

CONCLUSIONS

1. The incidence of hypoproteinemia in patients with cancer of the rectum and colon was found to be 36 per cent. This incidence is increased to 86 per cent after the patients have been subjected to surgical procedure.

2. In the early preoperative period, hypoproteinemia is best treated by intravenous plasma protein. Later in the convalescence, sufficient amounts of dietary nitrogen may be ingested to counteract the postoperative hypoproteinemia.

3. It is believed that the correction of the postoperative hypoproteinemia is, in great part, responsible for the decreased mortality among patients with rectal and colon cancer.

4. The presence of infection in the patients studied considerably impairs the effectiveness of the measures outlined to combat the hypoproteinemia.

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