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Studies on Gastrointestinal Plasma Protein Loss in Extensive Skin Disease

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Abstract. The gastrointestinal loss of plasma protein was determined in 9 patients with extensive skin disease. $^{51}CrCl_3$ was used as the test substance in 5 patients and [^{131}I]albumin in 4 patients. The fecal isotope excretion was within the normal limits in all patients, though they had hypoalbuminaemia and increased initial disappearance rate of tracer albumin, presumably reflecting an abnormal leakiness of the microvasculature. It is concluded that loss of albumin through the gut does not account for the depressed plasma albumin concentration in these patients.

Key words: Albumin; skin disease; Gastrointestinal protein loss; Microvascular permeability; Transcapillary escape rate of proteins; Hypoalbuminaemia

There is evidence that extensive skin disease may be accompanied by dermatogenic enteropathy[10]. Thus several authors have found malabsorption of fat, D-xylose, iron, vitamin B_{12}, lactose and structural changes of the intestine (1, 3, 9, 10).

It has been postulated that intestinal plasma protein loss follows this involvement of the gut, but experimental evidence is sparse (11).

Protein-losing gastroenteropathy is no remote suggestion as an explanation for the hypoalbuminaemia that is almost always present in patients with extensive skin disease, but dilution or displacement of the intravascular albumin mass, proteinuria, or increased endogenous catabolism might equally well be the cause. However, we have previously found no evidence of dilution and proteinuria (5, 6).

The present study was designed to elucidate whether patients with extensive skin disease and hypoalbuminaemia have an abnormal leakage of plasma protein to the gastrointestinal tract.

METHODS

Nine patients, 4 females and 5 males aged 42–78 (mean 58 years) were examined. The clinical data are given in Table 1. Five patients had erythroderma, due to psoriasis in 4 and of an unknown cause in one (case no. 5).

Routine laboratory values, chest X-ray, ECG and clinical examination revealed no other major disease but the skin disease.

Measurements of gastrointestinal leakage of plasma protein

For technical reasons two methods were applied. In 4 patients a weighed dose of about 20 μCi ^{131}I-labelled albumin (code IK 21 S, Institute for Atomic Energy, Kjeller, Norway) was given intravenously. The thyroid gland was blocked with potassium iodine 100 mg daily (cases 1–4). In another 5 patients a weighed dose of about 50 μCi $^{51}CrCl_3$ (code CJS.2P, Radiochemical Centre, Amersham, England) was given intravenously (cases 5–9). The stools were collected from the time of injection until they became red following oral administration of 1 g carmine 96 h after injection of one of the tracers. The activity of ^{131}I or ^{51}Cr in the stools and in a standard solution of the injected tracer was determined twice in a shielded whole-body counter. The fecal loss of the isotope was expressed as a percentage of the injected dose.

Transcapillary escape rate (TER)

The transcapillary escape rate was calculated from the initial slope of the plasma disappearance curve after injection of [^{131}I]albumin or [^{125}I]albumin (code IT 21 S, Institute for Atomic Energy, Kjeller, Norway). [^{125}I]albumin (code IT 21 S, Institute for Atomic Energy, Kjeller, Norway). [^{125}I]albumin was used in 3 of the cases examined

Table 1. *Gastrointestinal protein loss determined with [^{131}I]albumin or $^{51}CrCl_3$, plasma albumin concentration, transcapillary escape rate of albumin (TER_{alb}), intravascular mass of albumin (IVM_{alb}) in 9 patients with extensive skin disease*

Case no.	Diagnoses	Skin involvement (%)	Fecal ^{131}I loss (% of injected dose)	Fecal ^{51}Cr loss (% of injected dose)	TER_{alb} (% IVM × h^{-1})	Albumin (g/l)	IVM_{alb} (g/m^2)
1	Eczema	80	0.17		6.9	31.0	53.0
2	Erythroderma	Generalized	0.21		8.7	29.3	54.4
3	Erythroderma	Generalized	0.19		11.4	36.4	51.4
4	Psoriasis	80	0.16		7.3	28.2	41.8
5	Erythroderma	Generalized		0.34	8.6	35.5	50.6
6	Erythroderma	Generalized		0.67	8.3	30.3	48.2
7	Eczema	80		0.43	7.5	32.8	60.7
8	Atopic dermatitis	75		0.60		31.9	
9	Erythroderma	Generalized		0.65		35.1	
Mean			0.18	0.54	8.4	32.3	51.4
± S.D.			0.02	0.15	1.5	2.9	5.8
Controls ($N=10$)							
Mean			0–0.40[a]	0–0.80[a]	5.2	41.5	68.0
± S.D.					1.1	2.4	9.6
$p<$			N.S.	N.S.	0.001	0.001	0.005

[a] Values from Jarnum et al. (4).

with $^{51}CrCl_3$. The technique and theoretical basis for the calculation of TER have been described previously (5).

Intravascular mass of albumin (IVM_{alb})

IVM_{alb} equals plasma volume × plasma albumin concentration.

Statistics

The fecal isotope excretion was compared with the normal values stated by Jarnum et al. (4). The other measurements were compared with those obtained in 10 normal adults by exactly the same technique. The control group matched the patients with regard to sex, age and surface area. Student's *t*-test was used for statistical evaluation.

RESULTS

The results are shown in Table 1. The isotope content in the stools was in all cases within the normal range. TER_{alb} (mean 8.4% IVM × h^{-1} ± 1.5 S.D.) was significantly higher than that of the control group (mean 5.2% IVM × h^{-1} ± 1.1 S.D.) ($p<0.001$). The mean plasma albumin concentration and the mean IVM_{alb} were significantly lower than the control values ($p<0.001$ and 0.005 respectively).

The patients examined with ^{131}I-albumin did not differ from those examined with $^{51}CrCl_3$, either with respect to the clinical data or to the results obtained.

DISCUSSION

The possible causes of hypoalbuminaemia in patients with extensive skin disease are increased loss of albumin, dilution due to increased plasma volume, displacement of albumin from the intravascular to the extravascular space and/or changes in the albumin metabolism. In a completely comparable group of patients we recently found the urinary albumin excretion to be normal (6), a slight decrease in plasma volume and a pronounced decrease of the intravascular mass of albumin even after the leakage of albumin from the microvasculature was normalized following treatment with systemic steroid (5).

The term dermatogenic enteropathy was introduced by Shuster & Marks (9), indicating that a skin disease might cause malabsorption, and that the severity of malabsorption was proportional to the extent of the skin disease (10). Subsequently somewhat conflicting results have been published (1, 3, 8).

Most studies have been based on determination of the fecal fat excretion, D-xylose absorption and the structural changes of the intestinal mucosa. Only very few studies have dealt with the problem of protein-losing enteropathy in such patients.

Fecal nitrogen content examined in one patient

with generalized dermatitis and hypoproteinaemia was within normal limits (7). Braverman (2) found normal fecal isotope excretion after intravenous injection of [^{131}I]albumin in 7 patients with severe pustular psoriasis and hypoalbuminaemia.

In contrast Shuster & Wilkinson (11) found increased loss of protein to the gut in 2 out of 5 patients with erythroderma and concluded that the hypoalbuminaemia in these patients was partly due to protein loss through the gut. In later reports Shuster and co-workers suggested that it might be due to a dermatogenic enteropathy or associated with increased capillary permeability (9, 10).

This study, however, demonstrates that patients with increased initial disappearance rate of tracer albumin—presumably reflecting an abnormal leakiness of the microvasculature—have no detectable gastrointestinal protein loss.

The diagnoses and extent of the skin diseases in this study seem to be comparable to those published by Shuster & Wilkinson (11). Differences in methodology might therefore explain the discrepancy.

$^{51}CrCl_3$ is almost non-absorbable from the gastrointestinal tract and has proved to be a reliable substance for the quantitative estimation of gastrointestinal protein loss (4, 12).

[^{131}I]albumin may underestimate the protein loss due to intestinal reabsorption of the isotope, though the method has proved valid as a diagnostic test (4). The normal results obtained in this study are substantiated by the normal results obtained with $^{51}CrCl_3$.

Shuster & Wilkinson (11) used [^{131}I]polyvinylpyrrolidase (PVP), a substance which is less reliable than $^{51}CrCl_3$ for quantitative measurements of the intestinal protein loss (4).

The urinary excretion of the isotope during the first 5 days after administration of [^{131}I]albumin and $^{51}CrCl_3$ is about 30% of the dose given, whereas the urinary isotope excretion after [^{131}I]PVP is considerable, and can amount to 90% of the dose (12). Urinary contamination of the stools is a source of error whichever test substance is applied, but will especially invalidate the results obtained with [^{131}I]PVP.

It seems reasonable to conclude that loss of albumin through the gut does not account for the lowered plasma albumin concentration in patients with extensive skin disease. Increased albumin catabolism was found in the studies of Shuster & Wilkinson (11) and of Braverman (2). It is likely that a leaky microvasculature as reflected by an increased TER_{alb} is accompanied by or causes changes in the endogenous metabolism and that this is the main cause of the hypoalbuminaemia.

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