Is There a Venoarterial Difference in α_1 -Antitrypsin Levels?

JACK LIEBERMAN

British Medical Journal, 1974, 3, 93-94

Summary

Serum trypsin inhibitory capacity and α_1 -antitrypsin concentrations were compared in venous and arterial bloods obtained simultaneously from patients with chronic airways obstruction. No significant venoarterial difference was observed in most patients, which was contrary to the published findings of Woolcock *et al.* (1972).

Introduction

α_1 -Antitrypsin in blood is postulated to protect the lungs from the destructive actions of leucocytic proteases during intrapulmonary infections or inflammation (Lieberman, 1973). Woolcock *et al.* (1972) published data suggesting that the level of α_1 -antitrypsin in arterial blood is lower than that in venous blood in the presence of chronic airways obstruction and pulmonary infections. They suggest that the immunological property of α_1 -antitrypsin is altered as it passes through the lungs, perhaps by attachment of the α_1 -antitrypsin to proteolytic enzymes, thereby causing an apparent venoarterial difference in concentration. Their data were based upon a radial immunodiffusion assay for α_1 -antitrypsin performed upon arterial and venous bloods drawn from patients with various types of lung disease. These authors found a mean percentage difference between venous and arterial α_1 -antitrypsin of 9.9% in the group with obstructive lung diseases (range 0-15.7%). A few individuals with known lung infection had even higher differences ranging up to 37% higher venous levels.

The present study was an attempt to confirm the observations of Woolcock *et al.*, and to extend the investigation to include a measure of the serum trypsin inhibitory capacity (S.T.I.C.) as well as α_1 -antitrypsin concentration via radial immunodiffusion assay.

Patients and Methods

Arterial and venous blood samples were drawn from 50 consecutive patients undergoing medical blood gas studies in the pulmonary physiology laboratories of the City of Hope National Medical Center. All of these patients were subjected to a complete panel of pulmonary function studies including measurements of the vital capacity (VC), forced expiratory volume in one second (FEV₁), and functional residual capacity (FRC). These data were used for identifying those individuals with significant chronic obstruction of airways.

S.T.I.C. was measured with benzoyl-L-arginine-ethyl ester substrate as described previously (Lieberman, 1969) in units representing mg trypsin inhibited by 1 ml serum. The α_1 -antitrypsin concentration was assayed with commercially obtained radial immunodiffusion plates (Kallestad Laboratories, Chaska, Minnesota) using the standards provided with these kits.

Results

The values for venous and arterial S.T.I.C. in 48 of the subjects are plotted on the graph. Data from two patients with S.T.I.C. values greater than 2.5 units are not shown. The data show that the venous S.T.I.C. was higher than the arterial value in only half of the patients and equal or lower than the arterial values in the others.

Comparison of serum trypsin inhibitory capacity (S.T.I.C.) values for arterial and venous blood from 48 patients. O = severe chronic airways obstruction, Δ = no chronic airways obstruction, ● = mild chronic airways obstruction.

Most patients had chronic airways obstruction consistent with a diagnosis of pulmonary emphysema (36 out of 50), but 21 of the 50 subjects were classified as having severe obstructive pulmonary disease in that their FRC was greater than 150% of normal and/or the FEV₁ was 50% or less of the VC (see table). In 12 of those with severe obstructive diseases the venous S.T.I.C. was greater than the arterial S.T.I.C., in three the values were identical, and in six the S.T.I.C. was higher in the arterial blood than in the venous blood. The mean venous-arterial difference ($\pm$ S.D.) expressed as a percentage of the venous level was $+2.50 \pm 6.6$. This was not considered to be a significant difference since it was within the acceptable range of variation for the S.T.I.C. assay in our laboratory. The mean venous S.T.I.C. of 1.317 ± 0.232 units was not significantly higher than the mean arterial S.T.I.C. of 1.285 ± 0.251 units.

Measurements of α_1 -antitrypsin by the radial immunodiffusion technique showed essentially no difference between the arterial and venous samples in most cases. Two patients with the greatest venoarterial differences in S.T.I.C. did show parallel differences by radial immunodiffusion. One patient had 19.5% higher venous S.T.I.C. and 15% higher α_1 -antitrypsin concentration by radial immunodiffusion. A second patient had 11.7% higher venous S.T.I.C. and 6.3% higher α_1 -antitrypsin level by radial immunodiffusion.

Discussion

Contrary to the findings of Woolcock *et al.* (1972) we did not

Department of Respiratory Disease, City of Hope National Medical Center, Duarte, California

JACK LIEBERMAN, M.D., Acting Director

Data from 21 Cases with Severe Chronic Airways Obstruction

Case No.	S.T.I.C.			α_1 -Antitrypsin			Pulmonary Function		
	Venous (Units*)	Arterial (Units*)	% Difference	Venous (mg/100 ml)	Arterial (mg/100 ml)	% Difference	VC (% of Predicted)	FRC (% of Predicted)	FEV ₁ (% of VC)
1	1.200	1.133	+5.6	180	180	0	84	300	29
2	1.043	0.970	+7.0	240	240	0	96	230	27
3	1.351	1.285	+4.9	200	200	0	85	222	33
4	1.209	1.209	0	240	240	0	67	198	35
5	1.000	0.805	+19.5	200	170	+15.0	111	193	29
6	1.444	1.425	+1.3	215	215	0	112	193	42
7	1.202	1.135	+5.6	191	194	-1.6	100	186	40
8	1.563	1.516	+3.0	275	275	0	57	185	42
9	1.240	1.178	+5.0	240	240	0	74	183	31
10	1.400	1.400	0	215	215	0	63	177	33
11	1.487	1.487	0	225	225	0	63	173	56
12	1.651	1.552	+6.0	275	275	0	76	175	19
13	1.486	1.425	+4.1	240	240	0	56	172	44
14	1.284	1.300	-1.3	220	220	0	61	168	37
15	1.000	1.105	-10.5	220	220	0	102	157	66
16	1.875	1.944	-3.7	215	240	-11.6	62	156	57
17	1.269	1.169	+7.9	200	215	-7.5	62	154	27
18	1.382	1.419	-2.7	235	235	0	81	146	37
19	1.400	1.438	-2.7	320	320	0	56	140	35
20	1.265	1.117	+11.7	240	225	+6.3	69	127	44
21	0.896	0.969	-8.2	240	240	0	32	100	33

S.T.I.C. = Serum trypsin inhibitory capacity.

*Units = mg trypsin inhibited by 1 ml serum.

find any significant venoarterial difference in α_1 -antitrypsin activity or concentration in individuals with chronic obstructive lung diseases. In only two out of 21 patients with severe airways obstruction was there a significantly higher level of α_1 -antitrypsin in the venous blood than in the arterial blood as determined by two assay procedures. This suggests that a venoarterial difference in α_1 -antitrypsin concentration may occur in some unusual instances, but certainly not in most patients with airways obstruction, as reported by Woolcock *et al.* (1972).

Woolcock *et al.* postulated that their findings were possibly due to the binding of α_1 -antitrypsin to a protease during passage of the blood through the lungs, with alteration of the antigenic properties of α_1 -antitrypsin. In our experience binding of α_1 -antitrypsin to a protease is most effectively observed by a loss of the α_1 -antitrypsin activity (reduced S.T.I.C.) rather than by any decrease in α_1 -antitrypsin concentration as detected by immunological assays. Thus, one would expect an assessment of S.T.I.C. to be more sensitive for showing such venoarterial differences in α_1 -antitrypsin. Protease-inhibitor complexes

usually have altered electrophoretic mobility but can be detected by immunological techniques (Ohlsson, 1971).

Thus, there is no significant venoarterial difference in α_1 -antitrypsin concentration in most individuals with severe obstructive lung diseases.

The author was supported by grant no. HL 13398 from the National Institutes of Health and by the Helen Galland Research Fund.

Requests for reprints should be addressed to: Dr. Jack Lieberman, City of Hope National Medical Center, 1500 East Duarte Road, Duarte, California 91010.

References

- Lieberman, J. (1969). *New England Journal of Medicine*, **281**, 279.
 Lieberman, J. (1973). *Medical Clinics of North America*, **57**, 691.
 Ohlsson, K. (1971). *Scandinavian Journal of Clinical Lab Investigation*, **28**, 225.
 Woolcock, A. J., Green, W., and Crockett, A. (1972). *British Medical Journal*, **2**, 134.

Prevention of Postoperative Deep Venous Thrombosis in Legs by Orally administered Hydroxychloroquine Sulphate

A. E. CARTER, R. EBAN

British Medical Journal, 1974, 3, 94-95

Summary

In a series of patients given hydroxychloroquine sulphate by mouth before and after major surgery the incidence of deep venous thrombosis in the legs, as assessed by iodine-125-tagged fibrinogen scanning and venography, was reduced to 5% compared with an incidence of 16% in a similar untreated group of patients.

Introduction

Past observations (Carter *et al.*, 1971) had suggested that hydroxychloroquine sulphate was an effective agent in reducing deep venous thrombosis in the leg after major surgery. Hydroxychloroquine sulphate is not an anticoagulant and is effective orally in safe doses. When given as a preoperative loading dose of 1,200 mg in divided doses during the 24 hours preceding operation followed by 800 mg daily in two divided doses until discharge from hospital the incidence of deep vein thrombosis, as assessed by ¹²⁵I-tagged human fibrinogen leg scanning and venography was reduced from a control level of 16% to 5% in treated patients ($P < 0.005$).

Patients and Methods

Patient Selection.—Male and female patients over the age of 45

King Edward Memorial Hospital, London W13 9NU

A. E. CARTER, F.R.C.S., Consultant Surgeon

R. EBAN, F.F.R., Consultant Radiologist