DMSO and colchicine therapy in amyloid disease^{*}

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SUMMARY There is no specific therapy for primary amyloidosis, and acquired generalised amyloidosis can be treated only if the underlying disease is eliminated. In this study we have investigated the role of colchicine therapy in primary amyloidosis, and dimethylsulphoxide (DMSO) in leprosy associated secondary amyloidosis. No effect on creatinine clearance or 24 h proteinuria could be observed in the patients with primary amyloidosis. In the DMSO group renal function was considerably improved in 3 patients with moderate renal failure but not in those with severe renal impairment (creatinine clearance < 10 ml/min). Serum SAA determinations were not particularly informative. These findings point to a beneficial effect of DMSO in human secondary amyloidosis when given at an early stage of renal involvement.

In the past few years dimethylsulphoxide (DMSO) and colchicine have been suggested as methods of treatment for human amyloidosis.¹⁻⁵ In the present study we have looked at the effects of oral DMSO in 5 patients with biopsy-proved renal amyloidosis secondary to lepromatous leprosy, and of colchicine in 5 patients with primary amyloidosis.

Materials and methods

Patients were admitted to Hospital Lauro Souza Lima, a special hospital for leprosy in the City of Bauru, State of St Paulo, and classified by histological examination of biopsy specimens according to the Ridley and Jopling system. Five patients were classified as polar lepromatous and were included in the biopsy proven associated renal amyloidosis study. Patients with primary amyloid disease were followed up as outpatients at the Division of Immunology, Instituto Arnaldo Vieira Carvalho.

SERUM AMYLOID PROTEIN (SAA) DETERMINATIONS

The level of SAA in serum samples was determined

by radioimmunoassay as previously described by means of antiserum to amyloid protein SAA and ¹²⁵I labelled amyloid protein (AA). The antiserum was prepared in rabbits by immunisation with purified AA.^{6,7}

DMSO ('Pro-analyse' quality obtained from Carlo Erba, Brazil) was administered by mouth as 1.0 g in 5 ml distilled water 3 times daily for 6 consecutive months.

Patients with primary amyloidosis were given 1.0 g of colchicine daily for 6 consecutive months. Both groups of patients received exclusively DMSO or colchicine; no other form of treatment was given.

Results and discussion

Table 1 summarises the results obtained with DMSO in secondary amyloidosis. Four patients showed some improvement in their renal function (patients 1, 2, 3, and 4) as judged by creatinine clearance and/or 24 h proteinuria. Fluctuations of serum SAA levels did not show any significant trend. All patients receiving DMSO had bad smelling breath (produced by partial conversion of DMSO into the radical sulphoxide).

Table 2 shows the results with the use of colchicine in patients with primary amyloidosis. On the protocol used colchicine did not appear to alter renal function during 6 months of continuous use.

We concluded that in patients with generalised amyloidosis secondary to chronic infection the

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Table 1 The effect of oral DMSO on renal function and SAA levels after 3 and 6 months' daily administration: secondary amyloidosis

Patient	Proteinuria 24 h (g/l)			Creatinine clearance (ml/min)			SAA (U/ml)		
	0	3	6	0	3	6	0	3	6
1	1.7	2.5	1.5	6.5	18.7	10.9	45	25	60
2	6.5	6.0	6.9	44.6	32.7	60.7	160	45	140
3	6.7	3.4	2.7	117	113	135	1350	1300	—
4	0.45	0.47	0.13	18	44.3	43	50	150	350
5	7.02	8.8	4.6	5.4	7.8	4.8	45	230	1700

continuous use of oral DMSO appeared to lead to modest improvement in renal function, particularly in patients who still retained some renal function. Similar results were obtained by other investigators in secondary amyloid disease.⁸⁻¹⁰ No considerations can be drawn with regard to the amount of amyloid deposited in the kidney, since none of the patients was examined by biopsy again after treatment.

The lack of correlation between renal function and serum SAA levels agrees with our previous experience.^{6,7}

The possible mechanisms of action of DMSO is still poorly understood. It is known to be an anti-inflammatory agent with a mode of action which includes stabilisation of lysosomal membranes.¹¹ The original work with DMSO in amyloidosis suggested that this compound could make the amyloid fibril soluble or accessible to proteolytic digestion.¹

Colchicine has been used extensively in the treatment of amyloidosis associated with familial Mediterranean fever.¹² In a preliminary report Rubinow *et al.*¹³ have suggested a beneficial effect on other forms of amyloidosis in man. Our experience has so far failed to show any beneficial effect of

colchicine in patients with the primary form of the disease.

Current pathogenetic studies of amyloidosis have pointed to similar mechanisms operating in primary and secondary amyloidosis.¹⁴ Colchicine appeared to be effective in the treatment of murine casein-induced amyloidosis, a model comparable to the secondary form of the disease in man. Our disappointing results with colchicine in primary amyloid disease await confirmation but suggest a heterogeneity of amyloidogenesis in man.¹⁵

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Table 2 The effect of colchicine on renal function after 3 and 6 months' daily administration: primary amyloidosis

Patient	Proteinuria 24 h (g/l)			Creatinine clearance (ml/min)		
	0	3	6	0	3	6
1	12.0	8.0	19.0	62	45	46
2	8.0	12.5	21.0	85	80	76
3	25.0	18.0	15.0	45	58	53
4	7.0	4.5	3.8	115	100	102
5	6.0	—	6.5	75	92	85

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