South African Medical Journal : Suid-Afrikaanse Tydskrif vir Geneeskunde

Cape Town, 22 April 1961 Volume 35 No. 16 Deel 35 Kaapstad, 22 April 1961

THE TREATMENT OF PLEURAL EFFUSION IN BANTU MINE LABOURERS

A FURTHER THERAPEUTIC TRIAL

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Pleurisy with effusion as an isolated finding is usually the result of tuberculosis, neoplasm, thrombo-embolic disease, or pneumonia, although other pathological processes may also be responsible. However, it is well known that the aetiological diagnosis may frequently remain in doubt even after full and prolonged study, including bacteriological and cytological examination of the fluid, pleural biopsy, and thoracoscopy. This difficulty applies equally to the pleural effusions which occur so commonly in the Bantu mine labourers employed in the gold-mining industry of South Africa, and although tuberculosis (in other populations) is generally regarded as the most likely cause of this condition, especially in young persons, this view is by no means accepted as far as these labourers are concerned.

We recently reported the results of a controlled therapeutic trial in which 4 different methods of treating these so-called 'idiopathic' pleural effusions in Bantu mine labourers were evaluated.[1] These treatments were: (1) Standard antituberculous therapy, (2) standard antituberculous therapy combined with prednisolone, (3) penicillin, and (4) ascorbic acid. The results indicated that antituberculous therapy combined with prednisolone was markedly superior to the other three methods of treatment. Although we had little doubt that the vast majority of these effusions were in fact tuberculous in nature, we were not surprised that the antituberculous drugs alone proved no better than treatment with penicillin or vitamin C, for it had previously been demonstrated[2,3] that, whereas antituberculous therapy was extremely effective in preventing subsequent frank tuberculosis, it had little influence on the actual rate of fluid absorption.

The view has been put forward[2-5] that pleural effusion is largely an allergic manifestation of the tuberculous process. We had thought therefore that the addition of adrenal steroid to the antituberculous therapy would have proved advantageous. The inclusion in our trial of a group of patients receiving adrenal steroids only was deemed inadvisable because of the hazard of causing dissemination of the supposed tuberculous process. As already mentioned, the trial included groups of patients receiving penicillin and ascorbic acid, but these drugs proved to have no appreciable effect on the disease. These groups served as controls against which the other two methods of treatment could be judged.

The superiority of antituberculous therapy combined with prednisolone was clearly demonstrated, but the trial was extended when the opportunity arose to use methylprednisolone ('medrol', Upjohn) instead of prednisolone. The present report details the outcome. Groups receiving penicillin and ascorbic acid were, for the reasons already stated, omitted on this occasion.

METHOD

The method which we followed was that employed in the original trial save that the treatment groups were reduced from 4 to 2. All cases of pleural effusion occurring in the Bantu mine labourers employed by the Central Mining-Rand Mines Group were admitted to a central hospital after the diagnosis was confirmed by an X-ray examination of the chest and the aspiration of 20 c.c. of fluid from the pleural cavity. Paracentesis was limited to this amount so as to avoid the possible beneficial effect of aspirating larger amounts. The fluid was submitted for full bacteriological examination including cultural and biological tests.

On admission to the central hospital, the X-ray examination was repeated. Each patient was subjected to a full clinical examination; and a blood count, a test for the erythrocyte sedimentation rate (Wintrobe), a Mantoux skin test (1/1,000 KOT), and a sputum examination for acid-fast bacilli were carried out. All cases showing evidence of additional pathology such as abdominal masses or cervical adenopathy were excluded.

A panel of doctors reviewed each case and allocated a score to the effusion ranging from 1 - 4, depending on whether it was considered to occupy $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ or the whole of the hemithorax respectively. Minimal effusions were not accepted and occasionally $\frac{1}{2}$ scores, e.g. $2\frac{1}{2}$ were given. One of two methods of treatment were allocated by means of drawing lots: *Treatment T*, 1 gram of streptomycin sulphate intramuscularly daily for 8 weeks and 200 mg. of isoniazid 3 times daily for 8 weeks; *treatment TS*, same as treatment T but with the addition of 8 mg. of methyl-prednisolone ('medrol') 3 times daily for 2 days followed by 4 mg. 3 times daily for the remainder of the 8 weeks.

The period of bed rest varied from case to case, but when allowed up all patients were confined to the pre-

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cincts of the ward. All patients received a standard hospital diet and in addition 3 tablets of vitamin B.Co. daily.

The X-ray examination and sedimentation rate were repeated after 4 weeks of treatment at which time the panel reviewed each patient without knowledge of the treatment received. The process was repeated on the completion of the trial at the end of 8 weeks.

TABLE I. CHANGES IN EXTENT OF EFFUSION

Treatment T				*Treatment TS*			
Patient	*Initial*	*4 weeks*	*8 weeks*	*Patient*	*Initial*	*4 weeks*	*8 weeks*
101	4	3½	3½	102	1	—	—
103	1½	1	1	104	1½	1	1
105	2	2	2	108	1½	1	½
107	2½	2	2	110	1	½	½
109	3	—	—	114	1½	½	—
111	2	1	—	116	1½	—	—
113	1	—	—	118	1	1	—
115	2	2	1½	120	1½	½	—
117	2½	2½	2	122	2½	—	—
119	3	1	1	124	1½	1	1
121	4	4	4	126	1	½	½
123	4	1½	—	128	1½	—	—
125	1½	1	—	130	4	3½	3½
127	2	1	—	132	2½	—	—
131	4	3½	2½	134	2	—	—
133	2	1	1	136	2	—	—
135	2	½	—	138	3	—	—
137	2½	1	1	140	3	—	—
139	3	1½	1	142	2½	—	—
141	3	2½	2	144	2	—	—
143	1	1	1	146	2	1	1
145	2	—	—	148	4	2	½
147	3	1½	½	150	2	1½	1
149	3	2	1½	152	1	½	—
151	2½	1½	1	154	1½	—	—
153	1½	1	—	156	1½	1	½
155	½	—	—	158	1	—	—
157	4	3	2½	160	4	—	—
159	2½	2	2	162	4	4	4
161	3	1½	1½	164	3½	1	—
163	1½	1	1	166	2½	½	—
165	1½	½	—	168	1½	½	—
167	2½	1	½	170	2½	1	½
169	2½	1	1	172	½	—	—
171	3½	2½	2	174	3	½	—
173	1½	—	—	176	2	½	—
175	1	½	½	178	4	2	½
179	2	—	—	180	3	½	—
181	1	½	—	182	2	½	—
				183	3	—	—
No. of cases	(39)				(40)		
Totals	91½	53	39½		86½	26½	15
Average condition	2·346	1·359	1·013		2·163	·663	·375
Average condition as % of initial	100%	58%	43%		100%	31%	17%

RESULTS

Seventy-nine patients completed the trial, 39 receiving treatment T and 40 TS. In no case were tubercle bacilli recovered from the sputum on direct examination, or from the pleural fluid after cultural and biological examinations. The tuberculin skin test was positive in all instances.

Table I sets out the details of the extent of each effusion initially, after 4 weeks, and after 8 weeks of treatment. At the foot of Table I appear the average sizes of the effusions in each group initially, after 4 weeks, and after 8 weeks. The latter values are also given in terms of percentages of the initial average size taken as 100%.

Using standard statistical techniques, the results show that treatment TS effected a greater average absorption of the fluid than treatment T over the 8 weeks (significant at the 99% level). This superiority is very marked over the first 4 weeks (the difference is significant at the 99% level) but over the second 4 weeks the improvements do not differ significantly between the two groups.

The results in terms of the numbers of totally resolved effusions appear in Table II. Analysis of the data in this

TABLE II. PROPORTION OF COMPLETE RESOLUTIONS

Treatment	*No. of patients*	*First 4 weeks*		*All 8 weeks*	
		Cures	*Cures*	*Cures*	*Cures*
T	39	6	15·4%	14	35·9%
TS	40	16	40%	27	67·5%
TS minus T ..			24·6%		31·6%

manner indicates that over the full 8 weeks treatment TS yields significantly more complete cures than treatment T (at the 99% level). Over the first 4 weeks treatment TS is also superior (significant at the 98·5% level).

The average initial weight was 133 lb. in each treatment group. The average final weights were 133 lb. with treatment T and 135 lb. with treatment TS. The average initial and final ESR values were 32 and 19 in group T, and 23 and 6 in group TS. These figures were not analysed statistically.

DISCUSSION

The results of the trial confirmed those of the previous one,[1] and demonstrated that antituberculous therapy in combination with adrenal steroids is considerably more effective in the treatment of the pleural effusions which are so commonly found in Bantu mine labourers, than is antituberculous therapy alone. In the dosage used, viz. 24 mg. daily for 2 days followed by 12 mg. daily for the remainder of the 8 weeks, methyl-prednisolone appeared to have no advantage over the prednisolone which was used in the original trial. The average amount of fluid remaining per patient was 17% with methyl-prednisolone and 19% with prednisolone, and the corresponding figures for total resolutions were 27 out of 40 cases and 12 out of 20. Possibly the results might have been better with either steroid in higher dosage.

Another aspect of the original trial which was confirmed is that the rate of resolution of fluid is greater in the first 4 weeks of treatment than in the second 4 weeks. If our view is correct that the adrenal hormones act by overcoming the allergic component of a tuberculous process, it is understandable that the effect of these drugs is greater initially. We are unable to say whether the advantage which accrued to the group receiving steroids would have been maintained in a more prolonged trial, nor what a long-term follow up of cases from both treatment groups would reveal. The answer to these and many

other questions which arise from this trial must await further study.

In conclusion, we should like to stress that it is not claimed that these results prove that the bulk of cases of pleurisy with effusion in Bantu mine labourers are in fact tuberculous. Our findings are also not in conflict with the seemingly paradoxical experience of Emerson[2] and Forgacs[3] that the clearing of the fluid in tuberculous pleurisy is not hastened by antituberculous therapy.

SUMMARY

A controlled therapeutic trial was carried out in which two methods of treatment of so-called 'idiopathic' pleural effusions in Bantu mine labourers were compared. These treatments were: (1) Streptomycin sulphate and isoniazid for 8 weeks, 39 cases. (2) The same treatment as (1), but with the addition of methyl-prednisolone ('medrol'), 40 cases.

The results indicated a considerable advantage in favour of the group receiving methyl-prednisolone, both with regard to the average rate of clearing of the pleural fluid and the total number of cases in which complete resolution of the effusion occurred.

In the dosage used, methyl-prednisolone appears to be no more effective than the prednisolone used in the previous trial.

It is recommended that antituberculous drugs with adrenal steroids should be used as a routine in the treatment of 'idiopathic' pleural effusions in Bantu mine labourers and possibly in other populations as well.

We wish to thank the Upjohn Company who supplied the medrol' for the trial. We are grateful to Dr. I. Webster and the staff of the Pneumoconiosis Research Unit of the South African Council for Scientific and Industrial Research who carried out the investigations on the pleural fluid.

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