

Adjunct therapy with corticosteroids or paracentesis for treatment of tuberculous pleural effusion

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المعالجة المساعدة بالكورتيكوستيرويدات أو بالبنزل لعلاج الانصباب الجنبي السلبي
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الخلاصة: أُجريت هذه الدراسة الأترابية الاستباقية في المدة من أيار/مايو 2003 إلى نيسان/إبريل 2004، بغرض التعرف على تأثير المعالجة المساعدة على 190 من المرضى المصابين بالانصباب الجنبي السلبي. وقد قسّم المرضى إلى ثلاث فئات. وتمت معالجة جميع هذه الفئات بالأدوية المضادة للسُّل لمدة 6 أشهر؛ أما الفئة الثانية (وعددتها 46 مريضاً) فقد أُضيف إليها البريدنيزولون بمعدل 30 مغ/يوم لمدة 10 أيام؛ وأما الفئة الثالثة (وعددتها 78 مريضاً) فأُجري لها البنزل لتزح السوائل. وقد لوحظ اختفاء أعراض الحمى والأعراض البنيوية بسرعة أكبر في الفئة الثانية ($P > 0.05$). وبعد 10 أيام لوحظ انخفاض أكبر بدرجة يُعتدُّ بها إحصائياً في حجم الانصباب الجنبي في الفئة الثانية، ولكن لم يكن الفرق بحيث يُعتدُّ به إحصائياً بعد 6 أشهر. واستنتج الباحثان من الدراسة أنه لا لزوم لإعطاء الكورتيكوستيرويدات أو البنزل العلاجي في علاج الانصباب الجنبي السلبي.

ABSTRACT To determine the effect of adjunct therapy, we carried out a prospective cohort study on 190 patients with tuberculous pleural effusion during May 2003–April 2004. Patients were divided into 3 groups. All groups were treated with anti-tuberculosis (TB) drugs for 6 months; in group 2 ($n = 46$) prednisolone, 30 mg/day for 10 days, was added; group 3 ($n = 78$) were given paracentesis to remove fluid. Fever and constitutional symptoms disappeared faster in group 2 ($P > 0.05$). After 10 days, there was a significantly greater reduction in the size of pleural effusion in group 2, but after 6 months the difference was not statistically significant. We found corticosteroids and therapeutic paracentesis are not necessary in the management of TB pleural effusion.

Corticothérapie adjuvante ou ponction pour le traitement de l'épanchement pleural tuberculeux

RÉSUMÉ Afin de déterminer l'effet de la thérapie adjuvante, nous avons réalisé une étude de cohorte prospective chez 190 patients atteints d'épanchement pleural tuberculeux entre mai 2003 et avril 2004. Les patients ont été répartis en trois groupes. Tous les groupes ont été traités par antituberculeux pendant 6 mois ; dans le groupe 2 ($n = 46$), on a donné en supplément 30 mg/jour de prednisolone pendant 10 jours ; dans le groupe 3 ($n = 78$), les sujets ont subi une ponction pour drainer le liquide. La fièvre et les symptômes constitutionnels ont disparu plus rapidement dans le groupe 2 ($p > 0,05$). Après 10 jours, il y avait une réduction significativement plus importante de la dimension de l'épanchement pleural dans le groupe 2, mais après 6 mois, la différence n'était pas statistiquement significative. On constate que les corticoïdes et la ponction évacuatrice ne sont pas nécessaires pour la prise en charge de l'épanchement pleural tuberculeux.

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Received: 20/09/04; accepted: 22/02/05

Introduction

According to World Health Organization (WHO) recommendations, tuberculous pleural effusion is treated according to the category III regimen: 2 months with 3 anti-tuberculosis (TB) drugs followed by 4 months with 2 anti-TB drugs [1].

Adjunct therapy with corticosteroids or pleural fluid aspiration until dryness have been recommended by some researchers [2–5]. Corticosteroids in conjunction with anti-TB drugs may be appropriate in particular forms of TB such as tuberculous meningitis and pericardial and pleural disease [6]. Cohen and Sahn, however, do not recommend routine use of corticosteroids in tuberculous pleural effusion unless there are acute symptoms such as fever, chest pain or dyspnoea that are disturbing to the patient [7]. It has even been suggested that there is insufficient evidence for the effectiveness of adjunctive corticosteroid treatment in such patients [8]. Drug interaction with rifampin should, naturally, be taken into consideration [9].

The aim of this study was to determine the effect of adjunct therapy (corticosteroids and paracentesis) on tuberculous pleural effusion with regard to symptoms, size of the effusion and pleural thickening (scarring).

Methods

We carried out a prospective cohort study of all patients with TB pleural effusion (all biopsy and biochemically confirmed) in Al-Faiha hospital in Basra, Iraq, from May 2003 to April 2004. The study protocol was explained for all patients and informed consent was taken from them. Patients were recruited in 3 groups: group 1 were enrolled in the first 4 months of the study, group 2 after 4 months and group 3 were enrolled in the last 6 months of the study. For all par-

ticipants, the total duration of anti-TB drugs was 6 months.

The patients in group 1 ($n = 66$) were treated with anti-TB drugs only for 6 months, in line with WHO recommendations [1]. Those in group 2 ($n = 46$) were given the same anti-TB drugs plus corticosteroids in the form of prednisolone, 30 mg/day for 10 days. The patients in group 3 ($n = 78$) were treated with the same anti-TB drugs plus ≥ 1 paracentesis on an as-needed basis to remove as much of the fluid as possible until near dryness. All patients were treated in hospital for at least 10 days. Daily records for presence or absence of malaise, anorexia, weakness and night sweating were completed by the doctor using a chart prepared specifically for the purpose.

The size of pleural effusion was estimated according to the chest X-ray findings. Opacified hemithorax of \geq two thirds of the hemithorax was classified as severe grade; if it involved $>$ one third of the hemithorax but $<$ two thirds, it was considered moderate grade; if it involved \leq one third of the hemithorax, it was considered mild grade pleural effusion.

A chest X-ray was taken on diagnosis, again after 10 days, and then monthly for the 6 months of treatment. Reduction in pleural effusion was considered to be 50% if the amount of fluid decreased to a lower grade or 25% if there was reduction in the amount of fluid but still within the same grade.

The size of residual pleural thickening (scarring) was estimated using the same measurement grades as pleural effusion (\geq two thirds of the hemithorax, $>$ one third but $<$ two thirds, and \leq one third). The term “obliteration of costophrenic angle” was used when the angle was $> 90^\circ$.

For statistical analysis, the chi-squared test was used as appropriate. $P < 0.05$ was considered significant throughout the analysis.

Results

The total number of patients was 190, 185 males and 5 females (2 in group 1, 2 in group 2 and 1 in group 3). Age range was 17–45 years. There were no significant differences between the 3 groups regarding age, sex or clinical symptoms (Table 1).

The time of disappearance of fever and constitutional symptoms (malaise, anorexia, weakness, and night sweating) in the group who were treated with adjunct corticosteroids was 4 [standard deviation (SD) 3.2] days compared to 1 (SD 1.3) week in the other 2 groups ($P > 0.05$). Two patients, 1 in the corticosteroid group and the other in group 1, showed paradoxical response to

anti-TB drugs with increase in fever and size of pleural effusion that lasted for 1 month.

Comparisons between lines of treatment of tuberculous pleural effusion are shown in Table 1. There were no differences between the 3 treatment groups with regard to extent of pleural thickening. After 10 days, there was > 50% reduction in the size of pleural effusion in the group having adjunct corticosteroid treatment (group 2) compared with 25% in the other groups. In all groups, there was progressive reduction of size of pleural effusion up to the third month of treatment. After 6 months there was, however, no statistically significant difference between the 3 groups.

Table 1 Comparison of 3 lines of treatment for tuberculous pleural effusion (size of pleural effusion before treatment and pleural thickening at the end of treatment)

Variable	Anti-TB alone ^a		Treatment With steroid ^b		With paracentesis ^c		Total No.
	No.	%	No.	%	No.	%	
<i>Size of pleural effusion before treatment^d</i>							
Severe	8	12.1	13	28.3	31	39.7	52
Moderate	23	34.8	18	39.1	13	16.7	54
Mild	35	53.0	15	32.6	34	43.6	84
<i>Pleural thickening after 6 months treatment^d</i>							
Severe	2	3.0	0	–	2	2.6	4
Moderate	4	6.1	0	–	3	3.8	7
Mild	12	18.2	17 ^e	37.0	11 ^e	14.1	40
Obliteration of costophrenic angle	43	65.2	16 ^e	34.7	59 ^e	75.6	118
Normal chest X-ray	5	7.6	13 ^e	28.3	3 ^e	3.8	21
Total	66		46		78		190

^aMean age 30 (standard deviation 12.5) years.

^bMean age 34 (standard deviation 11.4) years.

^cMean age 28 (standard deviation 10.6) years.

^dSevere: $\geq 2/3$ of the hemithorax; moderate: $> 1/3$ but $< 2/3$; mild: $\leq 1/3$.

^e P -value > 0.05 (compared with anti-TB drugs alone).

Table 2 Comparison of size of pleural effusion at presentation and residual pleural thickening after 6 months treatment

Residual thickening ^a	Mild		Moderate		Severe		Total No.
	No.	%	No.	%	No.	%	
Severe	–		1	1.8	3	5.7	4
Moderate	–		3	5.6	4 ^b	7.7	7
Mild	12	14.3	17 ^b	31.5	11 ^b	21.2	40
Obliteration of costophrenic angle	60	71.4	27 ^b	50.0	31 ^b	59.6	118
Normal chest X-ray	12	14.3	6 ^b	11.1	3 ^b	5.8	21
Total	84		54		52		190

^aSevere: $\geq 2/3$ of the hemithorax; moderate: $> 1/3$ but $< 2/3$; mild: $\leq 1/3$.

^bP-value > 0.05 .

No significant relation was found between size of effusion and later pleural scarring (Table 2).

Discussion

Corticosteroids have been shown to be beneficial in treatment of TB [6, 10, 11] although in the study of Kalita and Misra no benefit was shown, even in tuberculous meningitis [12]. This is not absolute fact, and adjunctive corticosteroid therapy appears to offer significant short-term, but minimal long-term, benefit for patients with TB [11].

In our study, corticosteroids hastened the recovery of constitutional symptoms and led to early reduction in symptoms, but after 6 months there was no difference between the groups. Some researchers are of the opinion that, although benefit has been shown in pleural disease, adjunct therapy is not routinely required unless there are significant systemic symptoms of fever or a particularly large effusion [6].

Though corticosteroids may bring about more rapid resolution of pleural effusion

with less pleural scarring, scarring only rarely presents a problem in any event [5, 13]. Some even advocate repeated paracentesis as superior to other treatments [5, 7].

Similar findings to those in our study were reported in 3 previous studies [3–5], but one of those showed no clinical differences, even in resolution of symptoms in the corticosteroid group, compared to placebo [5].

There were some limitations in this study. There may have been selection bias for the 3 groups, since there was no real randomization and the groups were divided according to the time they presented to us rather than any other parameter, and the duration of corticosteroid treatment may have been shorter and the dosage lower than in previous studies [3–5].

In conclusion, corticosteroid treatment and therapeutic paracentesis are not necessary in the management of tuberculous pleural effusion, and have no effect on extent of residual pleural thickening after 6 months treatment with anti-TB drugs.

References

1. Maher D et al. *Treatment of tuberculosis: guidelines for national programmes*, 2nd ed. Geneva, World Health Organization, 1997:29.
2. Satya Sri S. *Textbook of pulmonary and extrapulmonary tuberculosis*, 2nd ed. New Delhi, Interprint, 1995:82–6.
3. Lee C et al. Corticosteroids in the treatment of tuberculous pleurisy: a double-blind, placebo-controlled, randomized study. *Chest*, 1988, 94(6):1256–9.
4. Galarza I et al. Randomised trial of corticosteroids in the treatment of tuberculous pleurisy. *Thorax*, 1995, 50(12):1305–7.
5. Wyser C et al. Corticosteroids in the treatment of tuberculous pleurisy: a double-blind, placebo-controlled, randomized study. *Chest*, 1996, 110(2):333–8.
6. Alzeer AH, FitzGerald JM. Corticosteroids and tuberculosis: risks and use as adjunct therapy. *Tubercle and lung disease*, 1993, 74(1):6–11.
7. Cohen M, Sahn SA. Resolution of pleural effusions. *Chest*, 2001, 119(5):1547–62.
8. Matchaba PT, Volmink J. Steroids for treating tuberculous pleurisy. *Cochrane database of systematic reviews*, 2000, 2.
9. Grange JM, Winstanley PA, Davies PDO. Clinically significant drug interactions with antituberculosis agents. *Drug safety*, 1994, 11(4):242–51.
10. Alarifi A, Nysten ES. Dislodging sacred dogmas in combating systemic stress: the case for steroids. *Annals of Saudi medicine*, 2000, 20(5,6):358–9.
11. Dooley DP, Carpenter JL, Rademacher S. Adjunctive corticosteroids therapy for tuberculosis: a critical reappraisal of the literature. *Clinical infectious diseases*, 1997, 25(4):872–87.
12. Kalita J, Misra UK. Effect of methyl prednisolone on sensory motor functions in tuberculous meningitis. *Neurology India*, 2001, 49(3):267–71.
13. Hopewell PC. Tuberculosis and nontuberculous mycobacterial infections. In: Stein JH, Daly WJ, eds. *Internal medicine*, 2nd ed. Boston, Little, Brown & Co., 1987:1731–48.