Evidence Update

Tuberculosis Series

Are corticosteroid drugs effective in people with tuberculous meningitis?

Corticosteroids reduce deaths in HIV-negative patients on treatment for tuberculous meningitis.

Inclusion criteria

Studies:

Randomized controlled trials.

Participants:

People with clinically diagnosed tuberculous meningitis.

Intervention:

Intervention: corticosteroids plus antituberculous treatment.

Control: antituberculous treatment with or without placebo.

Outcomes:

Primary: death, death or disabling residual deficit at the end of follow up.

Adverse events: any adverse event.

Results

- Seven trials with 1140 participants were included; allocation concealment was adequate in one trial. Five trials assessed dexamethasone and two assessed prednisolone. Only one trial included HIV -positive participants.
- There were fewer deaths in participants treated with corticosteroids (relative risk 0.78, 95% confidence interval 0.67 to 0.91; 1140 participants, 7 trials). The effect was significant in participants with mild, moderately severe, or severe illness.
- The risk of death or disabling residual neurological deficit was reduced with corticosteroids (relative risk 0.82, 95% confidence interval 0.70 to 0.97; 720 participants, 3 trials).
- One trial stratified the results for death and death or disabling residual deficit by HIV status. The trial did not detect any difference in the effect of corticosteroids between the groups; however, the number of HIV-positive participants included was very small (n = 98).
- Five trials mentioned adverse events, and two reported incidence. Adverse events included gastrointestinal bleeding, bacterial and fungal infections, and hyperglycaemia; the number of events in participants receiving corticosteroids were no more than in the control groups.







Adapted from Prasad K, Singh MB. Corticosteroids for managing tuberculous meningitis. *Cochrane Database of Systematic Reviews* 2008, Issue 1. Art. No.: CD002244. DOI: 10.1002/14651858.CD002244.pub3. *Evidence Update* published in August 2008.

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Corticosteroid vs control: death (stratified by severity of illness)

Study	Corticosteroid n/N	Control n/N	Relative Risk (Fixed) 95% Cl	Weight ୯ଇ	Relative Risk (Fixed) 95% Cl
01 Stagel(mild) Girgis 1991	0/6	2/5 -		9.2	0.17 [0.01, 2.92]
🗙 Kumarvelu 1994	0/2	0/6		0.0	Not estim able
× O'Toole 1969	0/1	0/1		0.0	Not estim able
Thwaites 2004	15/90	26/86		90.8	0.55[0.31,0.97]
Subtotal (95% Cl) Total events: 15 (Cortio Test for heterogeneity Test for overall effect z	chi-square=0.63 df=	98 ol) 1 p=0.43 l² =0.0%	•	100.0	0.52 [0.30, 0.89]
02 Stage II (moderately Girgis 1991	severe) 10/42	18/45		22.3	0.60[0.31,1.14]
Kumarvelu 1994	5/19	5/13		7.6	0.68 [0.25, 1.90]
O'Toole 1969	3/6	5/8		5.5	0.80[0.31, 2.10]
Schoeman 1997	1/30	1/31		1.3	1.03 [0.07, 15.78]
Thwaites 2004	38/122	50/125		63.3	0.78 [0.55, 1.09]
Subtotal (95% CI) Total events: 57 (Cortic Test for heterogeneity Test for overall effect z	chi-square=0.63 df=		•	100.0	0.73 [0.56, 0.97]
03 Stage III (severe) Girgis 1991	10/42	18/45		22.2	0.60[0.31,1.14]
Kumarvelu 1994	0/3	2/4		2.8	0.25 [0.02, 3.86]
Lardizabal 1998	4/29	6/29		7.7	0.67 [0.21, 2.12]
O'Toole 1969	3/4	4/4		5.1	0.75[0.43,1.32]
Schoeman 1997	3/24	12/24		15.3	0.25 [0.08, 0.78]
Thwaites 2004	34/62	36/60		46.8	0.91 [0.67, 1.24]
Subtotal (95% Cl) Total events: 54 (Cortic Test for heterogeneity Test for overall effect z	chi-square=7.04 df=		•	100.0	0.69[0.54,0.90]
		0.0	1 0.1 1 10 avours steroid Favours c	100	

Study	Corticosteroid n/N	Control n/N	Relative Risk (Fixed) 95% Cl	Weight ୯ଇ	Relative Risk (Fixed 95% Cl
Kumarvelu 1994	5/20	8/21		4.5	0.66 [0.26, 1.67]
Schoeman 1997	18/67	32/67	—	18.3	0.56[0.35,0.90]
Thwaites 2004	121/274	134/271		77.2	0.89[0.75,1.07]
Total (95% CI) Total events: 144 (Cor Test for heterogeneity Test for overall effect :	chi-square=3.57 df:		•	100.0	0.82[0.70, 0.97]

Authors' conclusions

Implications for practice:

For HIV-negative people who are being treated for tuberculous meningitis, corticosteroids reduce the risk of death and of disabling residual neurological deficit. There is not enough evidence to assess whether corticosteroids benefit people who are HIV positive.

Implications for research:

New randomized controlled trials are needed to assess the relative effectiveness of different corticosteroids, and the optimum duration of corticosteroid treatment. Trials are also needed to assess the effect of corticosteroid treatment for HIV-positive people with tuberculous meningitis.