Menenjit Tedavisinde Kortikosteroitler

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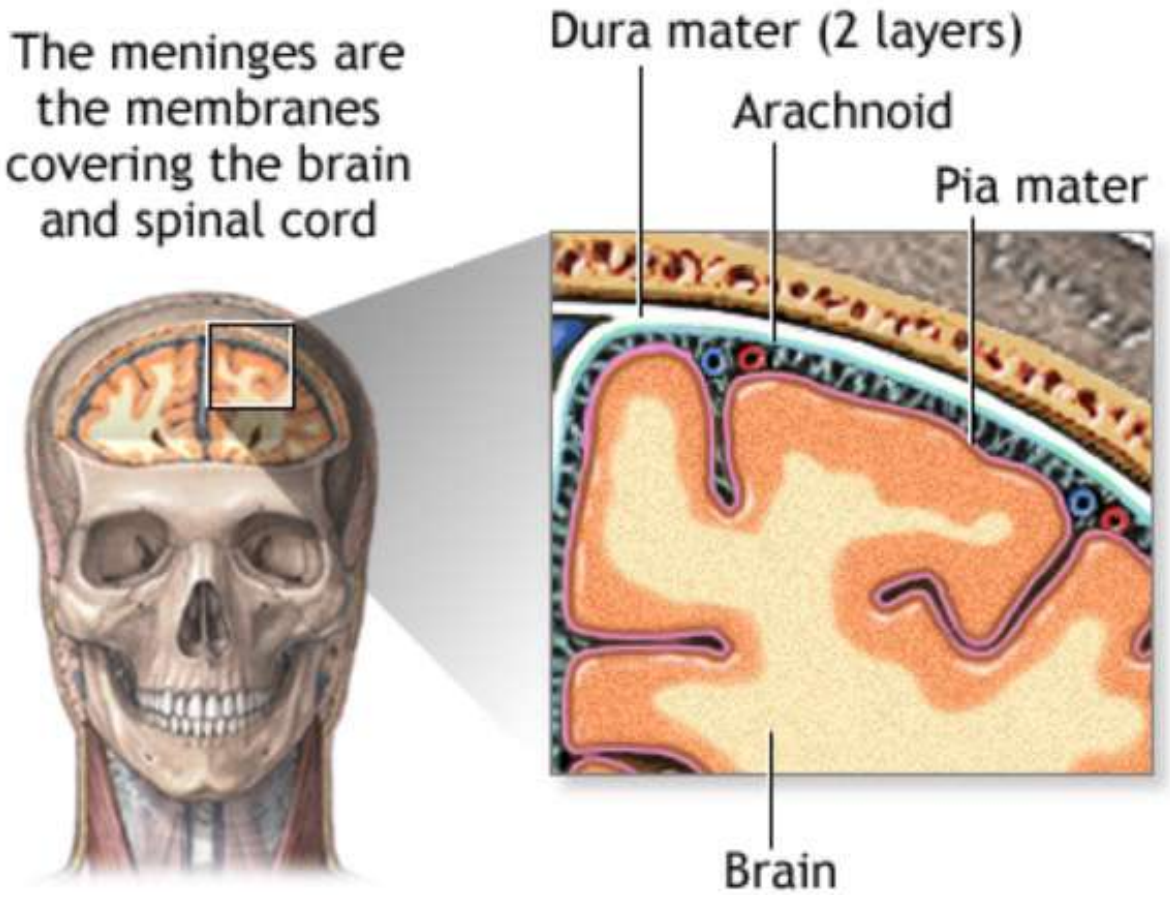
Sunum planı

- Tanım
- Patogenez
- Kortikosteroit kullanımı – Farklı ülke çalışmaları

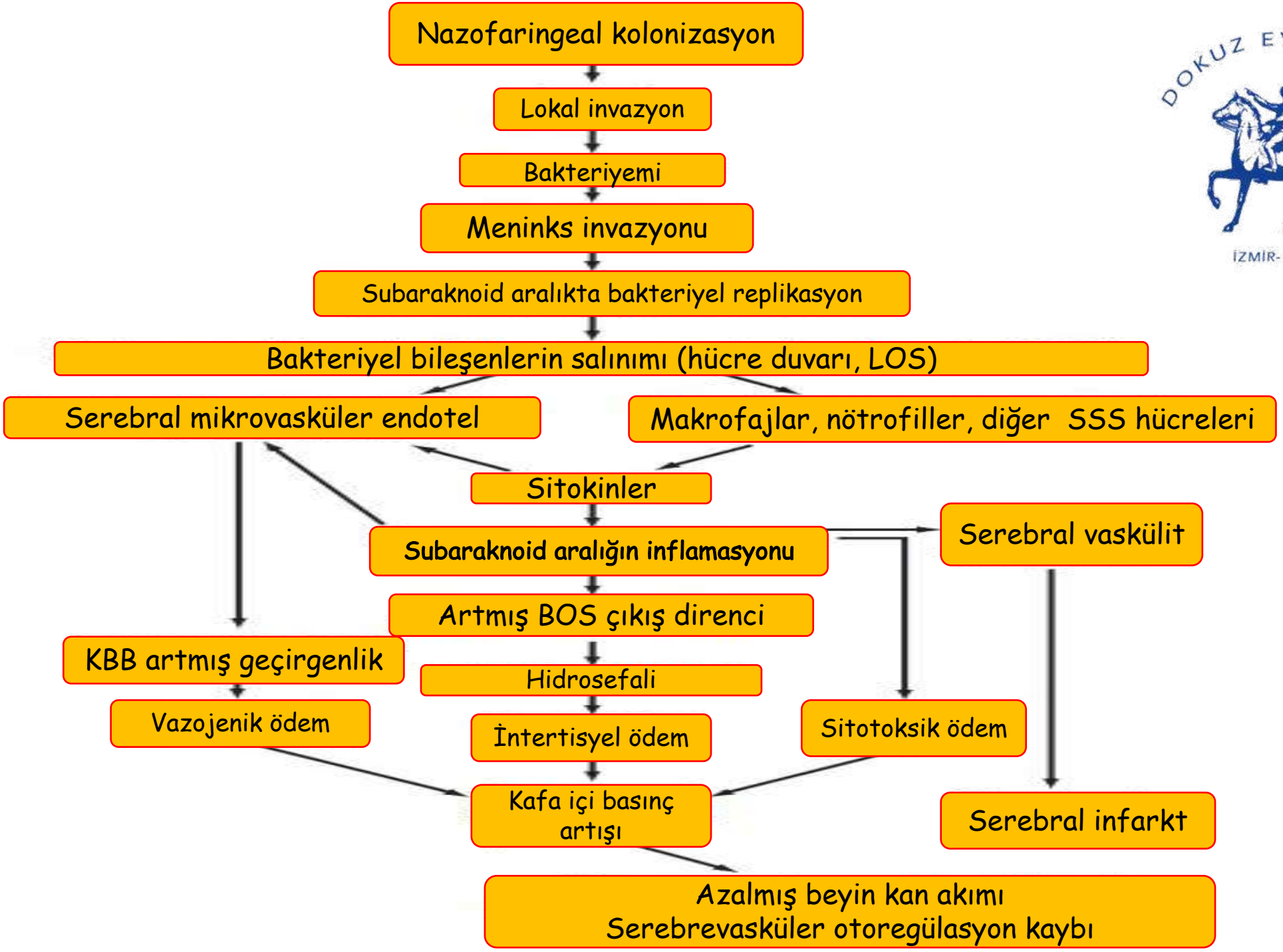
  Bakteriyel menenjitler

  Tüberküloz menenjit
- Sonuç

Tanım



Mikroorganizmaların neden olduğu, meninkslerin akut ve kronik seyirli inflamatuvar hastalığı


Nazofaringeal kolonizasyon
Lokal invazyon
Bakteriyemi
Meninks invazyonu
Subaraknoid aralıkta bakteriyel replikasyon
Bakteriyel bileşenlerin salınımı (hücre duvarı, LOS)
Serebral mikrovasküler endotel
Makrofajlar, nötrofiller, diğer SSS hücreleri
Sitokinler
Subaraknoid aralığın inflamasyonu
Serebral vaskülit
Artmış BOS çıkış direnci
KBB artmış geçirgenlik
Hidrosefali
Vazojenik ödem
İntertisyel ödem
Sitotoksik ödem
Kafa içi basınç artışı
Serebral infarkt
Azalmış beyin kan akımı
Serebrevasküler otoregülasyon kaybı

- Beyin yüzeyi inflamasyonu
- Arter ve ven inflamasyonu
- Beyin içinde basıncı
- Ölüm riski

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Corticosteroids for Bacterial Meningitis in Adults in Sub-Saharan Africa

Matthew Scarborough, M.R.C.P., Stephen B. Gordon, M.D., Christopher J.M. Whitty, F.R.C.P., Neil French, Ph.D., Yasin Njalale, Dip.Med.Sci., Alex Chitani, Dip.Med.Sci., Timothy E.A. Peto, Ph.D., David G. Lalloo, F.R.C.P., and Eduard E. Zijlstra, Ph.D.

- ✓ Randomize, çift kör, plasebo kontrollü
- ✓ 465 hasta (% 90 HIV pozitif)
- ✓ 233 Deksametazon- 232 plasebo
- ✓ Deksametazon mortalite ve morbiditeye etkisi Ø

N Engl J Med 2007;357:2441-50.

ABSTRACT

BACKGROUND

In sub-Saharan Africa, bacterial meningitis is common and is associated with a high mortality. Adjuvant therapy with corticosteroids reduces mortality among adults in the developed world, but it has not been adequately tested in developing countries or in the context of advanced human immunodeficiency virus (HIV) infection.

METHODS

We conducted a randomized, double-blind, placebo-controlled trial of dexametha- ily for 10 days) in adults with an admission diag- tyre, Malawi. The primary outcome was death at

n were HIV-positive, were randomly assigned to or placebo (232 patients) plus intramuscular cef- is ceftriaxone (235 patients). There was no sig- 0 days in the corticosteroid group (129 of 231 ebo group (120 of 228 patients) by intention-to- confidence interval [CI], 0.79 to 1.64) or when ts with proven pneumococcal meningitis (68 of s vs. 72 of 143 patients receiving placebo) (odds e were no significant differences between groups th combined, hearing impairment, and adverse ortality with intravenous ceftriaxone (121 of 230 ular ceftriaxone (128 of 229 patients) (odds ratio,

CONCLUSIONS

Adjuvant therapy with dexamethasone for bacterial meningitis in adults from an area with a high prevalence of HIV did not reduce mortality or morbidity. In this setting, intramuscular administration was not inferior to intravenous administration of ceftriaxone for bacterial meningitis. (Current Controlled Trials number, ISRCTN31371499.)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 13, 2007 VOL. 357 NO. 24

Dexamethasone in Vietnamese Adolescents and Adults with Bacterial Meningitis

Nguyen Thi Hoang Mai, M.D., Tran Thi Hong Chau, M.D., Guy Thwaites, M.D., Ly Van Chuong, M.D., Dinh Xuan Sinh, M.D., Ho Dang Trung Nghia, M.D., Phung Quoc Tuan, M.D., Nguyen Duy Phong, M.D., Nguyen Hoan Phu, M.D., To Song Diep, M.D., Nguyen van Vinh Chau, M.D., Nguyen Minh Duong, M.D., James Campbell, Constance Schultsz, M.D., Chris Parry, M.D., M. Estee Torok, M.D., Nicholas White, F.R.C.P., Nguyen Tran Chinh, M.D., Tran Tinh Hien, M.D., K

BACKGROUND

It is uncertain whether all adults with bacterial men with adjunctive dexamethasone.

METHODS

We conducted a randomized, double-blind, placebo- sone in 435 patients over the age of 14 years who ha tis. The goal was to determine whether dexamethaso 1 month and the risk of death or disability at 6 mon

RESULTS

A total of 217 patients were assigned to the dexame placebo group. Bacterial meningitis was confirmed able meningitis was diagnosed in 123 patients (28.3 sis was made in 12 patients (2.8%). An intention-to-t showed that dexamethasone was not associated with risk of death at 1 month (relative risk, 0.79; 95% co 1.39) or the risk of death or disability at 6 months (o 1.17). In patients with confirmed bacterial meningiti cant reduction in the risk of death at 1 month (relat 0.94) and in the risk of death or disability at 6 mon 0.32 to 0.98). These effects were not found in patients ingitis. Results of multivariate analysis indicated that patients with probable bacterial meningitis was signi increased risk of death at 1 month, an observation that ma of tuberculous meningitis in the treatment group.

CONCLUSIONS

Dexamethasone does not improve the outcome in all adolescents and adults with suspected bacterial meningitis; a beneficial effect appears to be confined to patients with microbiologically proven disease, including those who have received prior treatment with antibiotics. (Current Controlled Trials number, ISRCTN42986828.)

- ✓ Randomize, çift kör, plasebo kontrollü
- ✓ 435 hasta
  - 300 kesin tanı
  - 123 olası
- ✓ Deksametazon mortalite ve morbiditeye etkisi Ø
- ✓ Kesin menenjit tanılı hasta grubunda Morbidite ve mortalitede azalma

N Engl J Med 2007;357:2431-40

Immunological and Biochemical Correlates of Adjunctive Dexamethasone in Vietnamese Adults with Bacterial Meningitis

Nguyen Thi Hoang Mai,[1] Trung Vu Tuan,[2] Marcel Wolbers,[2,3] Dang Minh Hoang,[2] Tran Vu Thieu Nga,[2] Tran Thi Hong Chau,[1] Ly Van Chuong,[1] Dinh Xuan Sinh,[1] Ho Dang Trung Nghia,[1] Nguyen Duy Phong,[1] Nguyen Hoan Phu,[1] To Song Diep,[1] Hoang Thi Thanh Hang,[2] Nguyen van Vinh Chau,[1] Jeremy Farrar,[2,3] Constance Schultsz,[2,3,4] Tran Tinh Hien,[1] and Cameron P. Simmons[2,3]

[1]Hospital for Tropical Diseases and [2]Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam; [3]Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, University of Oxford, Oxford, United Kingdom; and [4]Academic Medical Center, Center for Poverty Related Communicable Diseases, University of Amsterdam, Amsterdam, the Netherlands

Adjunctive treatment to improve outcome from bacterial meningitis has centered on dexamethasone. Among Vietnamese patients with bacterial meningitis, cerebrospinal fluid (CSF) opening pressure and CSF:plasma glucose ratios were significantly improved and levels of CSF cytokines interleukin (IL)–6, IL-8, and IL-10 and were all statistically significantly lower after treatment in patients who were randomized to dexamethasone, compared with levels in patients who received placebo.

Clin Infect Dis. 2009 Nov 1;49(9):1387-92.

Table 2. Cerebrospinal Fluid (CSF) Opening Pressure, Leukocyte Count, and Biochemical Analysis Results for 341 Patients with Confirmed Bacterial Meningitis

CSF parameter	Dexamethasone group (n = 164) At baseline	Dexamethasone group (n = 164) At follow-up[a]	Placebo group (n = 177) At baseline	Placebo group (n = 177) At follow-up[a]	P for unadjusted comparison of follow-up values	Adjusted comparison of follow-up values: Estimate of dexamethasone effect (95% CI)	Adjusted comparison of follow-up values: P
Opening pressure							
No. of patients	128	135	144	143			
Median cm (IQR)	20 (14–34)	13.5 (9–18)	20 (15–28)	14 (11–20)	.04	−1.97 (−3.84 to −0.09)	.04
Leukocyte count							
No. of patients	164	153	176	164			
Median leukocytes per mm³ (IQR)	3785 (1065–8135)	825 (260–2630)	2808 (1138–7433)	865 (400–1943)	.40	0.95 (0.70–1.28)[b]	.74
Glucose level							
No. of patients	164	154	177	164			
Median mg/dL (IQR)	20 (10–36)	63 (45–80)	23 (10–38)	44 (27–55)	<.001	1.61 (1.41–1.84)[b]	<.001
Ratio of CSF glucose to plasma glucose							
No. of patients	162	154	177	162			
Median % (IQR)	15 (8–31)	40 (32–48)	17 (9–30)	37 (24–49)	.02	4.36 (0.84–7.89)	.02
Lactate level							
No. of patients	145	134	156	148			
Median mmol/L (IQR)	11.60 (7.07–17.10)	4.20 (3.33–6.28)	10.80 (6.82–15.72)	4.65 (3.23–6.13)	.73	0.99 (0.88–1.10)[b]	.79
Protein level							
No. of patients	162	148	172	159			
Median mg/L (IQR)	253 (155–419)	108 (69–176)	244 (159–421)	108 (66–165)	.84	1.03 (0.88–1.20)[b]	.70

NOTE. CI, confidence interval; IQR, interquartile range.

[a] The 318 follow-up samples were obtained on days 1–6 after randomization. Sampling day was day 1 for 19 (6%) of patients, day 2 for 218 (69%), day 3 for 69 (22%), day 4 for 5 (2%), day 5 for 3 (1%), and day 6 for 4 (1%).

[b] Because data was log-transformed before analysis, this corresponds to an (antilog-transformed) multiplicative effect (eg, follow-up CSF glucose level for patients who received dexamethasone is estimated to be higher than that for patients who received placebo by a factor of 1.61).

Table 3. Cerebrospinal Fluid (CSF) Cytokine Concentrations at Baseline and Follow-Up for 195 Patients with Confirmed Bacterial Meningitis

CSF parameter	Dexamethasone group (n = 88)		Placebo group (n = 107)		P for unadjusted comparison of follow-up values	Adjusted comparison of follow-up values	
	Baseline	Follow-up[a]	Baseline	Follow-up[a]		Estimate of dexamethasone effect (95% CI)	P
IL-6							
No. (%) of patients with detectable values	83 (94)	83 (94)	103 (96)	105 (98)			
Median $\log_{10}$ pg/mL (IQR) for patients with detectable values	4.97 (4.38–5.37	3.23 (2.43–4.19)	4.89 (4.5–5.5)	3.65 (2.8–4.33)	.01	−0.43 (−0.73 to −0.12)	.006
IL-8							
No. (%) of patients with detectable values	86 (98)	86 (97)	106 (99)	106 (99)			
Median $\log_{10}$ pg/mL (IQR) of patients with detectable values	4.33 (3.81–4.68)	3.24 (2.66–3.69)	4.3 (3.82–4.68)	3.45 (2.94–3.89)	.03	−0.21 (−0.41 to −0.008)	.04
IL-10							
No. (%) of patients with detectable values	83 (94)	43 (49)	106 (99)	74 (69)			
Median $\log_{10}$ pg/mL (IQR) of patients with detectable values	2.58 (2.06–3.09)	1.57 (1.19–1.94)	2.53 (2.04–3.06)	1.52 (1.25–1.87)	.02	−0.24 (−0.42 to −0.06)	.01
IL-12							
No. (%) of patients with detectable values	14 (16)	5 (6)	17 (16)	5 (5)			
Median $\log_{10}$ pg/mL (IQR) of patients with detectable values	1.33 (1.18–1.64)	1.27 (1.26–1.46)	1.3 (1.22–1.69)	1.20 (1.15–1.22)	.71[b]	0.08 (−0.26 to 0.42)	.64
IL-1β							
No. (%) of patients with detectable values	72 (82)	38 (43)	90 (84)	51 (48)			
Median $\log_{10}$ pg/mL (IQR) of patients with detectable values	2.63 (2.13–3.3)	1.77 (1.42–1.92)	2.44 (2.17–3.24)	1.87 (1.51–2.02)	.27[b]	−0.17 (−0.45 to 0.10)	.22
TNF-α							
No. (%) of patients with detectable values	64 (72)	12 (14)	73 (68)	11 (10)			
Median $\log_{10}$ pg/mL (IQR) of patients with detectable values	2.28 (1.49–3.16)	1.23 (1.16–1.39)	2.07 (1.57–3.35)	1.31 (1.17–1.51)	.50[b]	0.08 (−0.23 to 0.38)	.62

NOTE. IL, interleukin; TNF, tumor necrosis factor.

[a] Samples were obtained on days 1–4 after randomization. Sampling day was day 1 for 6 (3%) of the patients, day 2 for 144 (74%), day 3 for 44 (23%), and day 4 for 1 (1%).

[b] Comparisons of the rates of detectable values by Fisher's exact test were also nonsignificant. P values were .76 (IL-12), .57 (IL-1β), and .51 (TNF-α).

Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data

Diederik van de Beek, Jeremy J Farrar, Jan de Gans, Nguyen Thi Hoang Mai, Elizabeth M Molyneux, Heikki Peltola, Tim E Peto, Irmeli Roine, Mathew Scarborough, Constance Schultsz, Guy E Thwaites, Phung Quoc Tuan, A H Zwinderman

Summary

Background Dexamethasone improves outcome for some patients with bacterial meningitis, but not others. We aimed to identify which patients are most likely to benefit f

Methods We did a meta-analysis of individual trials of dexamethasone for bacterial meningit determined outcome measures were death at 1 month follow-up, death or any neurological s first follow-up. Combined odds ratios (ORs) Mantel-Haenszel statistics. We also did explora subgroup analyses by use of logistic regression.

Findings Data from 2029 patients from five tri infection was confirmed or likely in 580 (28·6% Dexamethasone was not associated with a sig *vs* 275 of 1010 [27·2%] on placebo; OR 0·97, 9 severe deafness (42·3% *vs* 44·3%; 0·92, 0·76– *vs* 57·4%; 0·89, 0·74–1·07), or death or severe dexamethasone seemed to reduce hearing lo Dexamethasone had no effect in any of the p dexamethasone antibiotic treatment, HIV status trials did not significantly change the results.

Interpretation Adjunctive dexamethasone in the treatment of acute bacterial meningitis does not seem to significantly reduce death or neurological disability. There were no significant treatment effects in any of the prespecified subgroups. The benefit of adjunctive dexamethasone for all or any subgroup of patients with bacterial meningitis thus remains unproven.

- ✓ 5 randomize, çift kör, plasebo kontrollü çalışma
- ✓ 2029 hasta
  - 833 hasta < 15 yaş
  - 580 hasta HIV+
- ✓ Deksametazon
  - Mortalite ve nörolojik sekel etkisi Ø
  - İşitme kaybında azalma (p=0.04)

Lancet Neurol 2010; 9: 254–63.

Nationwide implementation of adjunctive dexamethasone therapy for pneumococcal meningitis

ABSTRACT

Background: In this nationwide prospective cohort study, we evaluated the implementation of adjunctive dexamethasone therapy in Dutch adults with pneumococcal meningitis.

HOLLANDA

Çalışma dönemi	1988-2002	2006-2009	
Yaş grubu	>16	>16	
Hasta sayısı	352	357	
Deksametazon ilk doz AB ile kullanım	%3	%84	
Mortalite	%30	%20	p=0.001
İşitme kaybı	%22	%12	
Nörolojik komplikasyon	%75	%66	p<0.001

MC Brouwer, et al. Neurology. 2010 Oct 26;75(17):1533-9.

NEUROLOGY INDIA
Publication of the Neurological Society of India

Year : 2002 | Volume : 50 | Issue : 1 | Page : 63--7

Dexamethasone therapy for bacterial meningitis in adults : a double blind placebo control study.

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India

Abstract

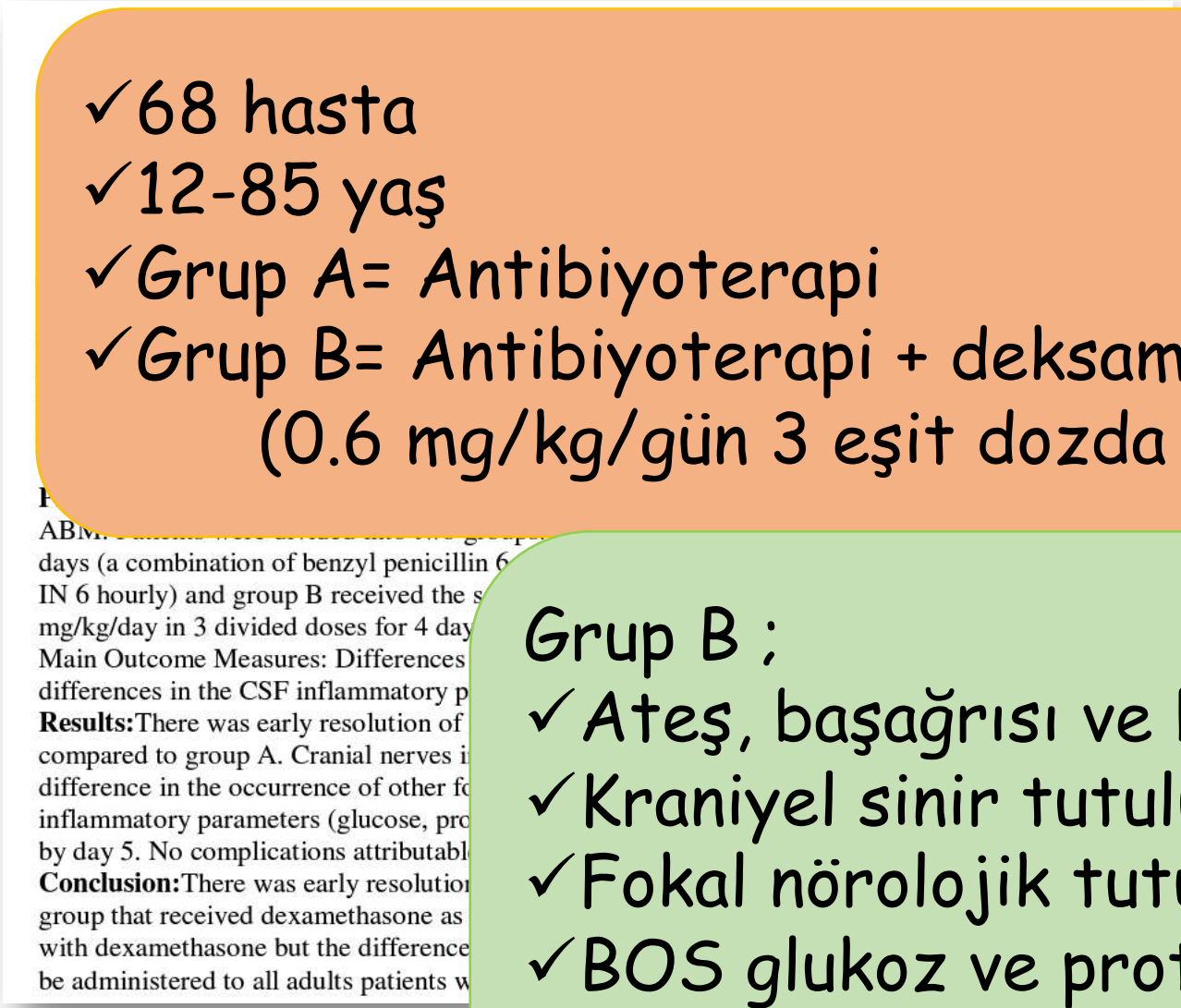
Routine use of steroids
controlled double blind
meningitis. The patien
addition to injection ce
phosphate was given i
dexamethasone was g
features of the two gr
dexamethasone group
fever, headache and v
15.00) and psychiatric
complications and hea
group (p<0.05). It is c
adults. A study with a

HİNDİSTAN

- ✓ Prospektif, çift kör, plasebo kontrollü
- ✓ 40 hasta (20/20)
  - >10 yaş
- ✓ Deksametazon
  - İlk doz antibiyotikten 15 dk önce
  - 0.6 mg/kg/gün 4 doza bölünmüş
- ✓ Meninks irritasyon bulgularında daha hızlı gerileme
- ✓ Ateş, GİS kanama ve psikiyatrik bulgular daha sık
- ✓ **Nörolojik komplikasyonlar ve işitme kaybı azalma (p<0.05)**

✓68 hasta
✓12-85 yaş
✓Grup A= Antibiyoterapi
✓Grup B= Antibiyoterapi + deksametazon
(0.6 mg/kg/gün 3 eşit dozda 4 gün)

PAKİSTAN


days (a combination of benzyl penicillin 6
IN 6 hourly) and group B received the s
mg/kg/day in 3 divided doses for 4 day
Main Outcome Measures: Differences
differences in the CSF inflammatory p
Results: There was early resolution of
compared to group A. Cranial nerves i
difference in the occurrence of other fo
inflammatory parameters (glucose, pro
by day 5. No complications attributabl
Conclusion: There was early resolution
group that received dexamethasone as
with dexamethasone but the difference
be administered to all adults patients w

J Pak Med As

Grup B ;
✓Ateş, başağrısı ve bilinç kaybında erken gerileme
✓Kraniyel sinir tutulumu daha az
✓Fokal nörolojik tutulum fark Ø
✓BOS glukoz ve protein 5. günde anlamlı azalma
✓Deksametazona atfedilecek yan etki Ø
✓Mortalite deksametazon grubunda daha az
(istatistiksel anlamlı değil)

- ✓ 147 hasta
- ✓ Ort yaş 62
- ✓ %31 immunsupresif
- ✓ KS almayan grupta mental değişiklik daha yüksek
- ✓ Mortalite etki Ø
- ✓ Komplikasyon gelişimi azalmış
- ✓ İleri yaş ve immunsupressif hastalarda kullanılabilir

ncis

Background The aim of this study was to evaluate the clinical outcome of patients with bacterial meningitis following the introduction of dexamethasone treatment in Denmark. **Methods** Adult patients with bacterial meningitis, admitted fro
were included retrospectively. Data at clinic
cerebrospinal fluid and blood biochemistry wer
interval (CI) was computed by Cox proportiona
and forty-seven patients were included in the st
and 31% had an immunosuppressive co-morl
outcome (GOS score = 1–4). Adjuvant treatme
0.76) was associated with a favourable outco
(RR = 2.36; 95% CI = 1.17–4.78) and age (RR =
associated with an unfavourable outcome. Adju
or long-term survival. Short-term mortality was
Long-term mortality was influenced by age
(RR = 1.81; 95% CI = 1.05–3.14). **Conclusion** T
treatment in acute bacterial meningitis improves
elderly population with high levels of immunos

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Table 3. Glasgow Outcome Score at discharge.

Score	All ($n = 147$)	No steroid ($n = 43$)	Steroid ($n = 104$)
1 (death)	49 (33%)	21 (49%)	28 (27%)
2 (vegetative state)	1 (1%)	0 (0%)	1 (1%)
3 (severe disability)	10 (7%)	7 (16%)	3 (3%)
4 (moderate disability)	29 (20%)	10 (23%)	19 (18%)
5 (mild or no disability)	58 (39%)	5 (12%)	53 (51%)

Klimik Derg • Cilt: 5, Sayı: 3 • 1992, s: 145-146

Akut Bakteriyel Menenjit Olgularında Steroid Kullanımı

Celal Ayaz, Sedat Arıtürk

Özet: Akut bakteriyel menenjitli 26 olgudan 13'üne nonselektif metodla antibiyotik ve steroid, 13'üne de sadece antibiyotik verildi. Her iki grupta da hastanede kalış süresi, şuurun erken açılması, ateşin düşmesi, nörolojik sekel, mortalite ve beyin-omurilik sıvısında lökosit sayısı, şeker ve protein değerleri parametre olarak alındı. Sonuç olarak ateşin erken düşmesi ve şuurun erken açılması istatistiksel açıdan anlamlı bulundu (P<0.05). Diğer parametreler istatistiksel açıdan anlamlı değildi (P>0.05).

- ✓ 26 hasta
- ✓ 13 hasta deksametazon
- ✓ Erken ateş yanıtı ve bilinç açılması anlamlı

Cochrane Library

Cochrane Database of Systematic Reviews

Corticosteroids for acute bacterial meningitis (Review)

Brouwer MC, McIntyre P, Prasad K, van de Beek D

Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD004405.

- 25 randomize kontrollü çalışma
- 4121 hasta
  - 2511 çocuk
  - 1517 erişkin
  - 93 çocuk +erişkin

- 25 çalışma
  - 4 yüksek kalite yanlılık yok
  - 14 orta kalite
  - 7 düşük kalite
  - Toplam analiz için orta düzeyde yanlılık

- 9 çalışma düşük gelir düzeyli ülke
- 16 çalışma yüksek gelir düzeyli ülke

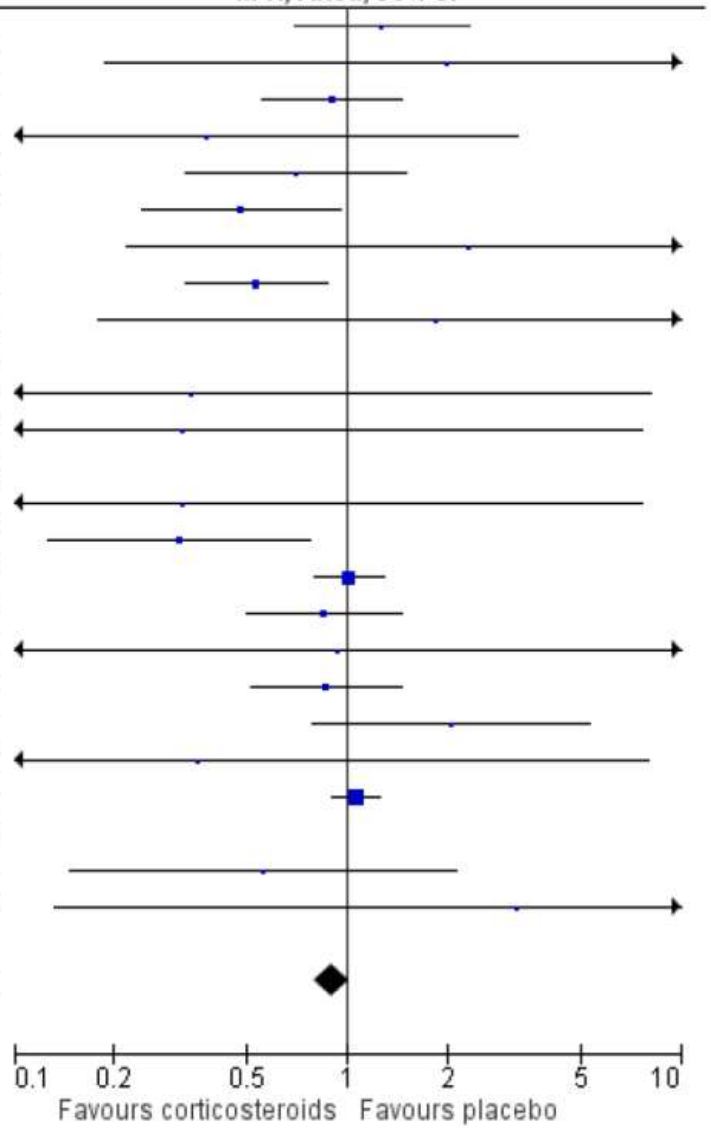
- Mortalite
- İşitme kaybı
- Nörolojik sekel
- Yan etki

Mortalite

Study or Subgroup	Corticosteroids Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bademosi 1979	12	24	11	28	2.5%	1.27 [0.69, 2.34]
Belsey 1969	2	43	1	43	0.2%	2.00 [0.19, 21.24]
Bennett 1963	16	38	22	47	4.8%	0.90 [0.56, 1.46]
Bhaumik 1998	1	14	3	16	0.7%	0.38 [0.04, 3.26]
Ciana 1995	8	34	12	36	2.8%	0.71 [0.33, 1.51]
de Gans 2002	11	157	21	144	5.3%	0.48 [0.24, 0.96]
DeLemos 1969	2	54	1	63	0.2%	2.33 [0.22, 25.03]
Girgis 1989	21	225	43	245	10.0%	0.53 [0.33, 0.87]
Kanra 1995	2	29	1	27	0.3%	1.86 [0.18, 19.38]
Kilpi 1995	0	32	0	26		Not estimable
King 1994	0	50	1	51	0.4%	0.34 [0.01, 8.15]
Lebel 1988a	0	51	1	49	0.4%	0.32 [0.01, 7.68]
Lebel 1988b	0	51	0	49		Not estimable
Lebel 1989	0	31	1	30	0.4%	0.32 [0.01, 7.63]
Mathur 2013	5	40	16	40	3.9%	0.31 [0.13, 0.77]
Molyneux 2002	96	305	91	293	22.6%	1.01 [0.80, 1.29]
Nguyen 2007	22	217	26	218	6.3%	0.85 [0.50, 1.45]
Odio 1991	1	52	1	49	0.3%	0.94 [0.06, 14.65]
Peltola 2007	23	166	26	163	6.4%	0.87 [0.52, 1.46]
Qazi 1996	12	48	5	41	1.3%	2.05 [0.79, 5.33]
Sankar 2007	0	12	1	13	0.4%	0.36 [0.02, 8.05]
Scarborough 2007	129	231	120	228	29.4%	1.06 [0.90, 1.26]
Schaad 1993	0	60	0	55		Not estimable
Thomas 1999	3	31	5	29	1.3%	0.56 [0.15, 2.14]
Wald 1995	1	69	0	74	0.1%	3.21 [0.13, 77.60]
Total (95% CI)		**2064**		**2057**	**100.0%**	**0.90 [0.80, 1.01]**
Total events	367		409			

Heterogeneity: Chi² = 26.68, df = 21 (P = 0.18); I² = 21%

Test for overall effect: Z = 1.80 (P = 0.07)



Mortalite

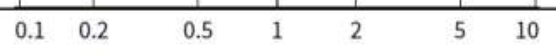
Analysis 3.1. Comparison 3 Adults, Outcome 1 Mortality.

Study or subgroup	Corticosteroids n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bennett 1963	16/38	22/47		19.94%	0.9[0.56,1.46]
Bhaumik 1998	1/14	3/16		2.36%	0.38[0.04,3.26]
de Gans 2002	11/157	21/144		14%	0.48[0.24,0.96]
Girgis 1989	5/68	18/79		9.51%	0.32[0.13,0.82]
Nguyen 2007	22/217	26/218		18.23%	0.85[0.5,1.45]
Scarborough 2007	129/231	120/228		30.5%	1.06[0.9,1.26]
Thomas 1999	3/31	5/29		5.46%	0.56[0.15,2.14]
Total (95% CI)	**756**	**761**		**100%**	**0.74[0.53,1.05]**

Total events: 187 (Corticosteroids), 215 (Placebo)

Heterogeneity: $Tau^2=0.09$; $Chi^2=13.07$, df=6(P=0.04); $I^2=54.08\%$

Test for overall effect: Z=1.7(P=0.09)

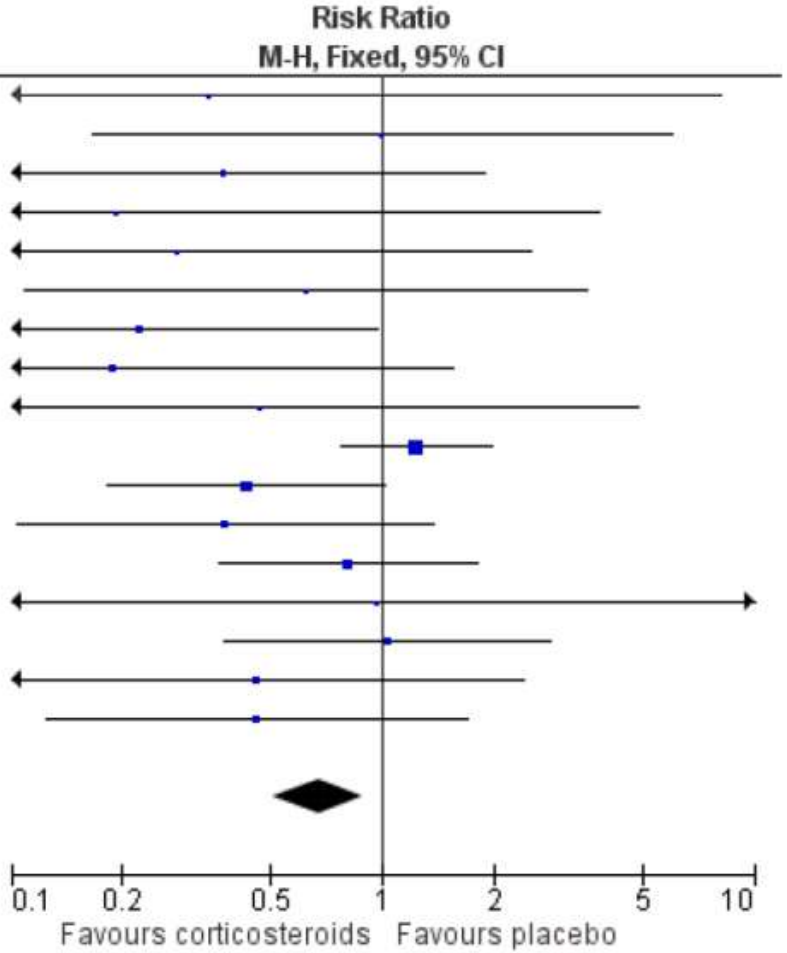


Ciddi işitme kaybı

Study or Subgroup	Corticosteroids Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Belsey 1969	0	41	1	42	1.3%	0.34 [0.01, 8.14]
Bhaumik 1998	2	13	2	13	1.8%	1.00 [0.16, 6.07]
Girgis 1989	2	190	5	177	4.5%	0.37 [0.07, 1.90]
Kanra 1995	0	27	2	26	2.2%	0.19 [0.01, 3.84]
Kilpi 1995	1	31	3	26	2.9%	0.28 [0.03, 2.53]
King 1994	2	48	3	45	2.7%	0.63 [0.11, 3.57]
Lebel 1988a	2	43	8	38	7.5%	0.22 [0.05, 0.98]
Lebel 1988b	1	49	5	46	4.5%	0.19 [0.02, 1.55]
Lebel 1989	1	31	2	29	1.8%	0.47 [0.04, 4.89]
Molyneux 2002	31	147	27	158	22.8%	1.23 [0.78, 1.96]
Nguyen 2007	7	180	16	177	14.2%	0.43 [0.18, 1.02]
Odio 1991	3	50	7	44	6.5%	0.38 [0.10, 1.37]
Peltola 2007	10	135	12	131	10.7%	0.81 [0.36, 1.81]
Qazi 1996	1	26	1	25	0.9%	0.96 [0.06, 14.55]
Scarborough 2007	7	96	7	99	6.1%	1.03 [0.38, 2.83]
Schaad 1993	2	60	4	55	3.7%	0.46 [0.09, 2.40]
Wald 1995	3	67	7	72	5.9%	0.46 [0.12, 1.71]
Total (95% CI)		**1234**		**1203**	**100.0%**	**0.67 [0.51, 0.88]**
Total events	75		112			

Heterogeneity: Chi² = 15.67, df = 16 (P = 0.48); I² = 0%

Test for overall effect: Z = 2.86 (P = 0.004)

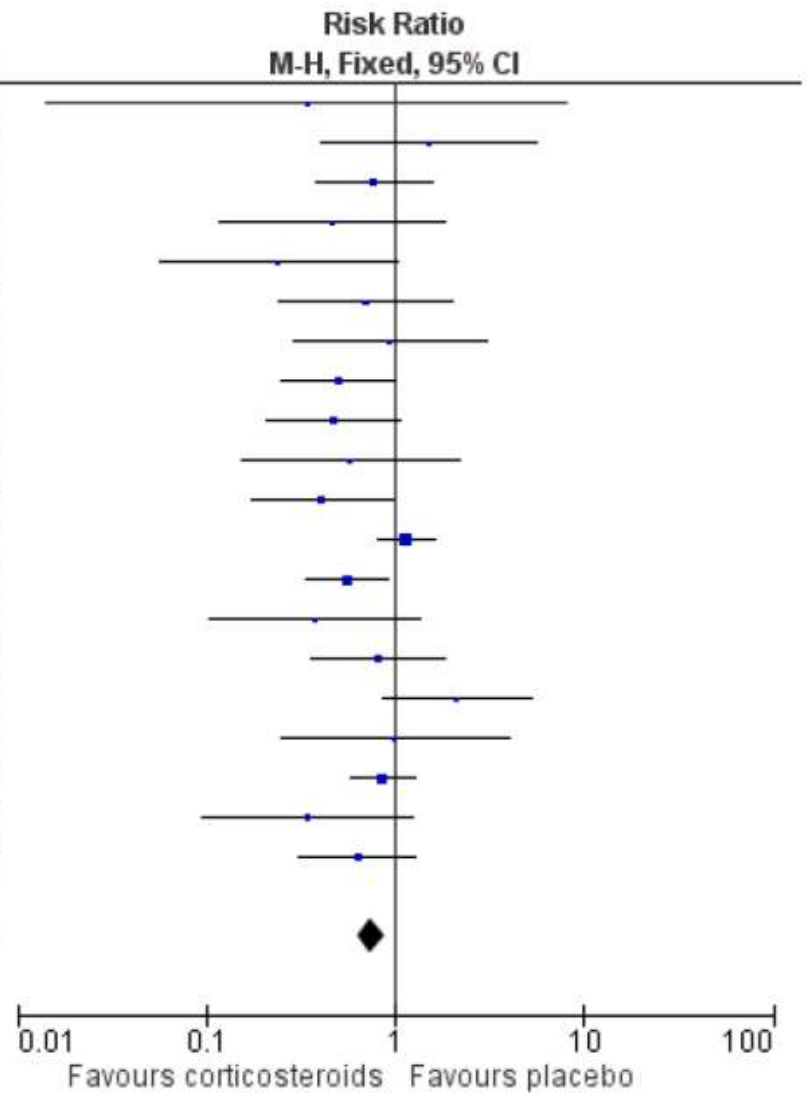


İşitme kaybı

Study or Subgroup	Corticosteroids Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Belsey 1969	0	41	1	42	0.6%	0.34 [0.01, 8.14]
Bhaumik 1998	4	14	3	16	1.1%	1.52 [0.41, 5.67]
de Gans 2002	13	143	14	119	5.8%	0.77 [0.38, 1.58]
Girgis 1989	3	190	6	177	2.4%	0.47 [0.12, 1.83]
Kanra 1995	2	27	8	26	3.1%	0.24 [0.06, 1.03]
Kilpi 1995	5	31	6	26	2.5%	0.70 [0.24, 2.03]
King 1994	5	48	5	45	2.0%	0.94 [0.29, 3.02]
Lebel 1988a	9	43	16	38	6.4%	0.50 [0.25, 0.99]
Lebel 1988b	7	49	14	46	5.5%	0.47 [0.21, 1.06]
Lebel 1989	3	30	5	29	1.9%	0.58 [0.15, 2.21]
Mathur 2013	6	35	10	24	4.5%	0.41 [0.17, 0.98]
Molyneux 2002	49	147	46	158	16.8%	1.14 [0.82, 1.60]
Nguyen 2007	21	180	37	177	14.2%	0.56 [0.34, 0.91]
Odio 1991	3	50	7	44	2.8%	0.38 [0.10, 1.37]
Peltola 2007	10	135	12	131	4.6%	0.81 [0.36, 1.81]
Qazi 1996	11	26	5	25	1.9%	2.12 [0.86, 5.22]
Sankar 2007	3	12	3	12	1.1%	1.00 [0.25, 4.00]
Scarborough 2007	30	96	36	99	13.4%	0.86 [0.58, 1.28]
Schaad 1993	3	60	8	55	3.2%	0.34 [0.10, 1.23]
Wald 1995	10	67	17	72	6.2%	0.63 [0.31, 1.28]
Total (95% CI)		**1424**		**1361**	**100.0%**	**0.74 [0.63, 0.87]**
Total events	197		259			

Heterogeneity: Chi² = 25.05, df = 19 (P = 0.16); I² = 24%

Test for overall effect: Z = 3.59 (P = 0.0003)



İşitme kaybı

Analysis 3.2. Comparison 3 Adults, Outcome 2 Any hearing loss.

Study or subgroup	Corticosteroids n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Bhaumik 1998	4/14	3/16		3.08%	1.52[0.41,5.67]
de Gans 2002	13/143	14/119		16.82%	0.77[0.38,1.58]
Nguyen 2007	21/180	37/177		41.07%	0.56[0.34,0.91]
Scarborough 2007	30/96	36/99		39.02%	0.86[0.58,1.28]
Total (95% CI)	**433**	**411**		**100%**	**0.74[0.56,0.98]**
Total events: 68 (Corticosteroids), 90 (Placebo)					
Heterogeneity: Tau²=0; Chi²=2.98, df=3(P=0.4); I²=0%					
Test for overall effect: Z=2.1(P=0.03)					

Favours corticosteroids 0.005 0.1 1 10 200 Favours placebo

Nörolojik sekel

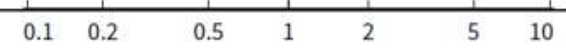
- Kısa dönem nörolojik sekel
- 13 çalışma - 1756 hasta
- Kortikosteroit alan grupta daha az (p= 0.05)

- Uzun dönem nörolojik sekel
- 12 çalışma - 1652 hasta
- İstatistiksel olarak anlamlı fark Ø

Nörolojik sekel

Analysis 3.3. Comparison 3 Adults, Outcome 3 Short-term neurological sequelae.

Study or subgroup	Corticosteroids n/N	Placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Bhaumik 1998	3/13	2/13		3.17%	1.5[0.3,7.55]
de Gans 2002	18/143	24/119		41.51%	0.62[0.36,1.09]
Scarborough 2007	21/98	26/104		39.97%	0.86[0.52,1.42]
Thomas 1999	5/28	9/24		15.36%	0.48[0.18,1.23]
Total (95% CI)	**282**	**260**		**100%**	**0.72[0.51,1.01]**
Total events: 47 (Corticosteroids), 61 (Placebo)					
Heterogeneity: $Tau^2=0$; $Chi^2=2.23$, df=3(P=0.53); $I^2=0\%$					
Test for overall effect: Z=1.88(P=0.06)					



Favours corticosteroids — Favours placebo

Alt grup analiz

Etkenler;

- Erişkinlerde

  S. pneumoniae menenjitlerinde mortalitede azalma

- Çocuklarda

  H. influenzae menenjitlerinde ciddi işitme kaybında azalma

Gelir dağılımı;

- Gelir düzeyi yüksek ülkelerde işitme kaybı ve kısa dönem nörolojik sekelde azalma

Yan etki

- 20 çalışma
- 16 gastrointestinal hemoraji
- 12 tekrarlayan ateş
- 6 reaktif artrit
- 5 herpes zoster
- 3 persistan ateş
- 1 fungal enfeksiyon

Rekürren ateş

Persistan ateş

ORIGINAL ARTICLE

ESCMID guideline: diagnosis and treatment of acute bacterial meningitis

D. van de Beek[1], C. Cabellos[2], O. Dzupova[3], S. Esposito[4], M. Klein[5], A. T. Kloek[1], S. L. Leib[6], B. Mourvillier[7], C. Ostergaard[8], P. Pagliano[9], H. W. Pfister[5], R. C. Read[10], O. Resat Sipahi[11] and M. C. Brouwer[1], for the ESCMID Study Group for Infections of the Brain (ESGIB)

1) *Department of Neurology, Academic Medical Center, Amsterdam, The Netherlands,* 2) *Department of Infectious Diseases, Hospital Universitari de Bellvitge, Barcelona, Spain,* 3) *Department of Infectious Diseases, Charles University, Third Faculty of Medicine, Prague, Czech Republic,* 4) *Pediatric Highly Intensive Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano, Milan, Italy,* 5) *Department of Neurology, Klinikum Großhadern, Munich, Germany,* 6) *Institute for Infectious Diseases, University of Bern, Bern, Switzerland,* 7) *Department of Intensive Care Medicine, Groupe Hospitalier Bichat-Claude Bernard, Paris, France,* 8) *Department of Clinical Microbiology, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark,* 9) *Department of Infectious Diseases, "D. Cotugno" Hospital, Naples, Italy,* 10) *Department of Infectious Diseases, Southampton General Hospital, Southampton, United Kingdom and* 11) *Department of Infectious Diseases and Clinical Microbiology, Ege University, Izmir, Turkey*

Keywords: Antibiotic, bacterial meningitis, ESCMID, guideline, *Neisseria meningitidis*, *Streptococcus pneumoniae*
Original Submission: 10 December 2015; **Accepted:** 11 January 2016
Editor: D. Raoult
Article published online: 7 April 2016

Conclusions

Level 1

KS'ler işitme kaybını ve nörolojik sekelleri anlamlı olarak azaltıyor
Mortaliteye etkisi yok
Tıbbi bakımın yüksek olduğu ülkelerde KS kullanımı öneriliyor
Düşük gelir düzeyi olan ülkelerde faydası saptanmamış
Neonatal menenjitlerde kullanımı önerilmiyor

Level 3

Antibiyoterapi başlanmış ise ilk 4 saat içinde deksametazon eklenebilir

Level 3

- ✓ Menenjit tanısı dışlanırsa
- ✓ *H. influenza* ve *S. pneumoniae* dışında bir etkenle menenjit gelişti̇ğinde

Deksametazon tedavisi kesilmeli

Recommendation

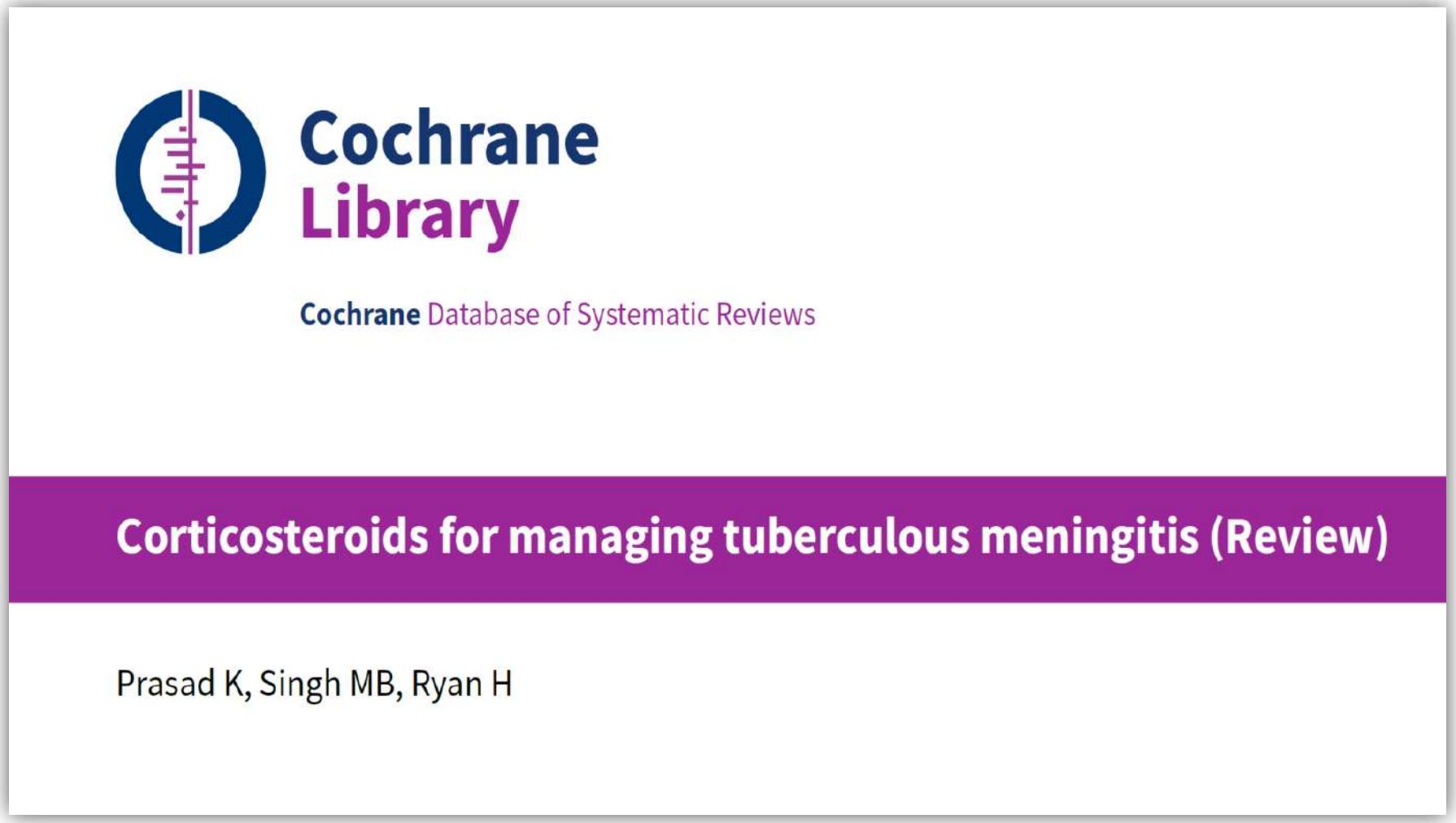
Grade A	Empiric treatment with dexamethasone is strongly recom all adults (10 mg qid for 4 days) and children (0.15 mg 4 days) with acute bacterial meningitis in the setting of countries.
Grade A	Treatment with dexamethasone is strongly initiated with the first dose of antibiotic
Grade C	If intravenous antibiotic treatment dexamethasone can still be adm of the first dose of intravenous
Grade B	It is recommended not to have bact meningitis is a sp although some e continued irresp

Yüksek gelir düzeyli ülkelerde
Erişkinlerde 10 mg qid 4 gün
Çocuklarda 0.15 mg/kg qid 4 gün

Deksametazon tedavisi ilk AB dozu ile birlikte başlanmalı

AB başlanmışsa ilk dozdan sonraki 4 saat içinde başlanabilir

Menenjit tanısı dışlanırsa
H. influenza ve *S. pneumoniae* dışında bir etkene bağlı
Deksametazon tedavisi kesilmeli



DOKUZ EYLÜL ÜNİVERSİTESİ
İZMİR-1982

Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD002244.

- 9 randomize kontrollü çalışma
- 1337 hasta
- Deksametazon/metilprednizolon/prednizolon+Anti-tbc tedavi

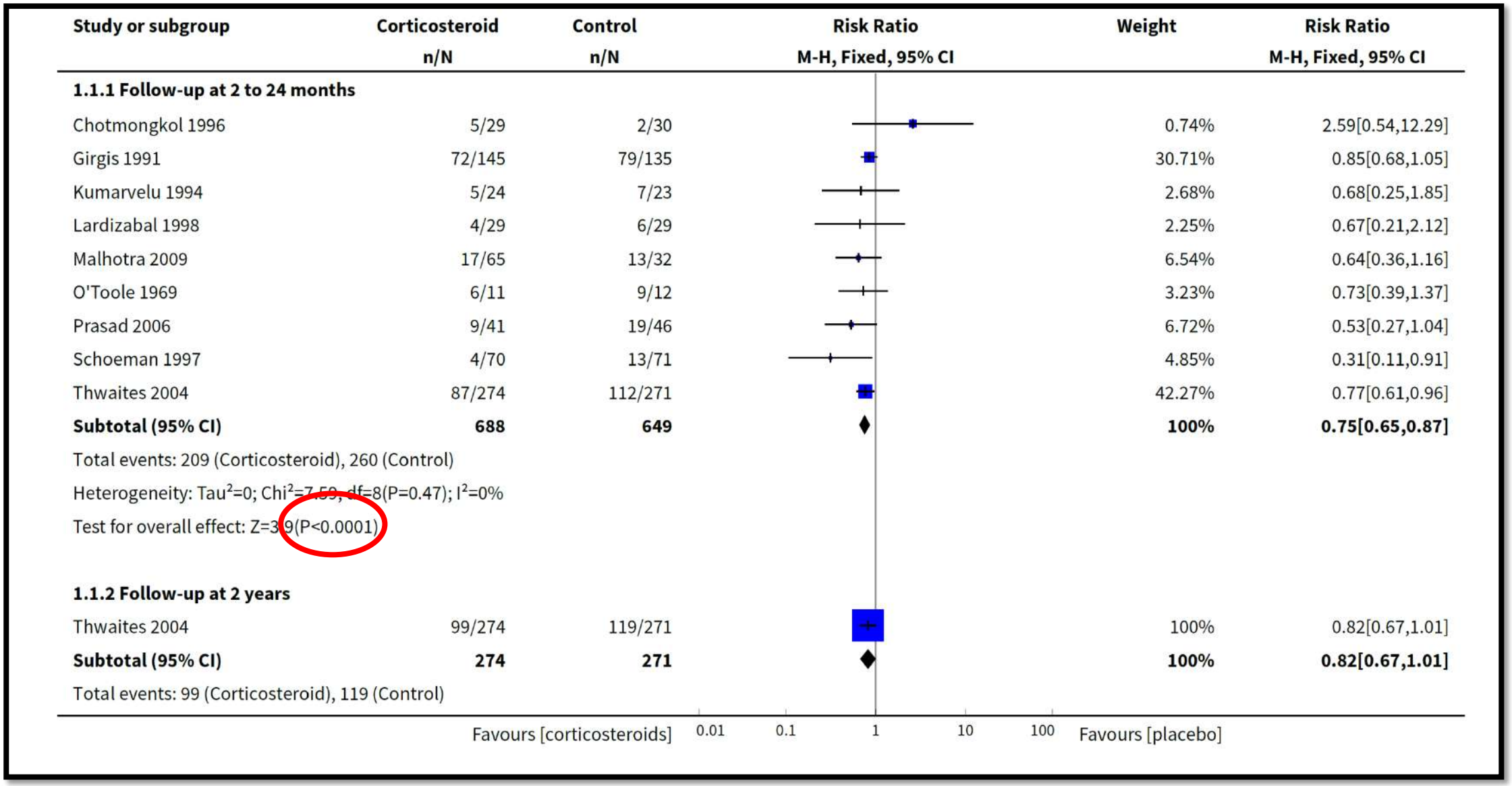
- Mortalite
- Nörolojik sekel
- Yan etki

ADDITIONAL TABLES

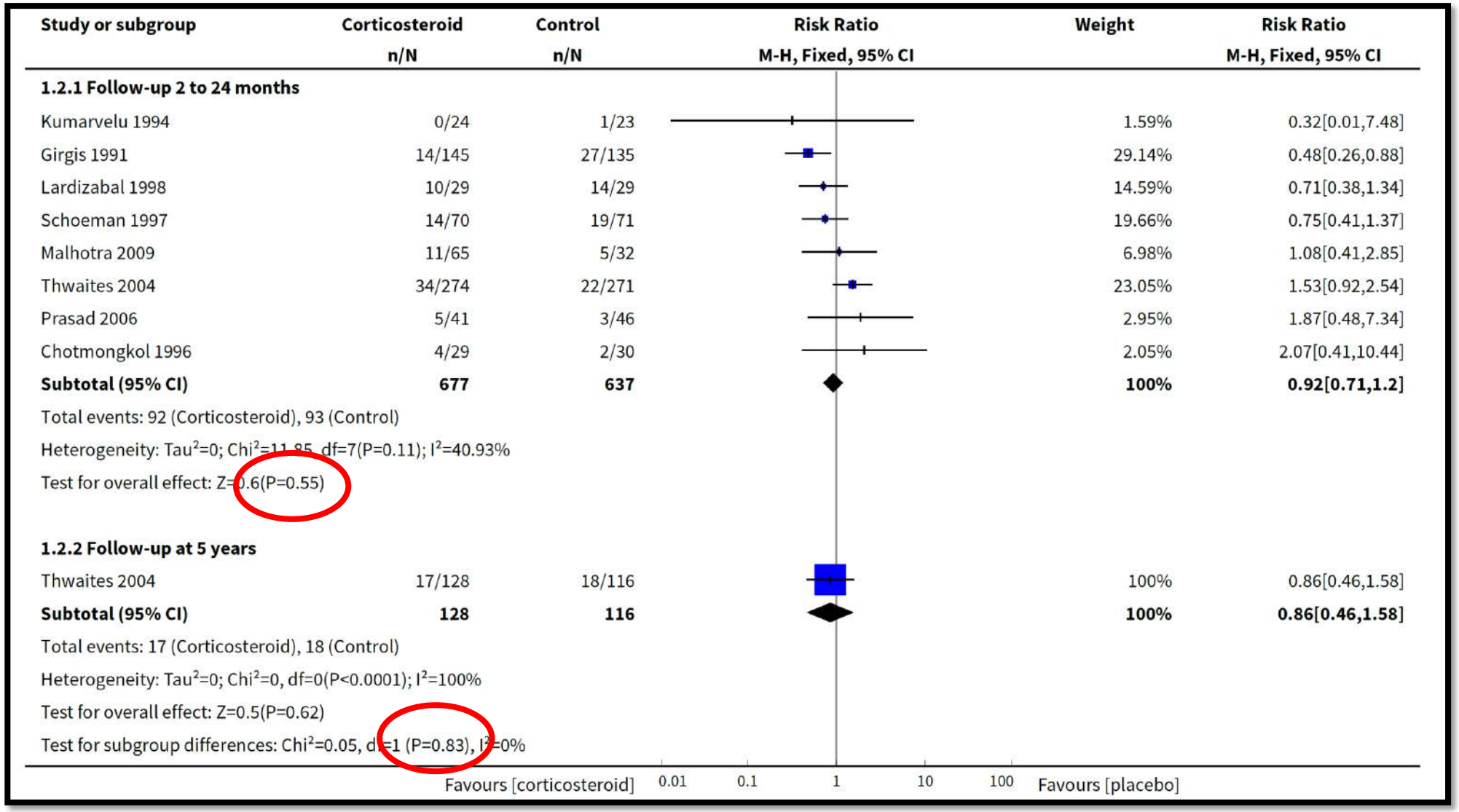
Table 1. Summary of characteristics of included trials

Trial ID	Country	Year	Setting	Age	TB meningitis MRC Grade[a]	HIV status reported	TB treatment regimen[b]	Steroid	Route	Starting dose	Duration
O'Toole 1969	India	1966 to 1967	Tertiary	All	II and III	No	HS (duration not specified)	Dexamethasone	IM/IV	Adults: 9 mg/day Children: unclear	4 weeks
Girgis 1991	Egypt	1982 to 1987	Research	All	All	No	24HE1.5S	Dexamethasone	IM	Adults: 12 mg/day Children: 8 mg/day	6 weeks
Kumarvelu 1994	India	1991 to 1992	Tertiary	> 12 years	All	No	12HRZ	Dexamethasone	IV	16 mg/day	4 weeks
Chotmongkol 1996	Thailand	1990 to 1992	Tertiary	> 15 years	All	Yes, HIV-positive participants excluded	2HRZS +4HR	Prednisolone	Oral	60 mg/day	5 weeks
Schoeman 1997	South Africa	Unclear	Tertiary	Children	II and III	No	6HRZE	Prednisolone	Oral	2 to 4 mg/kg/day	4 weeks
Lardizabal 1998	Phillipines	1996 to 1997	Tertiary	> 18 years	II and III	No	2HRZE +10HR	Dexamethasone	IV/oral	16 mg/day	7 weeks
Thwaites 2004	Vietnam	2001 to 2003	Tertiary	> 14 years	All	Yes, HIV participants included	3HRZE(or S)+6HRZ	Dexamethasone	IV	Grade II & III: 0.4 mg/kg/day Grade I: 0.3 mg/kg/day	8 weeks
Prasad 2006	India	1996 onwards	Tertiary	> 16 years	All	No	9RHZ	Dexamethasone	IV	0.6 to 12 mg/day	3 weeks then tapered
Malhotra 2009	India	2006 to 2007	Tertiary	> 14 years	All	Yes, HIV-positive participants excluded	2HRZE(or S)+7HR	Dexamethasone	IV	0.4 mg/kg/day	8 weeks
								Methylprednisolone	IV	20 mg/kg/day	5 days

Mortalite


Study or subgroup
Corticosteroid n/N
Control n/N
Risk Ratio M-H, Fixed, 95% CI
Weight
Risk Ratio M-H, Fixed, 95% CI
1.1.1 Follow-up at 2 to 24 months
Chotmongkol 1996 5/29 2/30 0.74% 2.59[0.54,12.29]
Girgis 1991 72/145 79/135 30.71% 0.85[0.68,1.05]
Kumarvelu 1994 5/24 7/23 2.68% 0.68[0.25,1.85]
Lardizabal 1998 4/29 6/29 2.25% 0.67[0.21,2.12]
Malhotra 2009 17/65 13/32 6.54% 0.64[0.36,1.16]
O'Toole 1969 6/11 9/12 3.23% 0.73[0.39,1.37]
Prasad 2006 9/41 19/46 6.72% 0.53[0.27,1.04]
Schoeman 1997 4/70 13/71 4.85% 0.31[0.11,0.91]
Thwaites 2004 87/274 112/271 42.27% 0.77[0.61,0.96]
Subtotal (95% CI) 688 649 100% 0.75[0.65,0.87]
Total events: 209 (Corticosteroid), 260 (Control)
Heterogeneity: Tau²=0; Chi²=7.59, df=8(P=0.47); I²=0%
Test for overall effect: Z=3.9(P<0.0001)
1.1.2 Follow-up at 2 years
Thwaites 2004 99/274 119/271 100% 0.82[0.67,1.01]
Subtotal (95% CI) 274 271 100% 0.82[0.67,1.01]
Total events: 99 (Corticosteroid), 119 (Control)
0.01
0.1
1
10
100
Favours [corticosteroids]
Favours [placebo]

Nörolojik sekel



Yan etki

- Gastrointestinal hemoraji
- İnvazif bakteriyel enfeksiyon
- Hepatit
- Hiperglisemi

Kortikosteroit –Tüberküloz menenjit

0,5-2 mg/kg prednizolon eşdeğeri dozda 4-6 hafta verilebilir.

Tüberküloz Tanı ve Tedavi Rehberi,
2. Baskı Ankara, Mayıs 2019

- Tedavide kortikosteroit, doz ve süre ?

Sonuç

Bakteriyel menenjit

- Deksametazon yüksek gelir düzeyli ülkelerde
- Sadece *H. influenza* ve *S. pneumoniae* menenjitlerinde
- İlk antibiyotik dozu ile birlikte
- 10 mg qid 4 gün

Tüberküloz menenjit

- 0,5-2 mg/kg prednizolon 4-6 hafta

Teşekkürler...