# PRETERM DOĞUMDA NÖRON KORUNMASINDA MAGNEZYUM SÜLFAT KULLANIMI

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**Kadın Hastalıkları ve Doğum Anabilim Dalı**

# Serebral Palsi (SP)

**Fetus veya bebek beyninde oluşan hasar veya hastalıklar sonucu kalıcı, ilerleyici olmayan, aktivite kısıtlamasına yol açan hareket ve duruş bozuklukları**

**Çocukluk çağında ağır motor bozukluğunun en sık nedeni**

**+ duyu, algı, bilişsel, iletişim, davranış bozuklukları**

# Klinik Sınıflama

1. Spastik
2. Atetoid veya Diskinetik
3. Ataksik
4. Mikst

**2 yş da güvenilir tanı**

**Tip ve ciddiliği 4-5 yş dek tanımlanamaz**

# Etyoloji

## Multifaktöriyel

### Obstetrik nedenler

| | |
|---|---|
| **Prematürite :** | **% 42*-78** |
| İntrauterin büyüme kısıtlılığı | %34 |
| Enfeksiyon | %28 |
| Antepartum kanama | %27 |
| Çoğul gebelik | % 20 |

Strijbis et al. Obstet Gynecol 2006;107(6):1357.

*(Australian Cerebral Palsy Registrer Group 2009)

# PRETERM SP

**İntrakranial Kanama**

< 28hf bebeklerde ciddi (Grade 3,4) kanama sık

**Beyaz Cevher Hasarı** en sık 28hf

# Serebral Palsi

**İnsidans: 1000 canlı doğumda/ 1- 2**

| | |
|---|---|
| **<1500g** | **1000/60** |
| **<1000g** | **1000/100** |

**Term gebelik ile karşılaştırıldığında**

**34-36 hafta : 3 kat**

**30-33 hafta : 8- 14 kat (%1.4)**

**28- 30 hafta : 46 kat (%6 )**

**< 28 hafta : 70- 80 kat artar (%10)**

Sibai, BM AJOG 2011

SOGC Clinical Practice Guideline No. 258, May 2011

# Serebral Palsi

**Preterm bebeklerde yaşama oranları dramatik olarak artmasına rağmen yaşayanlarda nörolojik bozukluklar özellikle motor hastalıklar SP gibi azalmamıştır**

**Tedavisi yok**

**Önleme girişimleri büyük  önem kazanıyor**

**Primer önleme önemli**

# SP - ÖNLEME GİRİŞİMLERİ

**Preterm fetüslerde: MgSO4**

**Term fetüslerde**: Hipotermi

(perinatal beyin hasarından şüphelenilen)

+

- **Kordonun geç klampe edilmesi**
- **Progesteron**
- **Enfeksiyonlardan kaçınma**

**Yenidoğan: Kordon kanı, Eritropoein…**

# MgSO4 Nöron Koruma

Gözlemsel çalışmalar

Randomize Kontrollü Çalışmalar

Meta-analizler

Rehberler ve görüşler

# Gözlemsel Çalışmalar

**Preeklamptik anneden doğan preterm bebeklerde santral sinir sistemi komplikasyonları daha azdır**

Levitonetal . Obstet Gynecol 1988;72:571–6.  Van de B  et al . J Perinat Med 1987;15:333–9.

**Doğum ağırlığı 1500gr'dan düşük olup antenatal dönemde MgSO4 alan bebeklerde SP sıklığı daha azdır**

Nelson & Grether,Pediatrics 1995; 95:263–9. (California Cerebral Palsy project)
Shendel De, JAMA 1996

**Table 1. Summary of Retrospective Studies**

| First Author, Year | Study Design | No. of Patients (Case/Control or Total) | Inclusion Criteria | Outcome Measure | Odds Ratio |
|---|---|---|---|---|---|
| Nelson, 1995 | Case control | 43/75 | <1500 g | Mod/ severe CP | 0.14 |
| O'Shea, 1998 | Case control | 80/240 | 500–1500 g | CP | NS |
| Wilson-Costello, 1998 | Case control | 72/72 | <1500 g | CP or other | NS |
| Grether, 2000 | Case control | 170/288 | <2000 g/33 weeks, no HTN | CP | NS |
| Matsuda, 2000 | Case control | 22/170 | 26–30 weeks | CP | 0.13 |
| Boyle, 2000 | Case control | 97/110 | <750 g, no HTN | CP | NS |
| Costantine, 2007 | Case control | 19/38 | <1000 g | CP | NS |
| Schendel, 1996 | Cohort | 1097 | <1500 g | Death/ CP/MR | NS death<br>0.11 CP |
| Paneth, 1997 | Cohort | 1105 | <2000 g | IVH/PVL/ CP | NS |

CP, cerebral palsy; IVH, intraventricular hemorrhage; HTN, hypertension; MR, mental retardation; NS, not significant; PVL, periventricular leukomalacia.

# Randomize Kontrollü Çalışmalar

## 1- MagNET Magnesium And Neurological Endpoints Trial

Mittendorf et al., Am J Obstet Gynecol 2002;186:1111–8 (+ tokoliz kolu)

## 2- MAGPIE: Eklampsi önlenmesi için MgSO4

Altman , et al, Lancet 2002;359 (9321) :1877–9 (+ preeklampsi kolu)

1&2 nöron koruma + diğer

# Randomize Kontrollü Çalışmalar

**3. ACTOMgSO4** The Australasian Collaborative Trial of MgSO4 Group

Crowther et al , JAMA. 2003;290(20):1062

**4. BEAM** Beneficial Effects of Antenatal MgSO4

Rouse et al , N Engl J Med. 2008;359(9):895

**5. PREMAG**

Marett et al., Gynecol Obstet Fertil. 2008;36(3):278

# Magnesium And Neurological Endpoints Trial
# MagNET

**ABD, tek merkez**

**1995- 1997, 149,** siyah/beyaz, tekil/ikiz

**25- 33hf** (25-28hf ve 29-33hf), 2 rejim

| | | | | |
|---|---|---|---|---|
| **Aktif doğum eylemi** | **<4 cm** | **tokolitik** | **MgSO4 46 gebe 4g bolus, 2-3g/st idame** | |
| | **Alternatif tokolitik** | | | 46 gebe/51 fetüs |
| **Nöron koruma** | **dilatasyon >4cm** | | **Mg 4g bolus,** | 29 gebe/30 fetüs |
| | | Plasebo %0.9 serum | fizyolojik | 28 gebe/29 fetüs |

Mittendorf R et al., Am J Obstet Gynecol 2002;186:1111–8.

# MagNET

**MgSO4 grubunda pediatrik mortalite yüksek olduğu için çalışma durdurulmuş** 10/85 vs 1/80 RR: 9.41(%95CI: 12.3-71.9)

**Serebral Palsi**

**MgSO4 grubu fark yok 3/85 vs 3/80 kontrol RR: 0.94(%95CI: 0.2- 4.5)**

**18 aylıkta SP oranı ve yaşayanlardaki sonuçlar ?**

**Motor fonksiyon bozuklukları ?**

} **rapor edilmemiş**

Mittendorf R et al., Am J Obstet Gynecol 2002;186:1111–8

# The Australian Collaborative Trial of Magnesium Sulphate Study ACTOMgSO4

**Avustralya ve Yeni Zellanda ,16 merkez**

**1996 – 2000, 1062 gebe, <30hf**

**MgSO4 535/ 629 fetüs vs Plasebo 527/ 626 fetüs**

**Doz: 4g bolus, 20dk, 1g/st-24st veya doğum olana dek**

Crowther et al , JAMA. 2003;290(20):1062.

# ACTOMgSO4

**Major sonuçları: 2. yaşta SP olmaması**

SP veya SP olmayan motor fonksiyon bozuklukları

**GMFCS**: Gross Motor Function Classification System

Kaba motor fonksiyon bozukluğu: ≥2GMFCS

2 yş da bağımsız olarak yürüyememe

Yaşayanların %99unun takibi var

# ACTOMgSO4

## Pediatrik mortalitede artış yok

MgSO4 27/629 vs Kontrol 107/626 RR: 0.81(%95CI:0.62-1.05)

## SP oranları benzer

MgSO4 36/629 vs Kontrol 42/626 RR: 0.85 (%95CI:0.55-1.31)

## Kaba motor fonksiyon bozukluğu MgSO4 grubunda belirgin olarak azalmış

MgSO4 18/629 vs Kontrol 34/626

**RR: 0.53(%95CI:0.30-0.92)**

DOI: 10.1111/j.1471-0528.2006.01162.x
www.blackwellpublishing.com/bjog



# Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial*

S Marret,[a] L Marpeau,[b] V Zupan-Simunek,[c] D Eurin,[d] C Lévêque,[e] M-F Hellot,[f] J Bénichou[g]
on behalf of the PREMAG trial group

Fransa, 18 merkez (13 merkezin datası var 564)

Doğum planlanan veya 24st içinde beklenen

573 gebe, <33hf tekil, ikiz, üçüz

**Doz: 4g MgSO4 yükleme**, 30dk içinde

Plasebo

Major sonuçlar

Kranial US de beyaz cevher hasarı varlığı

2 yıllık takip sonuçları var (%98)

Marett et al., Gynecol Obstet Fertil. 2008;36(3):278

# PREMAG

**Pediatrik mortalite yükselmemiş**

34/352 vs 38/336 RR:0.85(%95CI:0.55-1.32)

**SP oranı aynı**

22/352 vs 30/446 RR:0.70(%95CI: 0.41-1.19)

**Kaba motor fonksiyon bozukluğu oranı aynı**

18/352 vs 22/336 RR: 0.78(%95CI: 0.43-1.43)

# PREMAG

2 yıllık dataları

**Ölüm veya kaba motor fonksiyon bozukluğu MgSO4 grubunda istatistiksel anlamlı olarak az bulunmuş**

(OR 0.62; 0.41-0.93)

Marrett S, Pediatrics 2008 121: 225

# PREMAG

**TABLE 1** Mortality and Neurologic Outcomes at 2 Years of Age

| Outcome | No. (%) of Infants | | Adjusted OR (95% CI)[b] | *P*[b] |
|---|---|---|---|---|
| | $MgSO_4$ Group (*N* = 352)[a] | Placebo Group (*N* = 336)[a] | | |
| Pediatric mortality | 34 (9.7) | 38 (11.3) | 0.74 (0.42–1.32) | .31 |
| Gross motor dysfunction | 55 (17.6) | 64 (21.8) | 0.65 (0.41–1.02) | .06 |
| Cerebral palsy | 22 (7.0) | 30 (10.2) | 0.63 (0.35–1.15) | .13 |
| Cognitive dysfunction | 57 (18.2) | 62 (21.2) | 0.82 (0.52–1.28) | .38 |
| Combined death or gross motor dysfunction | 89 (25.6) | 102 (30.8) | 0.62 (0.41–0.93) | .02 |
| Combined death or cerebral palsy | 56 (16.1) | 67 (20.2) | 0.65 (0.42–1.03) | .07 |
| Combined death and motor or cognitive dysfunction | 121 (34.9) | 134 (40.5) | 0.68 (0.47–0.99) | .04 |
| Combined death and cerebral palsy or cognitive dysfunction | 102 (29.4) | 116 (35.0) | 0.68 (0.47–1.00) | .05 |

# BEAM Study: Beneficial Effects of Antenatal MgSO4

ABD, **2241** tekil, ikiz, 20 merkez

24-31hf doğum riski yüksek olan (%87 EMR)

**Doz: MgSO4 6g yükleme, 2g/st idame**

Plasebo

Rouse DJ et al , N Engl J Med. 2008;359(9):895

**2 yş da orta veya ciddi SP**

SP tanısı; pediatrist veya nöroloji uzmanı

Ciddiliği: GMFCS göre

Bayley Scales of Infant Developmental

<85 gelişim geriliği ( BSID-III)

%96 nın primer sonuçları var

Gross Motor Function Classification System for Cerebral Palsy (GMFCS)

**Before 2nd Birthday**

| | |
|---|---|
| Level I | Infants move in and out of sitting and floor sit with both hands free to manipulate objects. Infants crawl on hands and knees, pull to stand and take steps holding on to furniture. Infants walk between 18 months and 2 years of age without the need for any assistive mobility device. |
| Level II | Infants maintain floor sitting but may need to use their hands for support to maintain balance. Infants creep on their stomach or crawl on hands and knees. Infants may pull to stand and take steps holding on to furniture. |
| Level III | Infants maintain floor sitting when the low back is supported. Infants roll and creep forward on their stomachs. |
| Level IV | Infants have head control but trunk support is required for floor sitting. Infants can roll to supine and may roll to prone. |
| Level V | Physical impairments limit voluntary control of movement. Infants are unable to maintain antigravity head and trunk postures in prone and sitting. Infants require adult assistance to roll. |

**Between 2nd and 4th Birthday**

| | |
|---|---|
| Level I | Children floor sit with both hands free to manipulate objects. Movements in and out of floor sitting and standing are performed without adult assistance. Children walk as the preferred method of mobility without the need for any assistive mobility device. |
| Level II | Children floor sit but may have difficulty with balance when both hands are free to manipulate objects. Movements in and out of sitting are performed without adult assistance. Children pull to stand on a stable surface. Children crawl on hands and knees with a reciprocal pattern, cruise holding onto furniture and walk using an assistive mobility device as preferred methods of mobility. |
| Level III | Children maintain floor sitting often by "W-sitting" (sitting between flexed and internally rotated hips and knees) and may require adult assistance to assume sitting. Children creep on their stomach or crawl on hands and knees (often without reciprocal leg movements) as their primary methods of self-mobility. Children may pull to stand on a stable surface and cruise short distances. Children may walk short distances indoors using an assistive mobility device and adult assistance for steering and turning. |
| Level IV | Children floor sit when placed, but are unable to maintain alignment and balance without use of their hands for support. Children frequently require adaptive equipment for sitting and standing. Self-mobility for short distances (within a room) is achieved through rolling, creeping on stomach, or crawling on hands and knees without reciprocal leg movement. |
| Level V | Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and |

# BEAM Çalışması

**Pediatrik mortalite aynı**

MgSO4 103/1188 vs Kontrol 96/1256 RR:1.13(%95CI: 0.87-1.48)

**SP az bulunmuş**

MgSO4 41/1188 vs Kontrol 74/1256 RR:0.59(%95CI: 0.4-0.85)

**Kaba motor fonksiyon bozukluğu düşük bulunmuş**

MgSO4 20/1188 vs Kontrol 38/1256 RR:0.56(%95CI: 0.33-0.95)

Rouse et al , N Engl J Med. 2008;359(9):895

# MAGPIE: Eklampsi önlenmesi için MgSO4

Ağır preeklampsi, 10.141 gebe

1998-2001, Çok merkezli

**Doz**: **4g I.V, 10-15dk, 1g/st-24st** veya 5gI.M, 24st

Kontrol %0.9 serum fizyolojik

**Primer amaç nöron koruma değil**

Eklampsi profilaksisinde MgSO4 önemli

**Magpie Trial Collaborative Group. Lancet 2002 359 1977-90**

# MAGPIE

Preterm az, 2895 bebek 18.ay takip sonuç var

Neonatal mortalite, morbidite fark yok

Diğer çalışmalara göre pediatrik mortalite yüksek

Toplam mortalite benzer

Nörosensoryel bozukluk fark yok

BJOG 2007, 114:289-99

Cahill AG et al, 2010 Curr Opin Obstet Gynecol 22;122-27.

# MAGPIE

SP oranı diğer çalışmalara göre düşük

2/798, 2/795, RR: 0.40(0.08-2.05)

**SP ve kaba motor fonksiyon bozukluğunda önemli fark yok**

1/798, 0/795 RR:2.99(0.12-73.3)

**Magpie Trial Collaborative Group. Lancet 2002 359 1977-90**

**Table 6. Magnesium sulphate dosing in the randomized controlled trials of magnesium sulphate for fetal neuroprotection**

| Study | Women, n | Intervention: $MgSO_4$ Loading dose | Women who received the LD, % | Maintenance dose | Median (IQR) dose received (g) |
|---|---|---|---|---|---|
| **Neuroprotective intent** | | | | | |
| ACTOMgSO$_4$ Crowther et al. 2003[35] | 1062 | 4g IV over 20 mins | 90% | 1g/hr IV for 24 hr or until delivery, whichever comes first | 6.5 (4.5, 14) |
| PREMAG Marrett et al. 2006[36] | 564 | 4g IV over 30 mins | 99% | None given | 4 g IV over 30 mins |
| MAGnet Mittendorf et al. 2002—neuroprotective intent arm[37] | 57 | 4g IV bolus | Not reported | Neuroprotective arm: none (Tocolysis arm: 2–3g/hr) | Not reported |
| BEAM Rouse et al. 2008[38] | 2241 | 6g IV over 20–30 mins* | >90%† | 2 g/hr IV for a maximum of 12 hr or until delivery† | 31.5 (29.0, 44.6) |
| **Other primary intent** | | | | | |
| MAGnet Mittendorf et al. 2002—tocolytic arm[37] | 92 | 4g IV "bolus" | Not known | 2–3 g/hr | Not reported |
| MAGPIE 2006[41] | 10 141 | 4g IV over 10 to15 mins | 96% | 1g/hr IV (or 5g/4hrs IM) for 24 hours | 18 (9, 29)‡ |

LD: loading dose; NA: not available.

* 71.5% of women were eligible for re-treatment. 59.1% of women were re-treated and were on magnesium sulphate at delivery.

† Based on the fact that 91% of women were on magnesium sulphate for at least three hours.

‡ Estimated as value uncertain from published data.[33]

## Table 1. Characteristics of Included Studies

| Study (First Author) | Inclusions | Women (n) | Fetuses (n) | Magnesium Dose |
|---|---|---|---|---|
| MagNET (Mittendorf et al[17]) | 25–33 wk in preterm labor | 149 | 165 | Tocolytic arm; 4 g loading, 2–3 g/h maintenance. Neuroprotective arm; 4 g loading only |
| ACTOMgSO$_4$ (Crowther et al[18]) | <30 wk, likely to deliver within 24 h | 1,062 | 1,255 | 4 g loading, 1 g/h maintenance |
| MAGPIE (Duley et al[22,23]) | All gestations* with severe preeclampsia | 1,544* | 1,593* | 4 g loading, 1 g/h IV maintenance, or 5 g every 4 h IM |
| PREMAG (Marret et al[19]) | <33 wk of gestation in labor | 573 | 688 | 4 g loading only |
| BEAM (Rouse et al[13]) | 24–31 wk at high risk of spontaneous birth | 2,241 | 2,444 | 6 g loading, 2 g/h maintenance |

MagNET, Magnesium and Neurologic Endpoints Trial; ACTOMgSO$_4$, Australasian Collaborative Trial of Magnesium Sulphate. MAGPIE, Magnesium Sulphate for Prevention of Eclampis; IV, intravenously; IM, intramuscularly; BEAM, Beneficial Effects of Antenatal Magnesium Sulfate.

* Only less than 37 weeks and undelivered at enrolment included in this analysis.

| Çalışma | sayı | Gebelik haftası | MgSO4 dozu | SP'de azalma |
|---|---|---|---|---|
| ACTOMgSO4 | 1024 | <30 | 4 g yükleme<br>1 g/st idame | Orta - ağır SP<br>(3.4% Vs 6.6 % ) |
| BEAM | 2241 | 24-31 | 6 g yükleme<br>2 g/st idame | Orta - ağır SP<br>(1.9% Vs 3.5 %) |
| PREMAG | 537 | <33 | 4 g yükleme | Mortalite & kaba motor disfonksiyon<br>(0.6% Vs 0.4%) |

**MgSO4 preterm doğumda SP riskini anlamlı düzeyde azaltır**

# MgSO4- Etki Mekanizması

Çeşitli hücre içi olaylarda rolü var

Glikoliz, Oksidatif fosforilasyon, Protein sentezi, DNA, RNA agregasyonu, Plazma membran bütünlüğünün devamı

Hücre metabolizması, ölümü, yaralanması veya beyin kan akımı üzerine etkileri

Pretermlerde hayatın ilk 2 günü kan basıncını stabilize ederek hemodinamik yararlı etkiler

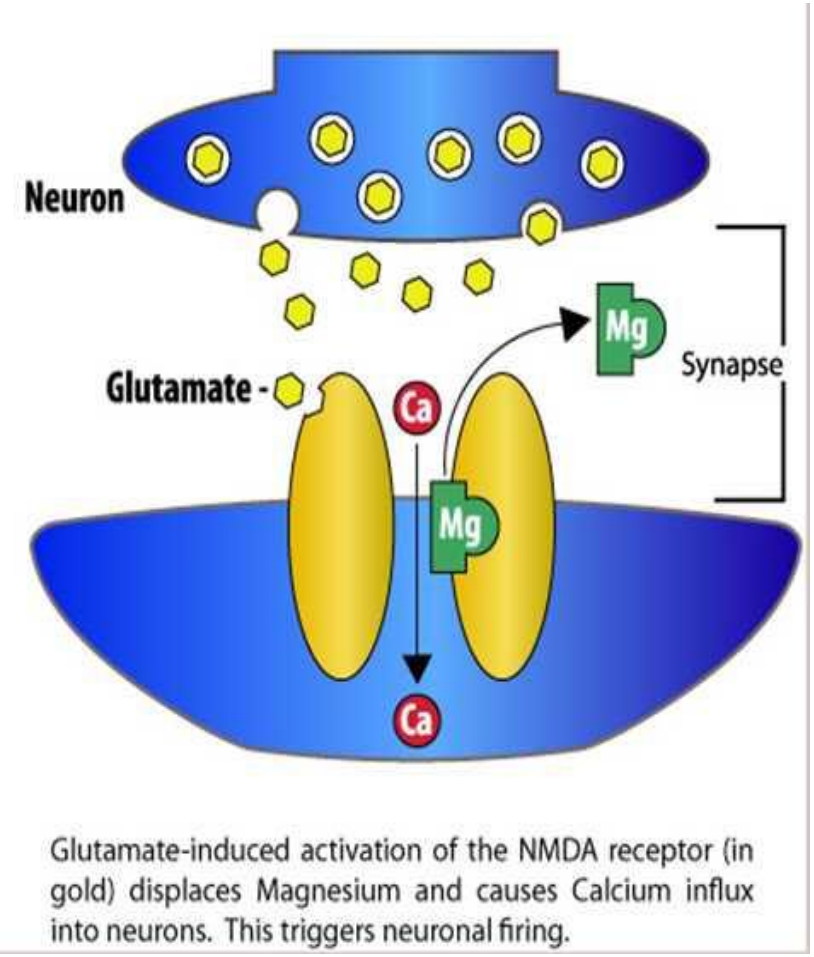
Serebral arterlerde vazokonstriksiyonu azaltarak beyin kan akımını arttırma

# Mg- Etki Mekanizması

Hipoksik iskemik reperfüzyon ve gebeliğin inflamatuar hastalık sırasında yükselen serbest radikal ve inflamasyon öncülerini azaltır

# MgSO4- Etki Mekanizması

## NMDA reseptörü




Glutamate-induced activation of the NMDA receptor (in gold) displaces Magnesium and causes Calcium influx into neurons. This triggers neuronal firing.

# Etki Mekanizması

**Antioksidan etki**

**Proinflamatuvar sitokinlerde azalma**

**Hücrelere kalsiyum girişinin engellenmesi**

**Membran stabilizasyonu**

**Serebral kan akımında artış**

Gathwala ,. Neuronal protection with magnesium. Indian J Pediatr 2001;68:417–9

Marret et al ., Semin Fetal Neonatal Med. 2007;12(4):311.

Hyagriv & Katherine .,UpToDate 19.3: January 2012

# MgSO4 Nöron Koruma

Gözlemsel çalışmalar

Randomize Kontrollü Çalışmalar

**Meta-analizler**

Rehberler ve görüşler

**ACOG , Committee Opinion 2010**

**Australian National Clinical Practice Guidelines 2010**

**SOGC Clinical Practice Guideline 2011**

**ACOG Patient Safety Checklist 2012**

**ACOG , Committee Opinion 2013**

**Institute Of Obstetricians &Gynecologist Royal College Of Physicians Of Ireland 2013**

# Meta- analizler

Doyle et al. Cochrane Database Syst Rev. 2009

Costantine et al. Obstet Gynecol. 2009;114(2 Pt 1):354.

Conde-Agudelo et al. Am J Obstet Gynecol 2009. 609-200:595,200

**MgSO4**

Pediatrik mortalite veya diğer nörolojik bozukluk veya yetersizlikte fark yok

RR: 1.04(%95CI: 0.92-1.17) 5 çalışma 6145

**Toplam SP ve ölüm oranlarında fark yok, ancak nöron koruma grubunda belirgin azalma var**

**RR: 0.85**(%95CI: 0.74-0.98) 4 çalışma 4446

Doyle et al., Cochrane Database Syst Rev. 2009

# Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks' gestation: a systematic review and metaanalysis

Agustín Conde-Agudelo, MD, MPH; Roberto Romero, MD

TABLE 3
**Effect of magnesium sulfate on cerebral palsy and pediatric mortality**

| Outcome | No. of trials | No. of events/total number | | Relative risk (95% CI) | $I^2$ (%) |
|---|---|---|---|---|---|
| | | Magnesium | No magnesium | | |
| Cerebral palsy | 6[30-32,34,35] | 104/2658 | 152/2699 | 0.69 (0.55-0.88) | 4.4 |
| Moderate/severe cerebral palsy | 3[31,34,35] | 45/2169 | 72/2218 | 0.64 (0.44-0.92) | 0.0 |
| Mild cerebral palsy | 3[31,34,35] | 54/2169 | 74/2218 | 0.74 (0.52-1.04) | 0.0 |
| Total pediatric mortality | 6[29,31,32,34,35] | 401/2658 | 400/2699 | 1.01 (0.89-1.14) | 38.9 |
| Fetal mortality | 5[29,31,34,35] | 17/2254 | 22/2298 | 0.78 (0.42-1.46) | 0.0 |
| Under 2 y of corrected age mortality | 5[29,31,34,35] | 217/2254 | 220/2298 | 1.00 (0.84-1.19) | 47.3 |
| Death or cerebral palsy | 6[30-32,34,35] | 505/2658 | 551/2699 | 0.92 (0.83-1.02) | 43.3 |

*CI*, confidence interval.

*Conde-Agudelo. Antenatal magnesium sulfate for preventing cerebral palsy in preterm infants. Am J Obstet Gynecol 2009.*

TABLE 6

## Effect of magnesium sulfate on infant neurodevelopmental outcomes

| Outcome | No. of trials | No. of events/total number | | Relative risk (95% CI) | $I^2$ (%) |
|---|---|---|---|---|---|
| | | Magnesium | No magnesium | | |
| Substantial gross motor dysfunction | 3[31,34,35] | 56/2169 | 94/2218 | 0.60 (0.43-0.83) | 0.0 |
| Major neurologic disability | 2[31,32] | 93/1033 | 85/1027 | 1.09 (0.83-1.43) | 15.3 |
| Any neurologic impairment | 2[31,32] | 198/1033 | 194/1027 | 1.02 (0.86-1.20) | 0.0 |
| Bayley mental development index < 85 | 3[31,34,35] | 639/2169 | 660/2218 | 1.00 (0.91-1.09) | 0.0 |
| Bayley mental development index < 70 | 1[35] | 165/1188 | 171/1256 | 1.02 (0.84-1.24) | NA |
| Bayley psychomotor development index < 85 | 1[35] | 299/1188 | 315/1256 | 1.00 (0.88-1.15) | NA |
| Bayley psychomotor development index < 70 | 1[35] | 134/1188 | 144/1256 | 0.98 (0.79-1.23) | NA |
| Blindness | 2[31,34] | 2/981 | 2/962 | 0.97 (0.14-6.90) | 0.0 |
| Deafness | 2[31,34] | 8/981 | 11/962 | 0.51 (0.05-4.96) | 58.7 |

*CI*, confidence interval; *NA*, not applicable.

*Conde-Agudelo. Antenatal magnesium sulfate for preventing cerebral palsy in preterm infants. Am J Obstet Gynecol 2009.*

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# MgSO4

**Major yan etki yok**

**Maternal komplikasyonlarda artış saptanmamış**

- **Ölüm** **(RR=1.25; 95%CI:0.51-3.07)**
- **Kardiak arrest** **(RR=0.34; 95%CI:0.04-3.26)**
- **Solunum arresti** **(RR=1.02; 95%CI:0.06-16.25)**

**Doyle et al Cochrane Database Syst Rev. 2009**

THE COCHRANE COLLABORATION®

## MgSO4 ile

**Minör yan etkiler: kızarma, terleme, baş ağrısı, çarpıntı**

**hipotansiyon, taşikardi artar**

- **Maternal solunum depresyonu**
- **Postpartum kanama**
- **C/S**

} **değişmez**

**Doyle et al Cochrane Database Syst Rev. 2009**

## MgSO4

THE COCHRANE COLLABORATION®

**Serebral palsi**

**2 yaşında kaba motor fonksiyon bozukluğu (yardımsız yürüyememe) risklerini anlamlı düzeyde azaltır**

**Pediatrik (fetal, neonatal) mortaliteyi azaltmaz**

Doyle et al., Cochrane Database Syst Rev. 2009

# Meta- analizler

**Fetal nöron koruma amaçlı verilen MgSO4**
**SP riskini azaltır**

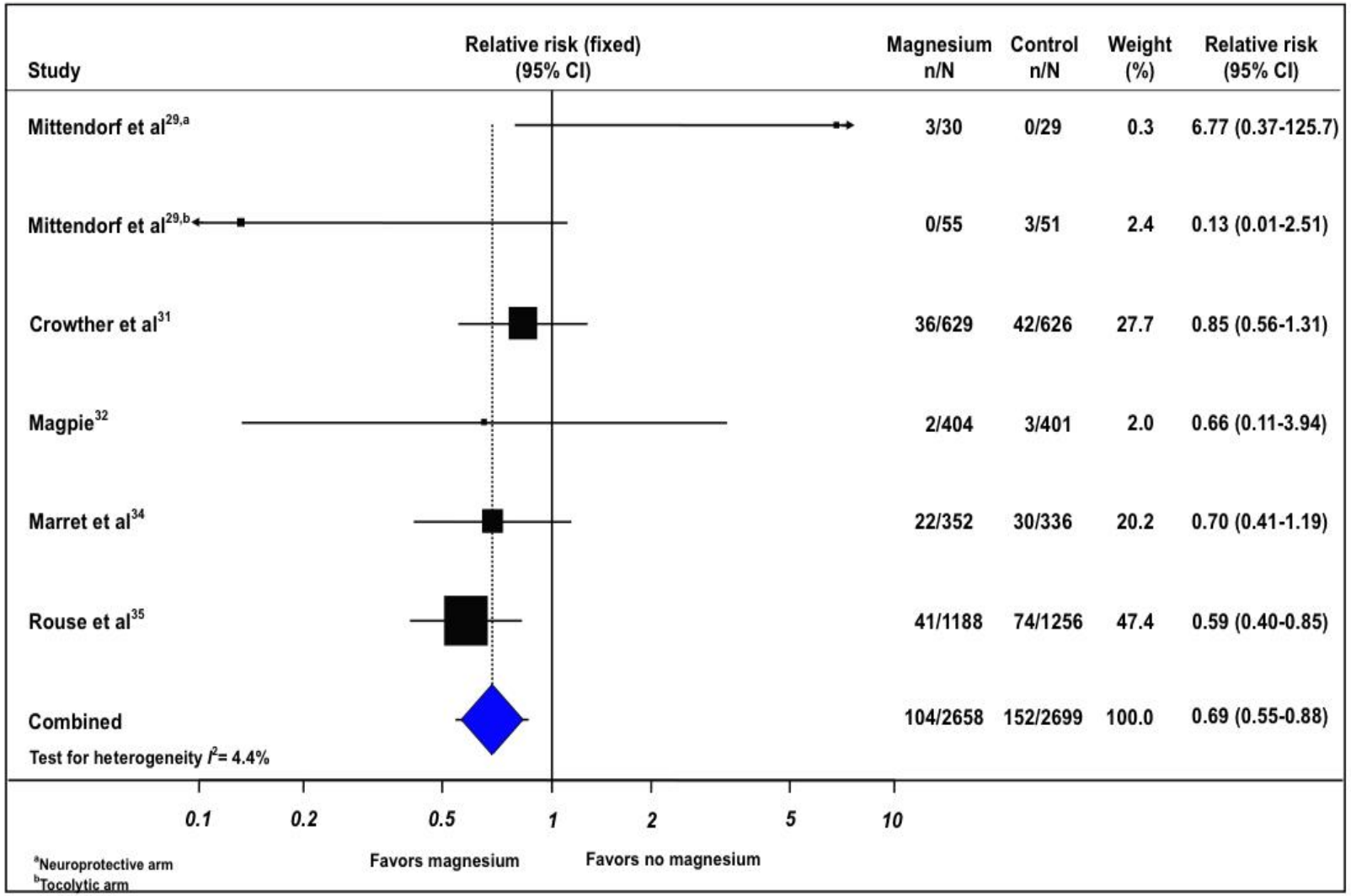
Doyle et al. Cochrane Database Syst Rev. 2009

Costantine et al. Obstet Gynecol. 2009;114(2 Pt 1):354.

Conde-Agudelo et al. Am J Obstet Gynecol 2009. 609-200:595,200

FIGURE 2

## Effect of magnesium sulfate on cerebral palsy




*Conde-Agudelo. Antenatal magnesium sulfate for preventing cerebral palsy in preterm infants. Am J Obstet Gynecol 2009.*

THE COCHRANE COLLABORATION®

**MgSO4, SP riskini %32 oranında azaltır ( 5.4% vs 3.7%)**

**Bir serebral palsiyi önlemek için magnezyum tedavisi alması gereken (Number Needed to Treat) gebe sayısı 63 ***

**Bir eklampsiyi önlemek için MgSO4 verilen gebe sayısı 70****

Doyle et al Cochrane Database Syst Rev. 2009 *

Sibai , Obstet Gynecol. 2005;105(2):402 **

Table 4b. Subgroup analyses by gestational age at randomization: all trials[26,35-38,41]

| | RR (95% CI) | | NNT to prevent harm | | |
|---|---|---|---|---|---|
| Weeks | Death or CP | CP | Death or CP | CP | Trials, n, infants, n |
| <34 | 0.94 (0.78 to 1.12) | 0.68 (0.54 to 0.87) | 105 | 63 | 5 trials, 6145 infants |
| <32 | 0.95 (0.76 to 1.18) | 0.69 (0.52 to 0.91) | 71 | 56 | 3 trials, 3981 infants |
| <30* | 0.97 (0.78 to 1.21) | 0.70 (0.49 to 0.99) | 71 | 56† | 3 trials, 2475 infants |
| <28* | 0.95 (0.74 to 1.22) | 0.45 (0.23 to 0.87) | 91 | 30 | 1 trial, 938 infants |

* Includes the <28 week subgroup of Rouse et al.,[38] which had women as the denominator.

This also includes the <30 week subgroup data provided by the MAGPIE trial.

† In the Cochrane review,[34] the <30 week subgroup did not include the BEAM trial data for <28 week[38] and the NNT was 50.

Table 4a. Subgroup analyses by gestational age at randomization: neuroprotective trials only[35–38]

| | RR (95% CI) | | NNT to prevent harm | | |
|---|---|---|---|---|---|
| Weeks | Death or CP | CP | Death or CP | CP | Trials, n, infants, n |
| <34 | 0.85 (0.74 to 0.98) | 0.71 (0.55 to 0.91) | 43 | 53 | 5 trials, 6145 infants |
| <32 | 0.86 (0.74 to 1.00) | 0.68 (0.52 to 0.91) | 43 | 50 | 3 trials, 3981 infants |
| <30* | 0.87 (0.74 to 1.03) | 0.69 (0.48 to 0.99) | 36 | 53† | 3 trials, 2475 infants |
| <28* | 0.95 (0.74 to 1.22) | 0.45 (0.23 to 0.87) | 91 | 30 | 1 trial, 938 infants |

* Includes the <28 week subgroup of Rouse et al.[38] which had women as the denominator.

† Inclusion of only the Crowther et al.[35] trial and exclusion of the BEAM data (Rouse et al.[38]) give an NNT of 24.

**Nöron koruma alt grubunda ise 1 SP den korunmak için 43 tedavi**

## Major nörolojik sonuçlarda fark yok

- Apgar 5dk <7
- Solunum desteğinin devamı
- IVK
- PLM
- Neonatal konvulsiyon
- Takipte(körlük, sağırlık, gelişim geriliği ve herhangi bir nörolojik, bozukluk


Doyle et al Cochrane Database Syst Rev. 2009

Costantine et al Obstet Gynecol. 2009;114(2 Pt 1):354.

Doyle Obstet Gynecol. 2009;113(6):1327.

# 3 Meta-analiz

**1. Gebelik yaşı**

**2. Optimal doz belli değildir**

3. İntraventriküler kanama
   Beyaz cevher hasarı
   İşitme kaybı
   Görme kaybı
   Gelişimsel geriliği

azaltmaz

**Öğrenme güçlükleri ve okul başarısındaki etkisi ile ilgili veri yoktur**

# MgSO4 Nöron Koruma

Gözlemsel çalışmalar
Randomize Kontrollü Çalışmalar
Meta-analizler

**Rehberler ve görüşler**

**ACOG , Committee Opinion 2010**

**Australian National Clinical Practice Guidelines 2010**

**SOGC Clinical Practice Guideline 2011**

**ACOG Patient Safety Checklist 2012**

**ACOG , Committee Opinion 2013**

**Institute Of Obstetricians &Gynecologist Royal College Of Physicians Of Ireland 2013**

The Society for Maternal Fetal Medicine

**The American College of Obstetricians and Gynecologists**
*Women's Health Care Physicians*

# COMMITTEE OPINION

Number 455 • March 2010

**Committee on Obstetric Practice**

*This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.*

*Reaffirmed 2013*

## Magnesium Sulfate Before Anticipated Preterm Birth for Neuroprotection

**Erken preterm doğumda MgSO4 verilmesi SP'yi azaltır**

**Gebelik haftasının sınırı konusunda farklı görüşler mevcuttur**

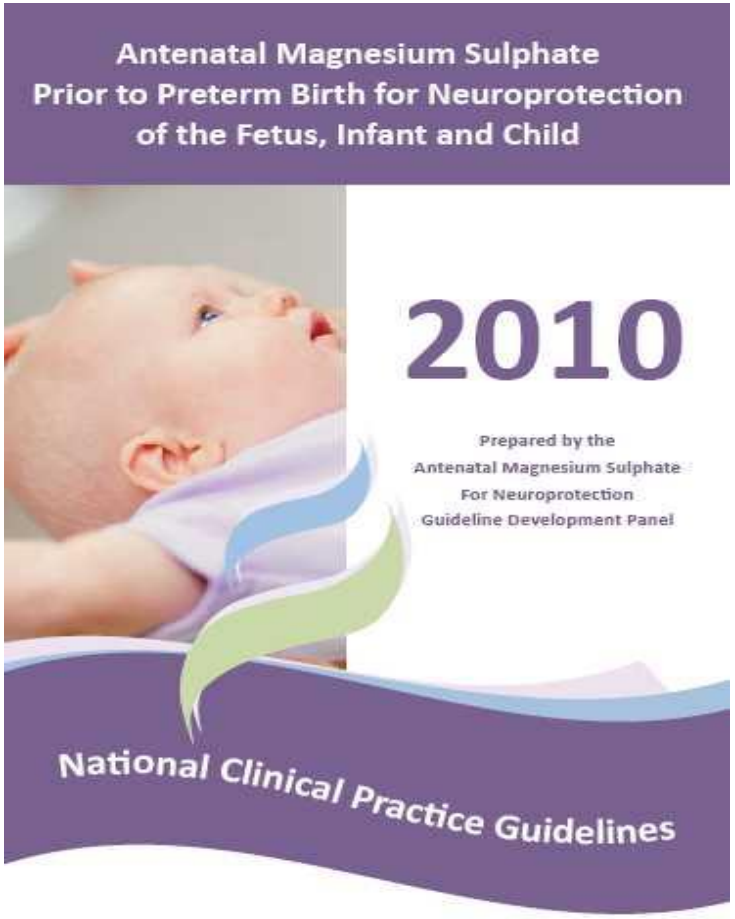
**Doz, tokoliz,takip ile ilgili rehberler oluşturulmalıdır**

Obstet Gynecol. 2010;115(3):669-71

# The Australian National Clinical Practice Guidelines

**Nöron koruma amaçlı**
**24 saat içerisinde doğum**
**beklenen preterm olgularda**

**<30 hafta**
**Doz: 4g yükleme (30 dk)**
**doğuma kadar 1gr/st idame**




The Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel. : National Clinical Practice Guidelines. The Australian Research Centre for Health of Women and Babies, The University of Adelaide; 2010

# SOGC Clinical Practice Guideline No. 258, May 2011

# MgSO4 for Fetal Neuroprotection

SOGC CLINICAL PRACTICE GUIDELINE

No. 258, May 2011

## Magnesium Sulphate for Fetal Neuroprotection

**32. haftadan önce doğumu öngörülen hastalara fetal nöron koruma amaçlı antenatal MgSO4 verilmesi önerilir (I- A)**

Magee et al . SOGC Clinical Practice Guideline. Magnesium sulphate for fetal neuroprotection. J Obstet 14. Gynaecol Can. 2011;33(5):516-29.

No. 258, May 2011

# Magnesium Sulphate for Fetal Neuroprotection

## Aşağıdakilerden herhangi biri varsa (II-2)

**Servikal dilatasyonun ≥ 4 cm'den fazla olduğu aktif travay**

**Fetal ya da maternal endikasyonlarla planlanmış preterm doğum**

No. 258, May 2011

# Magnesium Sulphate for Fetal Neuroprotection

**Gebelik haftası?**

**Viabilite - < 32 hafta (II-B)**

**MgSO4 başlanırsa, tokoliz kesilmelidir (III-A)**

SOGC Clinical Practice Guideline No. 258, May 2011

No. 258, May 2011

# Magnesium Sulphate for Fetal Neuroprotection

**Tekrar?**

**Tekrarı konusunda yeterli kanıt bulunmamaktadır. (III-E)**

**Doğum zamanlaması?**

**Doğum için acil maternal-fetal endikasyonlar varsa doğum geciktirilmemelidir(III-E)**

SOGC CLINICAL PRACTICE GUIDELINE

No. 258, May 2011

# Magnesium Sulphate for Fetal Neuroprotection

**Doz?**

**4g MgSO4 yükleme (30 dk)** doğuma kadar ya da 24 st boyunca 1gr/st idame (II-2B)

**Mg SO4 doğumdan en az 4 st önce verilmelidir (II-2B)**

SOGC Clinical Practice Guideline No. 258, May 2011

# 2012 - ACOG

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

*Patient Safety Checklist* ✓

Number 7 • August 2012

## MAGNESIUM SULFATE BEFORE ANTICIPATED PRETERM BIRTH FOR NEUROPROTECTION

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

*Patient Safety Checklist* ✓ Number 7 • August 2012

MAGNESIUM SULFATE BEFORE ANTICIPATED PRETERM BIRTH FOR NEUROPROTECTION

Date_____ Patient _____ Date of birth_____ MR # _____
Physician or certified nurse-midwife _____ Last menstrual period _____
Gravidity/Parity_____
Estimated date of delivery_____ Best estimated gestational age _____

Criteria (1):
- ❑ Gestational age less than or equal to 31 6/7 weeks

and
- ❑ Singleton or multiple pregnancy at risk for delivery within the next 30 minutes to 24 hours

and either
- ❑ Active preterm labor with cervix 4–8 cm dilated or preterm premature rupture of membranes if rupture occurred later than 22 weeks

or
- ❑ Indicated preterm birth within the next 24 hours. (If the planned delivery is for severe preeclampsia or hemolysis, elevated liver enzymes, and low platelet count [HELLP], the full antiseizure magnesium sulfate regimen should be administered as minimal therapy.)

Exclusions:
- ❑ Unwillingness to intervene for the benefit of the fetus
- ❑ Maternal contraindications to receiving magnesium sulfate

Counseling:
- ❑ Temporary side effects of magnesium sulfate administration
- ❑ No documented benefit in neonatal survival
- ❑ Risk of moderate to severe cerebral palsy decreased by approximately 30%
- ❑ In all other ways, routine care will be provided (steroids, tocolysis, antibiotics, or induction for preterm premature rupture of membranes if indicated)

Specific considerations with therapy:
- ❑ Consider the effect of administering magnesium sulfate if any other tocolytic agent, such as a calcium channel blocker, is being given
- ❑ Adjust the dose of magnesium sulfate appropriately if administered to women with altered renal function

Suggested treatment regimens from large trials (1):

Crowther Regimen (2):
- ❑ Bolus 4 g magnesium sulfate intravenously (IV) over 20 minutes
- ❑ Follow bolus with magnesium sulfate 1 g/hr IV until birth or up to 24 hours

Rouse Regimen (3):
- ❑ Bolus 6 g magnesium sulfate IV over 20–30 minutes
- ❑ Follow bolus with magnesium sulfate 2 g/hr IV for 12 hours

*(continued)*



Rouse Regimen (3) *(continued)*:
- ❑ Discontinue maintenance dose if delivery has not occurred within 12 hours and is no longer considered imminent. Resume the maintenance dose if the risk of imminent delivery recurs within 6 hours.
- ❑ Repeat loading dose and subsequent maintenance therapy as listed previously if risk of imminent delivery recurs after 6 hours

Marret Regimen (4):
- ❑ Bolus 4 g magnesium sulfate over 30 minutes
- ❑ No maintenance dose administered

Modification of any of the aforementioned regimens:
- ❑ Detailed description of the modified regimen entered in patient's chart

### Resource

Costantine MM, Weiner SJ. Effects of antenatal exposure to magnesium sulfate on neuroprotection and mortality in preterm infants: a meta-analysis. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Obstet Gynecol 2009;114:354–64.

### References

1. Magnesium sulfate before anticipated preterm birth for neuroprotection. Committee Opinion No. 455. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;115:669–71.
2. Crowther CA, Hiller JE, Doyle LW, Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. JAMA 2003;290:2669–76.
3. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network. N Engl J Med 2008;359:895–905.
4. Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Levaque C, Hellot MF, et al. Magnesium sulfate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial. PREMAG trial group. BJOG 2007;114:310–8.

*Standardization of health care processes and reduced variation has been shown to improve outcomes and quality of care. The American College of Obstetricians and Gynecologists has developed a series of Patient Safety Checklists to help facilitate the standardization process. This checklist reflects emerging clinical, scientific and patient safety advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Although the components of a particular checklist may be adapted to local resources, standardization of checklists within an institution is strongly encouraged.*

### How to Use This Checklist

The Patient Safety Checklist on Magnesium Sulfate Before Anticipated Preterm Birth for Neuroprotection should be completed by the health care provider during the patient's admission.

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Magnesium sulfate before anticipated preterm birth for neuroprotection. Patient Safety Checklist No. 7. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:432–3.

# 2012 - ACOG

## Tedaviye alınma kriterleri

- <31hf +6
- 30dk ile 24 st içinde doğum yapacaklar
- Tekil, çoğul gebelik
- Dilatasyon  4- 8cm veya spontan EMR >22hf
- Elektif prematurite ve 24 st içinde doğum yapacak ise(ciddi PE)

# 2012 - ACOG

**Dışlanma kriterleri**

- Maternal kontrendikasyonlar

- Fetusa gerçek bir fayda sağlayacağı düşünülmüyorsa (tam olarak tanımlanmamış)

# Doz, rejim

Suggested treatment regimens from large trials (1):

Crowther Regimen (2):

- ❑ Bolus 4 g magnesium sulfate intravenously (IV) over 20 minutes
- ❑ Follow bolus with magnesium sulfate 1 g/hr IV until birth or up to 24 hours

Rouse Regimen (3):

- ❑ Bolus 6 g magnesium sulfate IV over 20–30 minutes
- ❑ Follow bolus with magnesium sulfate 2 g/hr IV for 12 hours

Rouse Regimen (3) *(continued)*:

- ❑ Discontinue maintenance dose if delivery has not occurred within 12 hours and is no longer considered imminent. Resume the maintenance dose if the risk of imminent delivery recurs within 6 hours.
- ❑ Repeat loading dose and subsequent maintenance therapy as listed previously if risk of imminent delivery recurs after 6 hours

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- ❑ No maintenance dose administered

Modification of any of the aforementioned regimens:

- ❑ Detailed description of the modified regimen entered in patient's chart

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Society for Maternal-Fetal Medicine

# COMMITTEE OPINION

Number 573 • September 2013

**The American College of Obstetricians and Gynecologists Committee on Obstetric Practice**
**Society for Maternal-Fetal Medicine**

*This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.*

## Magnesium Sulfate Use in Obstetrics

**ABSTRACT:** The U.S. Food and Drug Administration advises against the use of magnesium sulfate injections for more than 5–7 days to stop preterm labor in pregnant women. Based on this, the drug classification was changed from Category A to Category D, and the labeling was changed to include this new warning information. However, the U.S. Food and Drug Administration's change in classification addresses an unindicated and nonstandard use of magnesium sulfate in obstetric care. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine continue to support the short-term (usually less than 48 hours) use of magnesium sulfate in obstetric care for appropriate conditions and for appropriate durations of treatment, which includes the prevention and treatment of seizures in women with preeclampsia or eclampsia, fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery, and short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal corticosteroids in pregnant women between 24 weeks of gestation and 34 weeks of gestation who are at risk of preterm delivery within 7 days.

# Obstetride MgSO4

**Endikasyonsuz ve standart olmayan dozlarda kullanılmamalı**

**∗Preeklampsi ve eklampside önleme**

**∗ Erken doğum beklenenlerde <32hf nöron koruma**

**∗ Tokolitik**

7 gün içinde doğum riski varsa, kortikosteroid etkinliği sağlamak için 24- 34hf

# Obstetride $MgSO_4$

**Dikkatli ve önerilen protokollere göre uygulanmalıdır**

**Uzun süreli kullanımda fetal ve neonatal uzun kemiklerde demineralizasyon ve kırıklar**

**Anne ve bebekte; Ca, P, Mg düzeylerinde bozukluk**

**FDA : Gebelik kategorisi A dan D ye çevirdi**

# Obstetride MgSO4

**YENİ DOĞAN**

**Hipermagnezemi**

Emme zayıflığı,apne,hipoventilasyon, zayıflık,hipotoni,hiporefleksi

Nadiren ventilasyon gerektiren solunum depresyonu

Stüpor, koma

Ölüm: 4.5 meq/L

**Anne ve fetusun monitorizasyonu**

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

INSTITUTE OF OBSTETRICIANS & GYNAECOLOGISTS
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

# CLINICAL PRACTICE GUIDELINE

# ANTENATAL MAGNESIUM SULPHATE FOR FETAL NEUROPROTECTION

Institute of Obstetricians and Gynaecologists,
Royal College of Physicians of Ireland
And
Directorate of Strategy and Clinical Care
Health Service Executive

## Key Recommendations

1. Data from several large randomized controlled trials and a Cochrane meta-analysis give evidence for a beneficial effect for magnesium sulphate in reducing the risk of cerebral palsy in infants delivered at preterm gestations. Thus administration of magnesium sulphate should be considered in all cases of planned or anticipated preterm delivery

2. Use of magnesium sulphate should be considered in all patients at risk of imminent preterm delivery before 32 weeks. However, in situations of limited resources, emphasis should be placed on ensuring that women delivering at 28 weeks or less, when the greatest benefit has been shown, receive antenatal magnesium sulphate.

3. Optimal benefit is seen with use of a loading dose of magnesium sulphate followed by and infusion. The recommended dosing regimen is 4g loading dose followed by an infusion of 1g/hr continued until delivery or for 24 hours, whichever occurs sooner.

4. In cases of limited resources for maternal monitoring, or limited time, it is reasonable to administer a 4g loading dose only, without a subsequent infusion.

5. Am to commence magnesium sulphate approximately 4 hours prior to delivery. If it is not possible to achieve a 4 hour window prior to delivery, magnesium sulphate should still be administered, as it is likely that some benefit will be seen when administered within this time

6. No evidence available at present to guide management regarding repeated doses of magnesium sulphate in those patients that do not deliver and have magnesium sulphate discontinued. It is reasonable to consider giving a repeat dose in the event of imminent preterm delivery if 24 hours have elapsed since discontinuing the magnesium sulphate.

7. Given the potential for adverse maternal and fetal effects of magnesium sulphate both maternal and fetal monitoring must be employed during magnesium sulphate administration.

**<32 hf (*<28hf)**

**Doz: 4g I.V bolus, 1g/st idame**

*** 4g.İ.V bolus**

Different magnesium sulphate regimens for neuroprotection of the fetus for women at risk of preterm birth (Review)

Bain E, Middleton P, Crowther CA

THE COCHRANE COLLABORATION®

**Rejim, Doz, Süre,Tekrar dozu ve zamanı: Fikir birliği yok**

**Doz? Farklı doz protokollerini karşılaştıran çalışma bulunmamaktadır**

**Bain et al. Cochrane Database Syst Rev. 2012 Feb 15;2:CD009302**

İdeal çift kör plasebo kontrollü çapraz çalışma yok

çeşitli protokoller var

**Hangi protokolden çok tedaviye başlanması önemli**

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:91
http://www.biomedcentral.com/1471-2393/13/91

BMC
Pregnancy & Childbirth

STUDY PROTOCOL Open Access

# Magnesium sulphate at 30 to 34 weeks' gestational age: neuroprotection trial (MAGENTA) - study protocol

Caroline A Crowther[1,2*], Philippa F Middleton[1], Dominic Wilkinson[1], Pat Ashwood[1], Ross Haslam[2,3] and for the MAGENTA Study Group

RCT, çok merkezli, 1676

Doğum planlanan veya 24st içinde beklenen

Tekil, ikiz, 30-34hf

**Doz: 8g MgSO4, I.V, 30dk,** Plasebo, %0.9 NaCl

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:91
http://www.biomedcentral.com/1471-2393/13/91

BMC
Pregnancy & Childbirth

STUDY PROTOCOL Open Access

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Caroline A Crowther[1,2*], Philippa F Middleton[1], Dominic Wilkinson[1], Pat Ashwood[1], Ross Haslam[2,3] and for the MAGENTA Study Group

**Mg kontrendike:**

Solunum depresyonu, hipotansiyon, renal yetmezlik, miyastenia gravis

**Yazılı onam**

100ml inf / 50ml 8g mg, 30dk

TA,Nb,Solunum: infüzyon öncesi ve 15dk sonra bitene dek 15dk da

Bu dozda toksisite beklenmez**, serum Mg gerek yok**

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:91
http://www.biomedcentral.com/1471-2393/13/91

BMC
Pregnancy & Childbirth

STUDY PROTOCOL Open Access

# Magnesium sulphate at 30 to 34 weeks' gestational age: neuroprotection trial (MAGENTA) - study protocol

Caroline A Crowther[1,2*], Philippa F Middleton[1], Dominic Wilkinson[1], Pat Ashwood[1], Ross Haslam[2,3]
and for the MAGENTA Study Group

Teorik olarak Mg ve nifedipin hipotansiyon ve nöromuskuler blokaj etkisi var, fakat klinik uygulamada nadir

- Solunum sayısı dk bazalin <4 veya <12 ise
- Diastolik kan basıncı bazalden <15mm ise

İnfüzyonu kes, normale gelirse tekrar başla

- Solunum depresyonu varsa 1g kalsiyum glukonat 10ml %10 luk solusyon i.v yavaş 10dk
- Resüsitasyon desteği hazır

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:91
http://www.biomedcentral.com/1471-2393/13/91

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Caroline A Crowther[1,2*], Philippa F Middleton[1], Dominic Wilkinson[1], Pat Ashwood[1], Ross Haslam[2,3] and for the MAGENTA Study Group

Doğumdan 2 yıllık takiplerine dek onay (6,12,18,2 yş)
Sağlık
Nörogelişimsel
Davranış
Büyüme
GMFCS(0-5)
Psikolojik değerlendirme: Kognitif  motor, dil
BAYLEY skala (BSID-III)
Görme keskinliği

**Table 3 Neurosensory Disability Classifications [51]**

| | |
|---|---|
| **Severe Disability** | Any severe cerebral palsy (child non-ambulant and likely to remain so; GMFCS level 4 or 5), severe developmental delay (standardised score <−3 SD) or blindness. |
| **Moderate Disability** | Moderate cerebral palsy (child non-ambulant at 2 years of age but who is likely to ambulate subsequently; GMFCS level 2 or 3), or deafness, or moderate developmental delay (standardised score from −3 SD to <−2 SD). |
| **Mild Disability** | Mild cerebral palsy (child walking at 2 years of age with only minimal limitation of movement (GMFCS level 1), or suspect developmental delay (standardised score from −2 SD to <−1 SD). |
| **No Neurosensory Disability** | Children without any neurosensory impairment. |

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:91
http://www.biomedcentral.com/1471-2393/13/91

BMC
Pregnancy & Childbirth

STUDY PROTOCOL Open Access

# Magnesium sulphate at 30 to 34 weeks' gestational age: neuroprotection trial (MAGENTA) - study protocol

Caroline A Crowther[1,2*], Philippa F Middleton[1], Dominic Wilkinson[1], Pat Ashwood[1], Ross Haslam[2,3]
and for the MAGENTA Study Group

**Analiz ve sonuçların rapor edilmesi bekleniyor**

Crowther et al. BMC Pregnancy and Childbirth 2013, 13:239
http://www.biomedcentral.com/1471-2393/13/239

BMC Pregnancy & Childbirth

STUDY PROTOCOL Open Access

# Working to improve survival and health for babies born very preterm: the WISH project protocol

Caroline A Crowther[1,2*], Philippa F Middleton[1], Emily Bain[1], Pat Ashwood[1], Tanya Bubner[1], Vicki Flenady[3], Jonathan Morris[4], Sarah McIntyre[5] for the WISH Project Team

Avustralya 600 SP/yıl, Yeni Zellanda 150 SP/yıl

%40' ı preterm doğuma bağlı, yıllık 4 milyon Avustralya doları

Avustralya, Yeni Zellanda, 25 tersiyer merkez

Rehber uygulanırsa erken preterm doğumlarda ölüm ve SP ve uzun dönem sorunlardan >90 bebek korunacak

Crowther CA et al, Pregnancy and Childbirth 2013

Crowther *et al. BMC Pregnancy and Childbirth* 2013, **13**:239
http://www.biomedcentral.com/1471-2393/13/239

BMC
Pregnancy & Childbirth

STUDY PROTOCOL Open Access

# Working to improve survival and health for babies born very preterm: the WISH project protocol

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28hf SP, 30 kat terme göre, Kombine ölüm veya SP için NNT 42-43

Audit, 22-34hf

Bilgilendirme

Onam;12-24 ay, 2- 3 yaş takipleri için

Implementation of a clinical practice guideline for antenatal magnesium sulphate for neuroprotection in Australia and New Zealand

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25 merkez
Mart- Haziran 2012

22 si anketi yanıtlamış

**%76 rehberi uyguluyor,** %36 audit

Bain E et al, WISH Project Team, ANZJOG 2012

DOI: 10.1111/1471-0528.12535
www.bjog.org



# Maternal adverse effects with different loading infusion rates of antenatal magnesium sulphate for preterm fetal neuroprotection: the IRIS randomised trial

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<30hf, 52 gebe

4g İ.V 20 vs 60dk, 1g/st idame

Yan etkilerde fark yok; kızarma ve sıcaklık hissi 60dk daha az

ES Bain et al, BJOG 2014

# Termde MgSO4

## Magnesium sulphate for women at term for neuroprotection of the fetus (Review)

Nguyen TMN, Crowther CA, Wilkinson D, Bain E

1 çalışma, RCT
135 gebe
hafif PE, fark yok
6 çalışma sonuçları ?

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**Authors' conclusions**

There is currently insufficient evidence to assess the efficacy and safety of magnesium sulphate when administered to women for neuroprotection of the term fetus. As there has been recent evidence for the use of magnesium sulphate for neuroprotection of the preterm fetus, high-quality randomised controlled trials are needed to determine the safety profile and neurological outcomes for the term fetus. Strategies to reduce maternal side effects during treatment also require evaluation.

# ?

MASP Study: Danimarka, İsveç,Norveç, İzlanda

5g bolus 1g/st, <32hf , 1240, 2011 de başladı

MAGENTA: Avustralya

WISH : Yeni Zellanda

WISH : Avustralya

In Utero Magnesium Sulfate Exposure: Effects on Extremely low Birth Weight Infants : 401-1500g ABD

ACTOMgSO4 : Takip sürüyor

# Maliyet-etkin

ABD de <32hf gebeler %2

1000/3-4, 800 000 SP yıl, her yıl 8000 ekleniyor

MgSO4 ile yılda 1000 olgu SP den korunur

**Hayat boyu maliyeti: 2013: 1.1milyon $**

2003 toplam: 11.5 milyar $

MgSO4 maliyeti 180 dolar, 1SP önlemek için **10.200 $** (NNT 56)

Heyborne KD ,Postgraduate Obstetrics and Gynecology 2010, 30

**MgSO4**

Ucuz, kolay bulunur, uygulama kolay, uygun şekilde kullanılırsa güvenilir

Sıcaklık hissi, kızarma, injeksiyon bölgesi ağrısı gibi minör yan etkiler

Rousse JD, AJOG 2011

ES Bain et al, BJOG 2014

# ONAM

Pretermlerde nörolojik bozukluk, ölüm riski yüksek

MgSO4 ın bu riski azalttığına dair bazı veriler var, ancak bu risk yaşayanlarda tamamen yok edilemez

MgSO4 alanlarda yan etkiler nedeniyle sıkı monitorizasyon gerekir

Cahill AG et al, 2010 Curr Opin Obstet Gynecol 22;122-27

# SON SÖZ

# FETAL NÖRON KORUMA YAPALIM

# TEŞEKKÜRLER

# Obstetride MgSO4

Periferik vazodilatatör etki ile sıcaklı hissi kızarma

Dozaj ve infüzyon hızına bağlı

Bulantı kusma, başağrısı, çarpıntı, hipotansiyon ve solunum depresyonu gibi ciddi riskler

Tendon reflekslerini kaldırarak nöromuskuler blokan ajan gibi görevi görür

Diğer ilaçların( betamimetik, kalsiyum kanal blokerleri ve gentamisin gibi) kardiovasküler ve nöromusküler yan etkilerini arttırabilir.

Terapotik sınırların dışına çıkarsa hayatı tehdid eden solunum ve kardiak arrest yol açabilir