PRETERM NÖRON KORUNMASINDA MAGNEZYUM SÜLFAT

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Perinatoloji Bilim Dalı

Serebral Palsi (SP)

Gelişmekte olan fetus veya bebek beynindeki hasar…

Çocukluk çağı ağır motor bozukluğunun en sık nedeni

Kalıcı, ilerleyici olmayan, aktivite kısıtlamasına yol açan hareket ve duruş bozuklukları

+ duyu, algı, bilişsel, iletişim, davranış bozuklukları

Prevalans: 1/323 çocuk

Klinik Sınıflama

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

2 yaşında güvenilir tanı

Tip ve ciddiliği 4-5 yaşa 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)

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

PRETERM SP

İntrakranial Kanama

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

Beyaz Cevher Hasarı en sık 28.hf

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: $MgSO_4$

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 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 uzman

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]

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

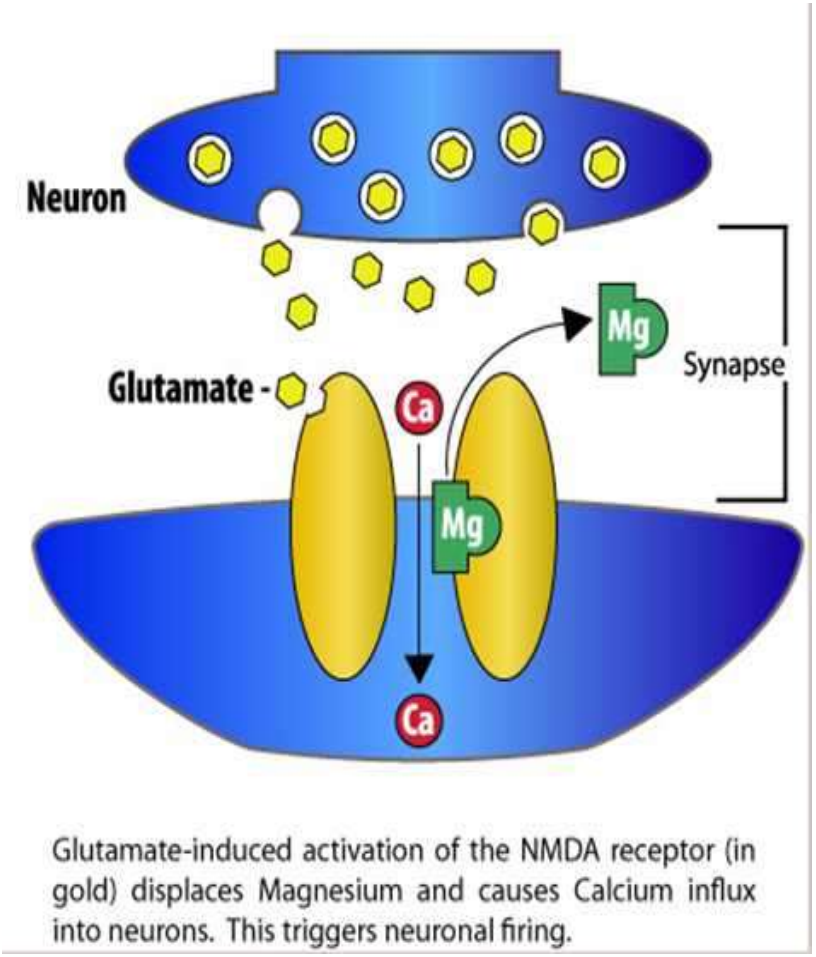
Hücre metabolizması, ölümü, yaralanması veya beyin kan akımı üzerine etkileri

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

Serebral arterlerde vazokonstriksiyonu azaltarak beyin kan akımını arttırma

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

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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

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

THE COCHRANE COLLABORATION®

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

Meta- analizler

Fetal nöron koruma amaçlı verilen $MgSO_4$
SP riskini azaltır

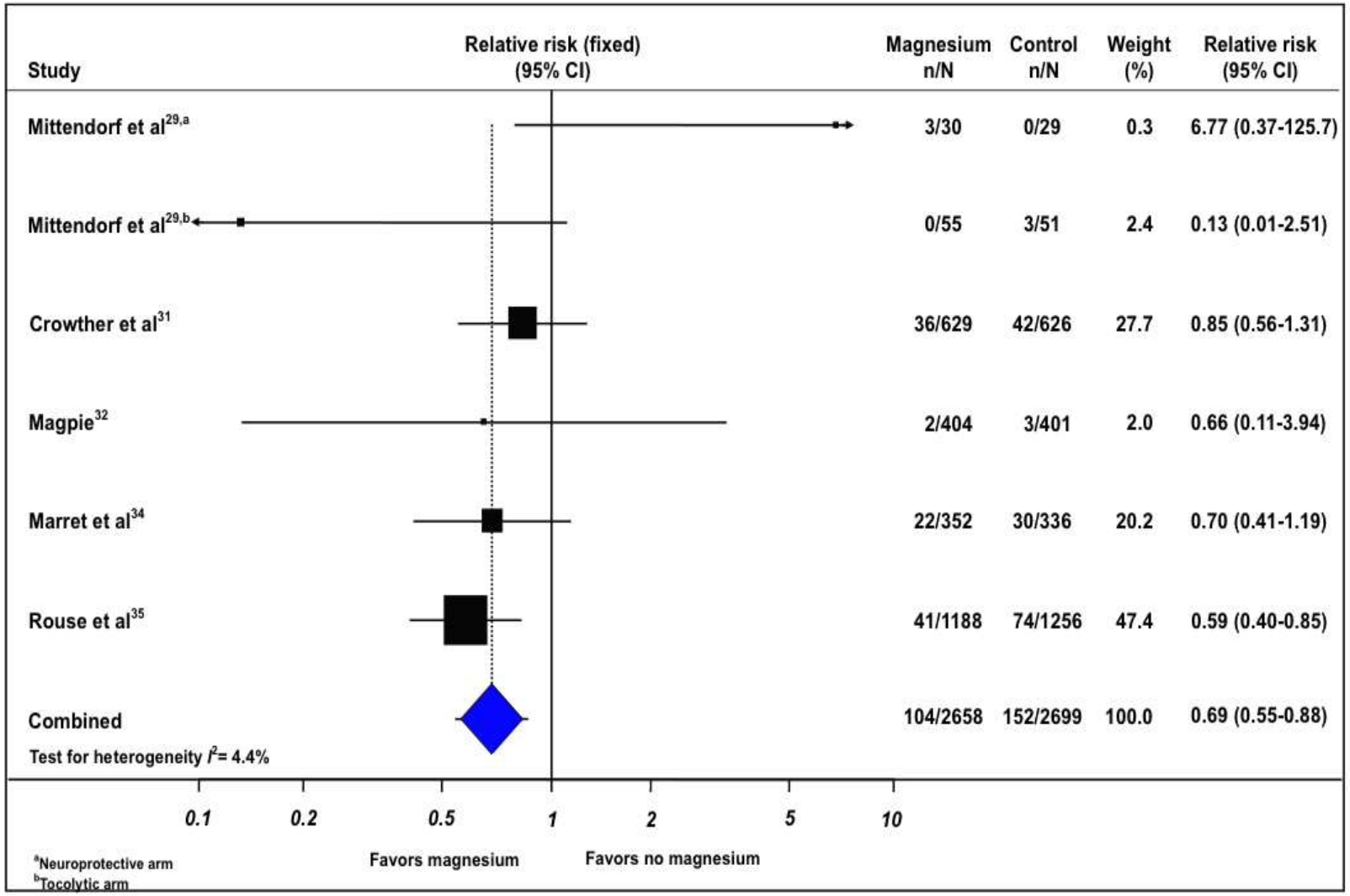
Doyle et al. Cochrane Database Syst Rev. 2009

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

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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

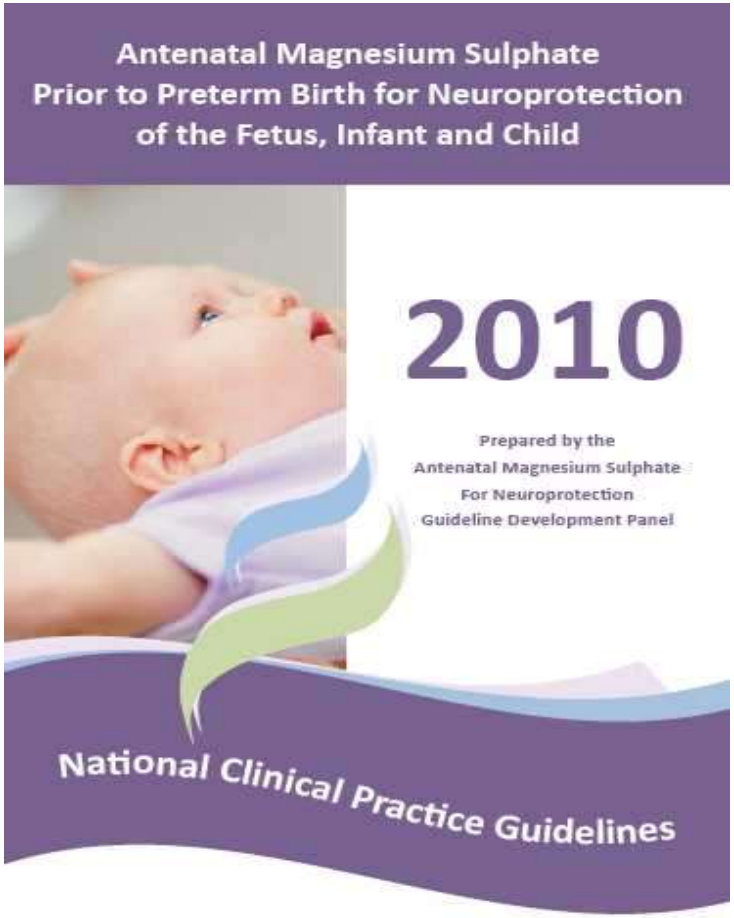
Doz, tokoliz,takip ile ilgili rehberler oluşturulmalıdır

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

SOGC Clinical Practice Guideline No. 258, May 2011

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

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, Leveque 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.

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

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

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

İdeal çift kör plasebo kontrollü çapraz çalışma yok, çeşitli protokoller var

Hangi protokolden çok tedaviye başlanması önemli

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

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, vs 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

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Mg kontrendike:

Solunum depresyonu, hipotansiyon, renal yetmezlik, miyastenia gravis

Yazılı onam

100ml inf / 50ml 8g $MgSO_4$, 30dk

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

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

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

BMC Pregnancy & Childbirth

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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 yavaş10dk

- Resüsitasyon desteği hazır olmalı

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

BMC Pregnancy & Childbirth

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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**

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28hf SP, terme göre 30 kat fazla, 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

Emily BAIN, Tanya BUBNER, Pat ASHWOOD, Caroline A. CROWTHER and Philippa MIDDLETON, for The WISH Project Team

Australian Research Centre for Health of Women and Babies, Discipline of Obstetrics and Gynaecology, Robinson Institute, The University of Adelaide, Adelaide, South Australia, Australia

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

ES Bain,[a] PF Middleton,[a] LN Yelland,[a] PJ Ashwood,[a] CA Crowther[a,b]

<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

CLINICAL AND LABORATORY OBSERVATIONS

www.jpeds.com • The Journal of Pediatrics

School-Age Outcomes following a Randomized Controlled Trial of Magnesium Sulfate for Neuroprotection of Preterm Infants

Clément Chollat, MD[1,2], Maya Enser, MD[3], Estelle Houivet, MSc[4], Delphine Provost, MD[3], Jacques Bénichou, MD, PhD[4], Loïc Marpeau, MD[2,5], and Stéphane Marret, MD, PhD[1,2]

In a French randomized trial, children at school-age demonstrated no evidence of harm from fetal exposure to $MgSO_4$ before very preterm birth. Motor dysfunction/death, qualitative behavioral disorders, cognitive difficulties, school grade repetition, and education services were decreased in the children exposed to $MgSO_4$, although the differences were not significant. *(J Pediatr 2014;165:398-400)*

2009- 2012, aile ile görüşme 48 soru-anket,
503 çocuğun uzun dönem sonuçları var (%26.9 takip dışı) ~11yş(7-14yş)

MgSO4 ın uzun dönemde zararlı etkisi yok.
Nörolojik sonuçları iyileştiriyor(ancak istatistiksel anlamlı farklılık bulunmamış)

www.jpeds.com • THE JOURNAL OF PEDIATRICS

School-Age Outcomes following a Randomized Controlled Trial of Magnesium Sulfate for Neuroprotection of Preterm Infants

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Table IV. Primary and secondary outcomes of death, motor impairment, cognitive deficity, health, and other

Outcome	$MgSO_4$ group, n/N (%)	Placebo group, n/N (%)	Unadjusted OR (95% CI)	OR adjusted for patient characteristics (95% CI)*	*P* value
Mortality and neurologic outcome†‡					
Death and/or motor deficit	138/252 (54.8)	147/249 (59.0)	0.81 (0.56-1.2)	0.79 (0.53-1.17)	.23
Death and/or cognitive deficits	173/252 (68.7)	175/249 (70.3)	0.93 (0.63-1.34)	0.89 (0.59-1.33)	.57
Death and/or psychiatric disorder	104/252 (41.3)	117/251 (46.6)	0.84 (0.58-1.22)	0.80 (0.54-1.20)	.29
Death and/or motor and/or cognitive deficits and/or psychiatric disorder	200/252 (79.4)	211/249 (84.7)	0.71 (0.44-1.15)	0.68 (0.41-1.11)	.16
Neuromotor deficits‖					
Severe CP	7/218 (3.2)	9/211 (4.3)	0.85 (0.58-1.26)	0.92 (0.62-1.36)	.66
Mild to moderate CP	23/218 (10.5)	24/211 (11.4)			
No CP, other motor disorder	74/218 (33.9)	76/211 (36.0)			
None identified	114/218 (52.4)	102/211 (48.3)			
Cognitive deficits/learning disabilities¶					
Severe	15/218 (6.9)	22/211 (10.4)	0.88 (0.60-1.29)	0.89 (0.60-1.33)	.58
Moderate	124/218 (56.9)	115/211 (54.5)			
None identified	79/218 (36.2)	74/211 (35.1)			
Association of motor and cognitive deficits#					
Motor only	18/218 (8.3)	29/211 (13.8)	0.88 (0.61-1.27)	0.94 (0.64-1.38)	.76
Cognitive only	53/218 (24.3)	57/211 (27.0)			
Motor and cognitive	86/218 (39.5)	80/211 (37.9)			
None	61/218 (27.9)	45/211 (21.3)			
Behavioral and psychiatric disorder†					
Moderate	70/218 (32.1)	79/213 (37.1)	0.87 (0.57-1.32)	0.84 (0.54-1.32)	.45
None identified	148/218 (67.9)	134/213 (62.9)			
Overall deficits†					
Severe	19/218 (8.7)	27/211 (12.7)	0.71 (0.47-1.08)	0.73 (0.47-1.11)	.14
Moderate	147/218 (67.4)	146/211 (68.5)			
None identified	52/218 (23.9)	40/211 (18.8)			
Learning and cognitive disabilities and special education services					
Language disorder§	19/67 (28.3)	19/60 (31.6)	0.85 (0.37-1.96)	0.80 (0.31-2.05)	.65
Schooling					
Regular school and classroom	200/212 (94.3)	198/210 (94.3)	0.9 (0.38-2.17)	1.18 (0.46-3.03)	.73
Specialized class room	7/212 (3.3)	8/210 (3.8)			
Specialized institution	4/212 (1.9)	4/210 (1.9)			
Repeated grades¶	9/212 (4.2)	17/210 (8.1)	0.5 (0.22-1.16)	0.44 (0.19-1.06)	.07
Specific education assistance‖	16/211 (7.6)	21/207 (10.1)	0.73 (0.36-1.45)	0.72 (0.34-1.54)	.40
Home education services	7/207 (3.4)	18/207 (8.7)	0.37 (0.15-0.9)	0.42 (0.16-1.06)	.07
Health					
Hospital admissions	102/216 (47.2)	116/204 (56.9)	0.69 (0.47-1.03)	0.66 (0.44-1.01)	.05
Asthma	42/214 (19.6)	57/210 (27.1)	0.67 (0.42-1.08)	0.7 (0.43-1.15)	.16
Health as assessed by parents					
Excellent or good	210/218 (96.3)	194/210 (92.3)	0.38 (0.15-0.95)	0.4 (0.15-1.09)	.07
Fair or poor	8/218 (3.7)	16/210 (7.6)			
Sleep disorder**	25/213 (11.7)	14/214 (6.5)	1.85 (0.91-3.7)	1.52 (0.7-3.33)	.29
Eating disorder**	17/212 (8.0)	22/210 (10.5)	0.67 (0.33-1.35)	0.66 (0.33-1.35)	.26
Neurosensory deficiencies††					
Hearing deficiency	9/218 (4.1)	14/211 (6.6)	0.60 (0.26-1.43)	0.61 (0.25-1.49)	.28
Visual deficiency	105/218 (48.2)	98/211 (46.5)	1.06 (0.72-1.56)	0.99 (0.66-1.49)	.97

School-Age Outcomes following a Randomized Controlled Trial of Magnesium Sulfate for Neuroprotection of Preterm Infants

Clément Chollat, MD[1,2], Maya Enser, MD[3], Estelle Houivet, MSc[4], Delphine Provost, MD[3], Jacques Bénichou, MD, PhD[4], Loïc Marpeau, MD[2,5], and Stéphane Marret, MD, PhD[1,2]

In a French randomized trial, children at school-age demonstrated no evidence of harm from fetal exposure to $MgSO_4$ before very preterm birth. Motor dysfunction/death, qualitative behavioral disorders, cognitive difficulties, school grade repetition, and education services were decreased in the children exposed to $MgSO_4$, although the differences were not significant. *(J Pediatr 2014;165:398-400).*

Table V. SDQ

Scale	$MgSO_4$ (n = 218), n (%)	Placebo (n = 213), n (%)	Unadjusted OR (95% CI)	OR adjusted for patient characteristics (95% CI)*	*P* value
Emotional Symptoms Scale					
Normal	133 (61.0)	126 (59.2)	1.14 (0.65-2)	1.51 (0.85-2.7)	.16
Borderline + abnormal	85 (39)	87 (40.9)			
Conduct Problem Scale					
Normal	162 (74.3)	161 (75.6)	1.14 (0.73-1.79)	1.43 (0.89-2.33)	.14
Borderline + abnormal	56 (25.7)	52 (24.4)			
Hyperactivity Scale					
Normal	169 (77.5)	157 (73.7)	0.83 (0.53-1.31)	0.9 (0.56-1.47)	.71
Borderline + abnormal	49 (22.5)	56 (26.3)			
Peer Problems Scale					
Normal	160 (73.4)	151 (70.9)	0.91 (0.59-1.41)	0.92 (0.57-1.45)	.71
Borderline + abnormal	58 (26.6)	62 (29.1)			
Prosocial Scale					
Normal	205 (94.0)	201 (94.4)	1 (0.99-1.01)	1.22 (0.49-3.03)	.66
Borderline + abnormal	13 (6)	12 (5.6)			
Total Difficulties Score					
Normal	165 (75.7)	143 (71.8)	0.70 (0.45-1.09)	0.72 (0.45-1.15)	.17
Borderline + abnormal	53 (24.3)	70 (32.9)			

Am J Perinatol, July 2014

Effect of Magnesium Sulfate Administration for Neuroprotection on Latency in Women with Preterm Premature Rupture of Membranes

Amanda L. Horton, MD[1] Yinglei Lai, PhD[2] Dwight J. Rouse, MD[3] Catherine Y. Spong, MD[4] Kenneth J. Leveno, MD[5] Michael W. Varner, MD[6] Brian M. Mercer, MD[7] Jay D. Iams, MD[8] Ronald J. Wapner, MD[9] Yoram Sorokin, MD[10] John M. Thorp, MD[11] Susan M. Ramin, MD[12] Fergal D. Malone, MD[13] Mary J. O'Sullivan, MD[14] Gary D. V. Hankins, MD[15] Steve N. Caritis, MD[16] for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network

Abstract

Objective This study aims to evaluate whether magnesium sulfate administration for neuroprotection prolongs latency in women with preterm premature rupture of membranes (PPROM) between 24 and $31^{6/7}$ weeks' gestation.

Study Design This is a secondary analysis of a randomized controlled trial of magnesium sulfate prophylaxis for cerebral palsy. Gravid women with singleton pregnancy between 24 and $31^{6/7}$ weeks' gestation with PPROM without evidence of labor were randomized to receive magnesium sulfate, administered intravenously as a 6-g bolus followed by a constant infusion of 2 g per hour until 12 hours, or placebo. Maternal outcomes for this analysis were delivery in less than 48 hours and in less than 7 days from randomization. Neonatal outcomes included a composite of respiratory distress syndrome, interventricular hemorrhage grades 3 or 4, periventricular leukomalacia, sepsis, necrotizing enterocolitis, retinopathy of prematurity, or death.

Results A total of 1,259 women were included. The rate of delivery < 48 hours was not different in the magnesium sulfate and the placebo groups (22.2 and 20.7%, $p = 0.51$). Delivery < 7 days was similar between groups (55.4 and 51.4%, $p = 0.16$). Median latency was also similar between groups (median [interquartile range], 6.0 days [range, 2.4–13.8 days] and 6.6 days [range, 2.4–15.1 days], $p = 0.29$). Composite neonatal outcomes did not differ between groups.

Conclusion Magnesium sulfate administration given for neuroprotection in women with a singleton gestation with PPROM and without labor before 32 weeks does not impact latency.

EMR de latent süreyi uzatmıyor

Neonatal sonuçlarda fark yok

Keywords
- latency
- magnesium sulfate
- neuroprotection
- preterm premature rupture of membranes

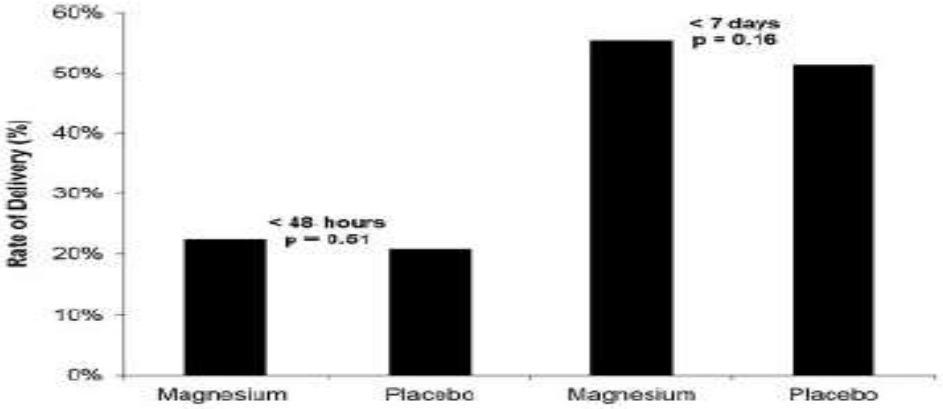

Fig. 1 Rates of delivery within 48 hours and 7 days from randomization among study group.

Table 2 Neonatal outcome according to treatment group[a]

	Magnesium sulfate ($N = 621$)	Placebo ($N = 638$)	Odds ratio[b] (95% CI)
Birth weight (g), mean (SD)	1,468 ± 542	1,489 ± 583	$p = 0.76$[c]
5 min Apgar < 7, *n*/*N* (%)	90/621 (14.5)	103/636 (16.2)	0.88 (0.65–1.19)
Composite outcome[c], *n*/*N* (%)	339/605 (56.0)	350/623 (56.2)	0.99 (0.79–1.25)
RDS, *n*/*N* (%)	285/620 (46.0)	293/633 (46.3)	0.99 (0.79–1.23)
PVL, *n*/*N* (%)	8/589 (1.4)	14/602 (2.3)	0.58 (0.24–1.39)
IVH (grade 3 or 4), *n*/*N* (%)	4/589 (0.7)	13/602 (2.2)	0.31 (0.10–0.96)
Culture proven sepsis, *n*/*N* (%)	83/620 (13.4)	88/633 (13.9)	0.96 (0.69–1.32)
NEC, *n*/*N* (%)	50/620 (8.1)	49/633 (7.7)	1.05 (0.69–1.58)
ROP, *n*/*N* (%)	109/620 (17.6)	113/633 (17.9)	0.98 (0.73–1.31)
Death, *n*/*N* (%)	27/621 (4.4)	31/638 (4.9)	0.89 (0.52–1.51)

Magnesium sulphate for preventing preterm birth in threatened preterm labour (Review)

Crowther CA, Brown J, McKinlay CJD, Middleton P

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Authors' conclusions

Magnesium sulphate is ineffective at delaying birth or preventing preterm birth, has no apparent advantages for a range of neonatal and maternal outcomes as a tocolytic agent and its use for this indication may be associated with an increased risk of total fetal, neonatal or infant mortality (in contrast to its use in appropriate groups of women for maternal, fetal, neonatal and infant neuroprotection where beneficial effects have been demonstrated).

This review of 37 trials including 3571 women and their infants did not find that magnesium sulphate, given to women who go into labour too soon, prevented babies being born too soon or reduced the risks of the baby developing serious health problems. However, antenatal magnesium sulphate is effective in helping women who develop pre-eclampsia (high blood pressure and protein in the urine) and for helping to protect babies' brains.

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2014, Issue 8

http://www.thecochranelibrary.com

Original Research

Association of Duration of Neuroprotective Magnesium Sulfate Infusion With Neonatal and Maternal Outcomes

Jessica A. McPherson, MD, Dwight J. Rouse, MD, MSPH, William A. Grobman, MD, MBA, Anna Palatnik, MD, and David M. Stamilio, MD, MSCE

OBJECTIVE: To evaluate the association of duration of magnesium sulfate infusion with stillbirth or death, cerebral palsy, and select adverse maternal and neonatal outcomes.

METHODS: This is a secondary cohort analysis of women randomized to receive magnesium sulfate within a previously reported Maternal-Fetal Medicine Units Network prospective clinical trial. The association of antenatal infusion of magnesium sulfate for less than 12 hours, 12–18 hours, and greater than 18 hours on maternal and perinatal outcomes was compared. The primary outcome was cerebral palsy of any severity or death. Secondary outcomes included cerebral palsy, death, and select maternal and neonatal outcomes. Stratified and logistic regression analyses were used. The models were adjusted for race, gestational age at birth, time since last magnesium sulfate, any magnesium sulfate at delivery, and eligibility criteria as appropriate.

RESULTS: Of 933 women available for analysis, 356, 341, and 236 received antenatal magnesium sulfate infusion for a total of less than 12 hours, 12–18 hours, or greater than 18 hours, respectively. Any cerebral palsy or death occurred in 39 women (11.7%) who received magnesium sulfate less than 12 hours, 34 women (10.3%) who received 12–18 hours of magnesium sulfate, and 20 women (8.8%) who received greater than 18 hours of magnesium sulfate. There was no difference in death or cerebral palsy among groups (less than 12 hours as reference; adjusted odds ratio [OR] 1.03, 95% confidence interval [CI] 0.60–1.77 for 12–18 hours; adjusted OR 1.08, 95% CI 0.57–2.03 for greater than 18 hours). Select maternal adverse drug affects and neonatal morbidities were also similar across groups.

CONCLUSION: The duration of antenatal magnesium sulfate infusion is not associated with risk of death or cerebral palsy. The optimal treatment duration needed for maximal neuroprotection remains unknown.

(Obstet Gynecol 2014;124:749–55)

DOI: 10.1097/AOG.0000000000000467

LEVEL OF EVIDENCE: II

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The authors thank the Eunice Kennedy Shriver *National Institute of Child Health and Human Development, the Maternal-Fetal Medicine Units Network,*

Table 2. Outcomes of Women Receiving Magnesium Sulfate

Outcome	Duration of Magnesium Sulfate Administration (h)			Adjusted OR (95% CI) for 12–18 h or Longer	Adjusted OR (95% CI) for Longer Than 18 h
	Less Than 12 (n=334)	12–18 (n=331)	Longer Than 18 (n=227)		
Any cerebral palsy or death	39 (11.7)	34 (10.3)	20 (8.8)	1.03* (0.60–1.77)	1.08* (0.57–2.03)
Unadjusted OR (95% CI)	Reference	0.87 (0.53–1.41)	0.73 (0.41–1.29)		
Moderate-to-severe cerebral palsy or death	32 (9.6)	29 (8.8)	17 (7.5)	1.11† (0.62–1.97)	1.13† (0.57–2.24)
Unadjusted OR (95% CI)	Reference	0.91 (0.54–1.55)	0.76 (0.41–1.41)		
Any cerebral palsy‡	14 (4.2)	9 (2.7)	4 (1.8)	0.61§ (0.26–1.43)	0.44§ (0.14–1.38)
Unadjusted OR (95% CI)	Reference	0.64 (0.27–1.50)	0.41 (0.13–1.26)		
Moderate-to-severe cerebral palsy	6 (1.8)	4 (1.2)	1 (0.4)	0.64‖ (0.18–2.30)	0.26‖ (0.03–2.17)
Unadjusted OR (95% CI)	Reference	0.60 (0.17–2.05)	0.22 (0.03–1.76)		
Death	27 (8.1)	25 (7.6)	17 (7.5)	1.10¶ (0.60–2.03)	1.41¶ (0.70–2.85)
Unadjusted OR (95% CI)	Reference	0.90 (0.52–1.57)	0.89 (0.47–1.66)		

OR, odds ratio; CI, confidence interval

Table 3. Obstetric Outcomes and Adverse Events (N=933)

Outcome	Duration of Magnesium Sulfate Administration (h)					
	Less Than 12 (n=356)	12–18 (n=341)	Longer Than 18 (n=236)	OR* (95% CI)	OR† (95% CI)	P‡
Any adverse drug event§	273 (76.7)	257 (75.4)	187 (79.2)	0.93 (0.66–1.32)	1.16 (0.78–1.73)	.55
Significant adverse drug event§	9 (2.5)	2 (0.6)	5 (2.1)	0.23 (0.05–1.06)	0.83 (0.28–2.52)	.08
Pulmonary edema	3 (0.8)	2 (0.6)	1 (0.4)	0.69 (0.12–4.18)	0.50 (0.05–4.84)	.81
Respiratory depression	2 (0.6)	0 (0)	4 (1.7)	—	3.05 (0.55–16.79)	.18
Infusion stopped because of adverse event§ or patient refusal	45 (12.6)	12 (3.5)	8 (3.4)	0.25 (0.13–0.49)	0.24 (0.11–0.49)	<.001
Cesarean delivery	130 (36.5)	136 (39.9)	64 (27.1)	1.15 (0.85–1.57)	0.65 (0.45–0.93)	.01

Table 4. Neonatal Outcomes (n=948)

Outcome	Duration of Magnesium Sulfate Administration (h)			OR* (95% CI)	OR† (95% CI)	P‡
	Less Than 12 (n=356)	12–18 (n=341)	Longer Than 18 (n=236)			
Birth weight (g)	1,474±632	1,390±557	1,464±480			.12
5-min Apgar score less than 7	63 (17.7)	58 (17.1)	32 (13.6)	0.95 (0.64–1.41)	0.73 (0.46–1.16)	.37
Resuscitation in delivery room						.07
None						
Oxygen blow-by						
Oxygen bag, mask, or b						
Intubation						
Chest compressions						
Necrotizing enterocolitis					1.11 (0.61–1.86)	.96
Retinopathy of prematurity	81/354 (22.1)	84 (24.6)	40 (17.1)	1.16 (0.81–1.64)	0.73 (0.48–1.12)	.09
Respiratory distress syndrome	174/354 (49.2)	166 (48.7)	110 (47.1)	0.98 (0.73–1.32)	0.92 (0.66–1.28)	.87
Mechanical ventilation	187/354 (52.8)	174/341 (51.0)	115/234 (49.2)	0.93 (0.69–1.25)	0.86 (0.62–1.20)	.68
Bronchopulmonary dysplasia	67/354 (18.1)	60 (17.6)	38 (16.2)	0.96 (0.66–1.41)	0.87 (0.56–1.36)	.84
Seizures	6/354 (1.4)	6/341 (1.8)	3/234 (1.3)	1.25 (0.38–3.39)	0.91 (0.21–3.83)	.88
Cranial ultrasound findings						
Any intraventricular hemorrhage	67/335 (20.0)	58/327 (17.7)	43/230 (18.7)	0.86 (0.58–1.27)	0.92 (0.60–1.41)	.76
Grade III or IV intraventricular hemorrhage	4/335 (1.2)	5/327 (1.5)	1/230 (0.4)	1.28 (0.34–4.83)	0.36 (0.04–2.25)	.42

Based on our secondary analysis, we cannot make definitive clinical recommendations for a specific neuroprotective magnesium sulfate regimen. However, our study suggests that neuroprotection may be achieved equally at lower doses.

OBSTETRICS

Antenatal magnesium sulfate exposure and acute cardiorespiratory events in preterm infants

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OBJECTIVE: Antenatal magnesium (anteMg) is used for various obstetric indications including fetal neuroprotection. Infants exposed to anteMg may be at risk for respiratory depression and delivery room (DR) resuscitation. The study objective was to compare the risk of acute cardiorespiratory events among preterm infants who were and were not exposed to anteMg.

STUDY DESIGN: This was a retrospective analysis of prospective data collected in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network's Generic Database from April 1, 2011, through March 31, 2012. The primary outcome was DR intubation or respiratory support at birth for an [illegible] Secondary outcomes were invasive mechanical ventilation, hypotension treatment, neonatal morbidities, and mortality. Logistic regression analysis evaluated the risk of primary outcome after adjustment for covariates.

RESULTS: We identified 1544 infants <29 weeks' gestational age (1091 in anteMg group and 453 in nonexposed group). Mothers in the anteMg group were more likely to have higher education, pregnancy-induced hypertension, and antenatal corticosteroids, while their infants were younger in gestation and weighed less ($P < .05$). The primary outcome (odds ratio [OR], 1.2; 95% confidence interval [CI], 0.88—1.65) was similar between groups. Hypotension treatment (OR, 0.70; 95% CI, 0.51—0.97) and invasive mechanical ventilation (OR, 0.54; 95% CI, 0.41—0.72) were significantly less in the anteMg group.

CONCLUSION: Among preterm infants age <29 weeks' gestation, anteMg exposure was not associated with an increase in cardiorespiratory events in the early newborn period. The safety of anteMg as measured by the need for DR intubation or respiratory support on day 1 of life was comparable between groups.

Key words: antenatal magnesium, nasal continuous positive airway pressure, neonatal resuscitation, preterm infants

Cite this article as: De Jesus LC, Sood BG, Shankaran S, et al. Antenatal magnesium sulfate exposure and acute cardiorespiratory events in preterm infants. Am J Obstet [illegible]

- Primer

Doğumda veya ilk gün solunum desteği,
Doğum salonunda entübasyon ihtiyacı

- Sekonder

İnvazif mekanik ventilasyon
hipotansiyon tedavisi

Neonatal morbidite ve mortalite

MgSO4 grubunda daha az

<29hf MgSO4 kullanımı kardiorespiratuar riski arttırmıyor

ADC-FNN Online First, published on September 17, 2014 as 10.1136/archdischild-2013-305884

Intrapartum magnesium sulfate and need for intensive delivery room resuscitation

Dany E Weisz,[1] Sandesh Shivananda,[2] Elizabeth Asztalos,[1,3] Wendy Yee,[4] Anne Synnes,[5] Shoo K Lee,[3] Prakesh S Shah,[3,6] on behalf of the Canadian Neonatal Network

ABSTRACT

Objective To evaluate the association of intrapartum magnesium sulfate for fetal neuroprotection ($MgSO_4$-FN) with the delivery room resuscitation and neonatal outcomes of preterm infants in an era of minimisation of invasive mechanical ventilation.

Design Retrospective cohort study.

Setting Neonatal intensive care units in the Canadian Neonatal Network.

Patients and intervention Preterm infants (23^0 to 31^6 weeks gestational age) born in 2011 or 2012. Resuscitation requirements and neonatal outcomes were compared between infants exposed and unexposed to intrapartum $MgSO_4$-FN.

Main outcome measures The primary outcome was a composite outcome of 'intensive resuscitation', defined as the need for intubation and ventilation or chest compressions or epinephrine administration in the delivery room. Secondary outcomes included mortality and major neonatal morbidities.

Results Of 6015 eligible infants, 1387 (23.1%) were exposed to intrapartum $MgSO_4$-FN. Significantly fewer $MgSO_4$-FN infants (41.0% vs 44.6%, p=0.02) required intensive resuscitation. However, after adjustment for confounders, this difference was no longer significant (adjusted OR (AOR) 0.88; 95% CI 0.66 to 1.17). Infants exposed to $MgSO_4$-FN had decreased odds of death (AOR 0.61; 95% CI 0.40 to 0.94), but there was no difference in neonatal morbidities compared with the unexposed infants.

Conclusions Intrapartum $MgSO_4$ for fetal neuroprotection was not associated with an increased need for intensive delivery room resuscitation in this cohort of preterm infants.

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 , 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

FETAL NÖRON KORUMA YAPALIM

TEŞEKKÜR EDERİM

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

- Preterm bebeklerde ilk haftada ölüm riski fazla
- Yaşayanlarda nörolojik bozukluk,serebral palsi,körlük,sağırlık…
- Ekonomik, sosyal problemler…..

Mg- Etki Mekanizması

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

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.