Comparison of Single-Dose Versus-Ten Day Ampicillin-Sulbactam Therapy for Group B Streptococcal Infection in Pregnant Rabbit Model

GEBE TAVŞAN MODELİNDE GRUP B STREPTOKOK ENFEKSİYONLARINDA TEK DOZ VE 10 GÜNLÜK AMPİSİLİN-SULBAKTAM TEDAVİLERİNİN KARŞILAŞTIRILMASI

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Summary

In this study, success of single-dose versus ten day ampicillin-sulhactain (SAM) therapy was compared in a pregnant rabbit model infected with group B-streptococci. We inoculated KP-lO^/mL group B streptococci intraperitoneally at Group B streptococci were inoculated intraperitoneally to 21 pregnant rabbits at the 21st day of thirty-one-day gestation. Rabbits were seperated to 3 groups. First group did not receive therapy (Group I. n:7). Second group was administered SAM therapy J50 mg/kg/day in three divided doses every 8 hours intramuscularly (IM) beginning immediately after inoculation, and continued until delivery (Group II, n:7). Third group was administered SAM therapy 150 mg/kg IM as a single dose immediately after inoculation (Group III, n:7). Outcome parameters were delivery, fever, positive cultures (from maternal blood, from uterus, from fetus, from pup blood or heart) for GBS, any live fetuses and maternal death. Without antibiotic treatment, 6 from 7 rabbits (85.71%) died after intraperitoneal (IP) inoculation (in Group I) between 2 to 6 days of inoculation.

In group II there was no maternal death, but there were fever at 2 rabbits (28.57%), term deliveiy at all of them (100%,), and there were no positive cultures (all specimens) (0/7) (0%). In group III 4 rabbits (4/7) (57.14%) died between 3 to 6 days. Common complications were fever at 5 rabbits (71.41%), deliveiy at 3 rabbits (42.85%), positive maternal blood cultures obtained at 4 rabbits (57.14%), and positive intrauterine cultures at 4 rabbits (57.14%), positive fetus cultures in 4 (57.14 %). Live fetuses were present in only 3 rabbits (42.85%,). Only one pup had positive blood culture and died after 24 hours of delivery in group I.

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Özet

Bu çalışmada B grubu streptokokla enfekte edilmiş gebe tavşanlarda tek doz ampisilin-sulbaktam (SAM) ile 10 günlük SAM tedavisi karşılaştırıldı. Yirmi bir gebe tavşana 31 gün süren gebelik süresinin 21. gününde J0-I()°/mL B grubu streptokok intraperitonal inoküle ettik. Tavşanlar 3 gruba ayrıldı. Birinci grup (grup I)(7 hayvan) tedavi almadı, ikinci grup (7 hayvan), inokülasyondan hemen sonra intramuskuler (IM) SAM (150 mg/kg/gün,8 saatte bir, 3 eşit dozda) aldı ve doğuma kadar verildi. Üçüncü grup (grup III)(7 hayvan) inokülasyondan hemen sonra tek doz SAM 150 mg/kg IM aldı. Doğum, ateş, B grubu streptokoklar için pozitif kültürler (anne kanı, ıuterus, fetus, yavru kanı veya kalbinden), canlı fetus, anne ölümü gibi parametreler değerlendirildi.

Antibiyotik almayan grupta (grup I) inokülasyondan sonra 2-6 saat içinde 6/7 (%85.71) öldü. Grup ilde (10 günlük SAM tedavisi) anne tavşan ölümü yoktu, 2/7'de ateş (%28.57) vardı, zamanında doğum 7/7'de (%>100) gerçekleşti ve bütün spesimenlerde kültürler negatifti (0/7) (%0).

III.grupla (tek doz SAM tedavi) 4 hayvan (4/7) (57.14%) 3-6 gün içinde öldü. Yaygın komplikasyonlar; ateş 5/7 (%71.41), normal doğum 3/7 (%42.85), anneden pozitif kan kültürü 4/7 (%57.14), pozitif ıuterus kültürü 4/7 (%57.14), pozitif fetus kültürü 4/7 (%57./4) idi. Sadece 3/7 (%>42.85) fetus canlıydı. Yine yalnız bir yavru kan kültürü pozitif bulundu ve doğumdan 24 saat sonra öldü (grup I).

Üç grup karşılaştırıldığında, 10 günlük SAM tedavisi alan grupta ölüm, ateş, pozitif kültür sonuçları diğer gruplara göre anlamlı derecede azdı (p<0.05). 10 günlük SAM tedavisi, B grubu streptokok (GBS) İP inokülasyonıtndan sonra neonatal kolonizasyonıt, komplikasyonları, ölümü anlamlı

When three groups were compared, animals treated with SAM therapy for ten days period (ten-day therapy) were significantly less likely to have death, fever and positive cultures from all specimens (p<().()5). SAM therapy for ten clays significantly decreased neonatal colonization, complications, and death after IP inoculation with (GBS). This regime improved outcomes when compared with single dose SAM therapy (p<0.05).

Key Words: Animal model. Infection, Group B streptococci. Pregnancy, Ampicillin-sulbactam

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derecede azalttı. Bu rejim tek dozdan daha başarılı bulundu (p<0.05).

Anahtar Kelimeler: Hayvan modeli, Enfeksiyon, B grubu streptokok, Gebelik, Ampisilin-sulbaktam

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Although group B streptococci have become the leading cause of major perinatal bacterial infection, there has been no agreement on the best strategy to prevent these infections (1-4).

Centers for Disease Control and Prevention (CDC) have all issued statements favouring intrapartum prophylaxis but there has been disagreement regarding how to optimally identify candidates for prophylaxis (and these approches have their limitations) (5-6).

Previous studies demonstrated fulminant perinatal (GBS) infection and demonstrated significant benefits of antibiotic treatment (7-9).

In the rabbit, high rates of maternofetal, and neonatal infection were demonstrated after inoculation with GBS and these rates were decreased significantly. When animals were treated with SAM immediately after inoculation (1).

We compared single dose SAM and therapy SAM therapy for ten days period in pregnant rabbits with GBS infection.

Materials and Methods

This protocol was approved by Animal Laboratory, Department of Infectious Diseases, Department of Microbiology, Department of Parmacology School of Medicine of our university. We used timed pregnant Swecs Albino Rabbits on the 21st of 31-day-gestation and cared these animals as previously described (10).

After cleaning the abdomen with povidone-iodine solution, we inoculated 0.1 ml of lOMOVmL (used McFarlaiiL.j GBS intrapcritoncally.

Group I (7 rabbits) did not receive therapy. Group II (7 rabbits) was administered SAM therapy (150 mg/kg/day in divided doses every 8 hours) intramuscularly beginning immediately after inoculation, and continued until delivery for ten days period. Group III (7 animals) was administered SAM therapy 150 mg/kg IM, as a single dose, just after inoculation.

Rectal temperatures were taken before inoculation, after inoculation for 24 hour period. Maternal blood cultures were taken after inoculation, after 24 hours, and when the rabbit died. Intrauterin culture and fetus culture were taken when the rabbit died. Pup blood or heart culture was taken after 72 hours of delivery or when it died.

Cultures were obtained from uterine by swabs and from blood by aspiration into a syringe. Material was plated onto 5% sheep blood agar. GroupB streptococci were, identifed by gram stain, catalase test, Peterson test. Outcome measures were similar to those in previous experiments, namely, delivery, fever (rectal, above 37.5°C), positive cultures, any live fetus present, and maternal death (10). Categoric data were analysed by Fisher's exact test or x^2 test.

Results

We infected 21 pregnant animals, there was no perforation. The results were shown in Table 1.

Discussion

In this study, we gained two results related to perinatal group B streptococci infection in rabbits. First; GBS bacteremia led to high rate (mean 47.61%) of adverse infection related adverse outcomes, including death. Second; early initiated and continued treatment with an antibiotic against group B sterptococci improved outcome significantly.

Table 1. Outcome after intraperitoneal inoculation GBS.

Outcome	Group 1*		Group 11*		Group 111*	
n	n	%	n	%	n	%
21	7		7		7	
Fever	6	85.71	2	28.57	5	71.41
Delivery	1	14.28	7	100	3	42.85
Maternal death	6	85.71	—	0	4	51.14
Maternal blood culture (+)	7	100	—	0	4	51.14
Intrauterin culture (+)	6	85.71	--	0	4	51.14
Fetal culture (+)	6	85.71	—	0	4	51.44
Live fetus present	1	14.28	7	100	3	51.44
Pup blood / heart culture	1	14.28	--	0	--	0

*p< 0.05 between group 1 and 11,
between group II and 111,
between group 1 and III, for all parameters except between II and III for pup blood culture.

Some articles reported values for the transmission of fetus in GBS in experimental studies between 18% and 50% (1,6,9,10). We found 47.61% (10/21) transmission of GBS to fetus. This rate was minimum in group II (%0), and maximum in group 1(85.71%).

It was demonstrated that in treated animals maternal death rate was significantly lower than untreated animals (1,11,12). We found significant difference between groups (I and 11,1 and III, II and III) in terms of complications and death. S A M therapy for ten days period was succeesful than single-dose S A M therapy. McDuffie RS et al (11,1) found that single dose S A M therapy or a 24-48 hour S A M therapy before delivery decreased neonatal colonization and bacteremia in GBS infection.

Acute GBS infection in pregnant women is similar to animals (1,6). The high attack rate reported here (mean 47.61 %) remarkably higher than those of women colonized with group B streptococci. In humans the rate of pelvic infection in GBS -colonized women was reported to be 21% (compared with 12%> among uncolonized women) (11,13). The reason for the high rate of vimlancc of group B streptococi infection in the rabbit compared to humans could be the limited immune response in the former (11).

As a conclusion, early initratcd and continued S A M therapy (before delivery) decrease intrauterine infection and bacteremia and other complications in group B streptococci infected pregnant rabbits. S A M therapy for ten days period is more succesful than single-dose S A M therapy (p<0.05).

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