

Stenotrophomonas maltophilia Outbreak in Neonatal Intensive Care Unit and Outbreak Management

Yenidoğan Yoğun Bakım Ünitesinde *Stenotrophomonas maltophilia* Salgını ve Salgın Yönetimi

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Abstract

Objective: *Stenotrophomonas maltophilia* is a pathogen, which may cause serious outbreak, particularly in neonatal intensive care units, with increasing importance at present. The aim of this study was to assess the epidemiological and clinical features of *S. maltophilia* epidemic that we encountered in our neonatal intensive care unit and outbreak management.

Materials and Methods: Demographic, clinic features, and microbiological findings of the cases who were hospitalized in our neonatal intensive care unit between February 2014 and May 2014 with *S. maltophilia* was isolated from blood cultures were retrospectively evaluated. Also, the isolation of *S. maltophilia* in the tracheal aspirate fluid cultures was investigated in the neonatal intensive care unit in the outbreak period and in the previous year. Other patients hospitalized at the same period were considered as the control group. Assessments and measures taken in the outbreak period were studied.

Results: *S. maltophilia* bacteremia was detected in a total of 11 patients in the 4-month epidemic period. The same agent was also isolated from the tracheal aspirate culture in two of these patients. No factor was found to increase the risk of infection in terms of gestational age, birth weight, hospitalization time, and use of carbapenem, umbilical catheter, and total parenteral nutrition compared with the control group (15 patients). Overall mortality rate was found as 36% (4/11) in *S. maltophilia* cases and 7% (1/15) in the control group. Microorganisms were not isolated from the baticon bottles or medications in the form of ampoules (such as heparin) as well as those sent from the surroundings to find out the source of the outbreak. Source of the outbreak was accepted as cross-contamination among the cases. Baticon bottles were made smaller in volume, and their duration

Özet

Amaç: *Stenotrophomonas maltophilia* özellikle yoğun bakım ünitelerinde ciddi salgınlara neden olabilen ve günümüzde önemi gittikçe artan bir patojendir. Bu çalışmada yenidoğan yoğun bakım ünitemizde karşılaştığımız *S. maltophilia* salgınının epidemiyolojik, klinik özelliklerinin ve salgın yönetiminin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Şubat 2014 - Mayıs 2014 döneminde yenidoğan yoğun bakım ünitemizde yatmakta olan ve kan kültüründe *S. maltophilia* üreyen olguların demografik özellikleri, klinik, mikrobiyolojik bulguları geriye dönük olarak incelendi. Ayrıca salgın dönemi ve salgından önceki yılda trakeal aspirat kültüründe üreyen *S. maltophilia* izolasyonları araştırıldı. Aynı dönemde üniteye yatmakta olan diğer hastalar kontrol grubu olarak değerlendirildi. Salgın döneminde yapılan değerlendirmeler ve alınan önlemler irdelendi.

Bulgular: Dört aylık salgın döneminde toplam onbir hastada *S. maltophilia* bakteriyemisi tespit edildi. Bu olguların ikisinde aynı etken trakeal aspirat kültürlerinde de üredi. Kontrol grubuna göre (onbeş hasta), gestasyonel yaş, doğum ağırlığı, yatış günü, karbapenem, umbilikal kateter ve total parenteral nutrisyon kullanımları açısından enfeksiyon riskini arttıran bir faktör bulunamadı. Genel mortalite *S. maltophilia* bakteriyemili olgularda %36 (4/11), kontrol grubunda ise %7 (1/15) idi. Salgın kaynağının bulunması amacıyla, batikon, heparin ve ampül formundaki ilaçlardan ve çevreden gönderilen kültürlerde üreme görülmedi. Salgın kaynağı olgular arası çapraz bulaş olarak kabul edildi. Batikon şişeleri hacim olarak küçültülerek kullanım süreleri kısaltıldı. Küvöz nemlendiricilerinin günlük temizlenmesi sağlandı. Üniteye görevli tüm personele enfeksiyon kontrol önlemleri ile ilgili eğitimler düzenlendi.

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of use was shortened. Daily cleansing of the incubator humidifiers was performed. Training programs regarding the infection control measures for all staff working in the unit were organized.

Conclusion: It should be always kept in mind that *S. maltophilia* causing serious outbreaks may be seen in the neonatal intensive care units. We believe that it would be useful to investigate possible environmental sources, analyze protective measures, and increase personnel awareness in outbreak management. (*J Pediatr Inf 2015; 9: 147-52*)

Keywords: *Stenotrophomonas maltophilia*, newborn, intensive care unit, outbreak management

Introduction

Stenotrophomonas maltophilia is an anaerobic, non-fermentative gram-negative bacillus, which was previously known as *Xanthomonas maltophilia* or *Pseudomonas maltophilia*, and may cause nosocomial infections as the only member of *Stenotrophomonas* order (1). It may be found in water, sewage, soil, plants, and animals as well as may be isolated from many areas in hospitals such as the washbasins, respirators, and antiseptics (2). At present, the incidence of nosocomial infections developing because of *S. maltophilia* is increasing; in particular, intensive care units are leading areas with high risk of these infections. Resistance to many broad-spectrum antibiotics including carbapenems renders the treatment of infections caused by this microorganism difficult and causes an increase in the mortality and morbidity rates in the intensive care units (3). Management of the outbreaks because of *S. maltophilia* is a challenging process for clinicians in many aspects. There is limited data in the literature regarding the outbreaks caused by this bacterium, particularly in the neonatal intensive care units (NICUs) (1, 4-7). In this study, we assessed the outcomes of *S. maltophilia* outbreak that emerged in the NICU of our hospital and discussed outbreak management.

Material and Methods

This retrospective case control study was conducted in the 15-bed capacity NICU. Characteristic of the newborns from whom *S. maltophilia* was isolated from the blood cultures were studied in the course of outbreak, which began with the isolation of *S. maltophilia* in the blood culture of a newborn hospitalized in the NICU in February 2014 and lasted for 4 months. BACTEC Peds Plus/F (BD, Sparks, MD) culture bottles were used for the blood as well as cerebrospinal, pleural, and peritoneal fluid samples. Samples of tracheal aspirate fluid (TAF) were added to 5% sheep blood agar and eosin-methylene blue agar plaques. Newborns who were hospitalized in the NICU at the same period and who did not suffer from

Sonuç: Yenidoğan yoğun bakım ünitelerinde *S. maltophilia* kaynaklı ciddi salgınlara görülebileceği her zaman akılda tutulmalıdır. Salgın yönetiminde olası çevresel kaynakların araştırılması ile birlikte koruyucu önlemlerin irdelenmesi ve personel farkındalığının artırılmasının da faydalı olduğunu düşünmekteyiz. (*J Pediatr Inf 2015; 9: 147-52*)

Anahtar kelimeler: *Stenotrophomonas maltophilia*, yenidoğan, yoğun bakım, salgın yönetimi

an infection because of *S. maltophilia* were assessed as the controls. Gestational age, birth weight, hospitalization time, use of carbapenem, total parenteral nutrition (TPN), and overall mortality rates were compared between the groups. In the assessment of parameters, except gestational age and birth weight, time of positivity of the culture was used in the study group and for the entire hospitalization course in the control group. Because the number of patients was small, median values of the data were expressed together with maximum and minimum values in brackets, unless otherwise specified.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS for Windows, version 22.0, Armonk, NY, USA: IBM Corp.) software. Compliance of the data to normal distribution was analyzed using Shapiro–Wilk test. On comparing the data, Pearson’s chi-square and Fisher’s exact chi-square tests were used where appropriate, whereas Mann–Whitney U test was used in comparison of non-normally distributed variables. Real p values were used and p values of <0.05 were considered to be statistically significant.

Results

S. maltophilia was isolated for the first time in the blood culture of a patient who was admitted to the NICU owing to perinatal asphyxia 24 days ago. After 18 days from the first incidence of bacteremia, *S. maltophilia* bacteremia began to be observed in different patients in the same unit. *S. maltophilia* bacteremia was newly detected in four patients in February, three in March, and two in April and May, respectively. The same agent was also isolated from TAF cultures in two of these cases. It was found when data from the past were examined that *S. maltophilia* was isolated only from TAF cultures in a total of 15 cases and no bacteremia was detected in the last 1 year. Distribution of the cases with *S. maltophilia* culture-positive cases in the unit during the outbreak period and also during the previous year is given in Figure 1. Median

value of gestational age was 33 (28–39) weeks and birth weight was 1395 (690–4200) g in the patients with bacteremia. Patients were at the 15th (2–125) day of the hospitalization during the development of bacteremia, and 55% (6/11) of the cases were receiving carbapenem and 64% (7/11) were receiving TPN. Median days of carbapenem and TPN use were 7 (5–15) and 10 (1–23), respectively. Umbilical catheter was used in all the patients who developed bacteremia, whereas the median number of days for catheter usage was 11 (1–19) during the development of infection. Four patients died (4/11, 36%) and seven in the study group were discharged. All the isolated *S. maltophilia* strains were sensitive in vitro only against trimethoprim–

sulfamethoxazole, ciprofloxacin, and ticarcillin–clavulanate. Specifications and outcomes of patients involved in the outbreak are summarized in Table 1. Fifteen patients who were admitted to the unit at the time of outbreak and without an *S. maltophilia*-positive sterile site cultures were assessed as the controls. The control group consisted of the hospitalized cases with similar gestational age, birth weight, and risk factors. When features of the patients were compared with those of the controls hospitalized in the NICU during the outbreak, no statistically significant difference was observed between both groups in terms of gestational age, birth weight, hospitalization time, duration of umbilical catheter use, rate of use of broad-spectrum antibiotics or TPN. Overall mortality rate was 7% (1/15) in the control group. Although the rate of mortality was higher in the study group compared with those in the control group (36% vs 7%), this difference was not statistically significant (p=0.057). Comparisons of the study and control groups are shown in Table 2.

New patient admission to the NICU was limited during the outbreak. The microorganism was not isolated in the samples of medications used by the patients (baticon bottles and heparin ampoules), cocks, tap water outlets, portable humidifiers in the incubators and respirators, and TPN solutions to find out the source of the outbreak. Source of the outbreak could not be determined in our cases. Training programs regarding the isolation and

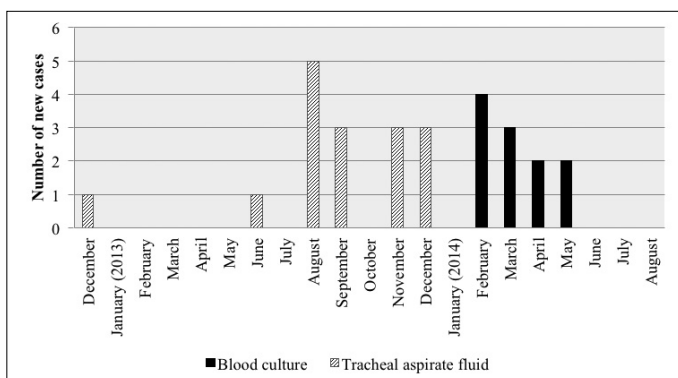


Figure 1. The number of new cases with *S. maltophilia* culture positive by months

Table 1. Gestational age, birth weight, admission diagnosis, hospitalization days, presence of other healthcare-associated infections, sites of positive cultures, antibiotic treatments, and outcomes of patients involved in the outbreak

Case No	GA (w)	BW (gr)	Diagnosis	Hosp. day (inf.)	Prior antibiotic treatment	Prior different HAI (s)*	Culture site	Treatment	Length of treatment (day)**	Hosp. day (total)	Outcome
1	39	4200	Perinatal asphyxia	25	AG, Car, Gly	BSI, VAP	Blood	Cipx, TMP-SMX	21	48	Discharge
2	33	2100	Prem.	2	Amp, AG	--	Blood	Cipx, TMP-SMX	17	20	Discharge
3	29	1200	Prem. & PROM	13	AG, Car, Gly, AF	VAP	Blood	Cipx, TMP-SMX	21	81	Discharge
4	33	1900	Prem.	2	Amp, AG	--	Blood	Cipx, TMP-SMX	16	32	Discharge
5	33	1300	Prem. & CHD	22	Car, Gly	BSI	Blood & TAF	Cipx, TMP-SMX	20	49	Discharge
6	31	1750	Prem. & CDH	125	AG, Car, Gly, AF	BSI (x2), VAP (x4)	Blood & TAF	Cipx, TMP-SMX	6	136	Exitus
7	34	825	Seckel Syndrome	21	Car, Gly, AF	VAP	Blood	Cipx, TMP-SMX	4	31	Exitus
8	30	885	Prem.	3	AG, Ceph	--	Blood	Cipx, TMP-SMX	20	62	Discharge
9	28	690	Prem.	15	Car, Gly, AF	--	Blood	Cipx, TMP-SMX	10	28	Exitus
10	31	1395	Prem.	38	AG, Ceph	--	Blood	Cipx, TMP-SMX	12	50	Discharge
11	39	2890	Perinatal asphyxia	4	AG, Ceph	--	Blood	Cipx, TMP-SMX	21	60	Exitus

*Different healthcare-associated infections (HAIs), which the patient had before *S. maltophilia* infection episode

**Treatment duration for *S. maltophilia* infection

AMP: ampicillin; AF: antifungal; AG: aminoglycosides; BSI: blood-stream infection; BW: birth weight (gr); Car: carbapenem; CDH: congenital diaphragmatic hernia; Ceph: cephalosporin; CHD: congenital heart defect; Cipx: ciprofloxacin; "Hosp. day (inf.)": the day of hospitalization before culture positivity was observed; "Hosp. day (total)": the total days of hospitalization; GA: gestational age (week); Gly: glycopeptides; Prem: prematurity; PROM: premature rupture of membranes; TAF: tracheal aspirate fluid; TMP-SMX: trimethoprim–sulfamethoxazole; VAP: ventilator-associated pneumonia

Table 2. Comparison of the study and control groups

	Case Group (n=11)	Control Group (n=15)	p
Gestational age median, week (min-max)	33 (28–39)	32 (29–39)	p=0.979
Birth weight median, gr (min-max)	1395 (690–4200)	1550 (953–4170)	p=0.574
Hospitalization day * Median, day (min-max)	15 (2–125)	33 (10–68)	p=0.055
Umbilical catheter usage (%)	10/11 (91%)	12/15 (80%)	p=0.614
Duration of umbilical catheter usage* median, day (min-max)	11 (1–19)	10 (1–38)	p=0.974
Carbapenem use (%)*	6/11 (55%)	6/15 (40%)	p=0.462
Carbapenem use* median, day (min-max)	7 (5-15)	13.5 (10–21)	p=0.065
Total parenteral nutrition use* (%)	7/11 (64%)	13/15 (87%)	p=0.348
Total parenteral nutrition use* median, day (min-max)	10 (1–23)	7 (3–53)	p=0.877
Overall mortality (%)	4/11 (36%)	1/15 (7%)	p=0.128
* In the assessment of these parameters, time of the culture positivity was used in the study group and the entire hospitalization course in the control group			

cleaning procedures for all the staff working in the unit were held. All the invasive interventional procedures including the collection of routine blood samples and culture were revised. Baticon bottles were made smaller in volume, and their duration of use was shortened. Daily cleansing of the incubator humidifiers was performed.

Discussion

S. maltophilia has been increasingly observed to causative pathogen of nosocomial infections in patients having underlying conditions such as malignancy and immunosuppression and in those who are admitted in hospitals, particularly in the neonatal intensive care units (3). Invasive interventions, invasive treatment methods, devices used in diagnosis and treatment, and non-rational use of antibiotics have important roles in this increase. In addition, *S. maltophilia* causes serious nosocomial infections in newborns, but nosocomial infections related to this agent have rarely been reported in the literature. The antimicrobial resistance among *S. maltophilia* increases the importance of effective outbreak management during epidemics. Contamination with cross-transmission should be prevented by isolating cases; the possible sources should be immediately investigated. Verweij et al. (2) reported *S.*

maltophilia outbreak in five preterm newborns in the NICU because of tap water contamination in 1996; Lanotte et al. (8) reported an epidemic from water tank in pediatric intensive care unit, and Abbassi et al. (7) reported an epidemic in eight newborns in the NICU arising from the sink used by healthcare staff for handwashing. It has been reported in the literature that disinfectants, ventilator sensors, water tanks, and fiberscopes may be the sources of *S. maltophilia* (1, 4, 6). However, the source cannot be always found in the outbreak control, and the revision of infection control measures is of paramount importance. Viedma et al. (4) reported *S. maltophilia* epidemic in seven newborns in 1999, and Gulcan et al. (5) reported three newborns in 2004; of these, all outbreaks resulted from cross-transmission. No pathogen was detected in the environmental cultures in our unit, suggesting dissemination primarily owing to cross-transmission. However, because molecular genome analysis could not be performed in the isolated strains, possible clonal link between the strains could not be demonstrated; this is another factor limiting this study.

Studies have reported that the main factors contributing to the increasing incidence of *S. maltophilia* in the intensive care units include long duration of hospital stay, long-term use of broad-spectrum antibiotics such as carbapenem, presence of a central venous catheter, mechanical ventilation, prematurity, and neutropenia (4, 9, 10). Likewise, another non-fermentative species, *S. maltophilia*, is also inherently resistant to many antibiotics. Limiting the use of antibiotics and shortening the duration of their use is important to prevent hospital-acquired *S. maltophilia* infections (11, 12). In our study, there were no factors increasing the risk of infection between the groups.

Mortality rate in *S. maltophilia* infections varies between 0% and 38% in the childhood period (9). However, this exceeds 50% in the cases with bacteremia. In a study by Çelebi et al. (3), the overall mortality rate in nosocomial *S. maltophilia* infections was 28.6%, whereas this rate was reported as 60% in cases of bacteremia. Although it is not seen statistically significant, in our study, the rate of mortality was observed to increase by five folds (7%–36%) compared with controls. It was considered that the lack of a significant difference between the groups in terms of risk factors and mortality rates might be a result of a small number of patients in the study and control groups.

Patient outcomes, including nosocomial infection rates, are directly caused by the behaviors of all bedside care providers. Continuing education programs on infection prevention and control can keep the awareness high; unfortunately, it is not always sufficient. Overcrowding and understaffing, i.e., a low nurse to patient ratio, can be factors for a breach in aseptic protocols resulting in outbreaks (13). Frequent hand washing between infant con-

tacts is difficult because of overcrowded and understaffed nurseries; this results in decreased practices in preventing other infections (14, 15). Haley and Bregman (14) showed that clustered infections were seven times greater after the periods of critically increased census than after periods of routine census. They also found the rate of clustered infections to be 16 times greater after the periods of critical understaffing (patient: nurse ratio exceeded by 7) than that after the periods of adequate staffing (14). In Level III NICUs, the recommended nurse to patient ratio is 1:1 or 1:2 (16). As a reference hospital, we have to frequently isolate complicated and infected newborns. In our NICU, there are usually four nurses working in a shift, and our nurse to patient ratio can decrease to 1:5 during certain night shifts with overcrowded times. In these situations, as mentioned below, education and behaviors of the all bedside care providers become a more critical issue for nosocomial infections. Hospitals need to focus on increasing the specialty nurse to infant ratios rather than decreasing the presence of properly trained registered nurses at bedside (15).

Conclusion

Neonatal intensive care units are the areas under risk in terms of nosocomial outbreaks, and *S. maltophilia* is one of the important outbreak agents resulting in high mortality rates. The most important factors in the outbreak control include investigating of the previously reported potential sources, revision of the infection control measures, isolation of the cases, and increasing personnel awareness. Despite the source of this outbreak, which we encountered at our center, could not be identified, the outbreak was brought under control owing to the measures taken. To prevent new outbreaks, increased awareness of all personnel about the infection control measures of the hospital after an outbreak should also be maintained.

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