Multi-drug Resistant Acinetobacter Baumannii (MDRAB) Infection: Experience from a Burn Center

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Background:

Multi-drug Resistant Acinetobacter Baubannii (MDRAB) has been bring the great concern for infection control in hospitalized patients, particularly those in intensive-care units (ICUs) such as burn unit in recent years. Prevent and control the infection from this organism can reduce the morbidity, mortality and length of hospital stay.

Aim and Objective:

We reviewed the incidence of the Acinetobacter Baubannii (AB) nosocomial infections (NIs) and among those the MDRAB NIs in Linkou Burn Center (LBC). We also reviewed our experience and internet literatures and try to find the way to control MDRAB NIs.

Materials and methods:

From 2001 to 2009, incidence of the Acinetobacter Baubannii (AB) nosocomial infections (NIs) and among those the MDRAB NIs in Linkou Burn Center (LBC) were evaluated. The demographic data of affected patients was also collected.

Results:

Seventeen patients including 12 males and 5 females developed 20 MDRAB NIs in LBC during 2001-2009. The incidence of MDRAB NIs is 0.27 NIs / 1000 patient days. The most common MDRAB NIs in LBC was blood stream infection (BSI) (55%). The mean age of these 17 patients was 49.8 +/- 25.7 years old (range, 2-85). The mean interval of MDRAB NIs confirmed by culture after ICU admission was 19.1 +/- 14.9 days (range, 4-56). Causes of burn injury were 9 flame burns (53%), 5 scald burns (29%), and one chemical burn (6%). Mean TBSA was 39.3 +/- 30.7% (range, 3-100%). The mean length of hospital stay was 53.5 +/- 32.2 days (range, 21-154). Five (29%) patient expired, including 2 BSI, 2 BWI and one LRI.

Conclusions:

MDRAB will persist and sporadic emerges in world, Taiwan, CGMH and LBC. The incidence is not high but the risks always exist. MDRAB may increase the morbidity, mortality, hospital stay and socioeconomic loss in burn unit. Proper antibiotic treatment, infection control, antibiotics stewardship and prevention measures can control or decrease the incidence. (J Taiwan Soc of Plast Surg 2012;21:107～115)

Key words: Multi-drug Resistant Acinetobacter Baumannii (MDRAB), infection control

Introduction

Besides Oxacillin Resistant Staphylococcus Aureus (ORSA) and Multi-drug Resistant Pseudomonas Aeruginosa (MDRPA), another multiply drug resistant organism, Multi-Drug Resistant *Acinetobacter Baubannii* (MDRAB), has been bring the greatest concern for infection control in hospitalized patients, particularly those in intensive care units (ICUs) such as burn unit in recent years. *Acinetobacter baumannii* (AB) is a non-fermentative, strictly aerobic, and non-motile, gram-negative (G-) coccobacillus, which is highly prevalent in nature.[1] AB is isolated from many areas in the hospital, including environmental surface, healthcare workers' hands, the respiratory, urinary, gastrointestine tract, wounds of patients, air ventilator and dialysis machines, mechanical ventilators, and water sources…etc. During past decades, AB emerged from an opportunistic G(-) bacillus to important nosocomial pathogen worldwide. Most alarming is the ability to accumulate diverse mechanisms of resistance.[2] Carbapenem resistant *Acinetobacter baumannii* (CRAB) was first reported in the United States in 1991.[3] Since then, CRAB nosocomial infections (NIs) and multihospital outbreaks reported worldwide.[4,5,6] Pandrug-resistant *Acinetobacter baumannii* (PDRAB), which is resistant to all antibiotics routinely tested was first recovered in May 1998 at NTUH (National Taiwan University Hospital), Taiwan.[7] Since then, PDRAB infections and nosocomial outbreaks persisted in hospitals in Taiwan.[8,9,10,11,]

Methods Definitions

- **Definition of nosocomial infection (NI)**:
  The diagnosis of NI was defined by centers for disease control (CDC) definitions for nosocomial infections, 1988[12].
- **Definition of PDRAB in Chang-Gung Memorial Hospital (CGMH)**:
  Acinetobacter baumannii(AB) which is resistant to all antibiotics routinely tested in CGMH except Ampicillin+Sulbactam, Piperacillin/ Tazobactam, and Tigecyclin. The data of PDRAB was reported in CGMH since 2004. However, the term PDRAB is inappropriate because it is not truly resistant to all antibiotics, so it was corrected to MDRAB in July 2008. The new definition of MDRAB in CGMH is AB resistant to : Amikacin, Aztreonam, Ceftazidime, Ciprofloxacin, Cefepime, Gentamicin, Imipenem, and Piperacillin-tazobactam.
- **Definition of MDRAB in this study**:
  There is no standard definition of MDRAB worldwide and the definition of MDRAB in CGMH is too complex. For uncomplicated study recording, we define MDRAB as isolates of AB resistant to three or all four antimicrobials: Ceftazidime, Ciprofloxacin, Gentamicin and Imipenem[13].

Study setting

A retrospective study was undertaken in Chang Gung Memorial Hospital (CGMH), Linkou. The CGMH, Linkou Burn Centre is the largest burn center in Taiwan, with a mean annual 487 admissions, account for one fourth to one fifth annual burn admission in Taiwan. The Burn Centre has 2 operation rooms and 30 bed facility, divided into a 6 isolated intensive care bed, 16 non-isolated intensive care bed and 8 bed observation ward. We collected AB NIs in CGMH during 2001-2007, PDRAB NIs in CGMH during 2004-2007 and total NIs, AB NIs and MDRAB NIs in burn center during 2001-2009. The data base was from Nosocomial Infection Control Committee of CGMH. Medical records were reviewed to obtain patients' data, including: gender, age, time of MDRAB infection, causes of burn injury, mean total body surface (TBSA), length of hospital stay and mortality. These data was expressed as mean +/- SD (standard deviation). The incidence of infection was showed as: NIs / 1000 patient days.

Results

Two thousands two hundreds and thirty six AB NIs was recorded in CGMH during 2001-2007. The incidence was 0.29 NIs / 1000 patient days (Figure1).

One hundred and eighty-three PDRAB NIs were recorded in CGMH during 2004-2007. The incidence was 0.042 NIs / 1000 patient days (Figure 2).

Three hundred and forty two NIs were recorded in Linkou Burn Centre (LBC) during 2001-2009 (Table 1). The incidence was 4.91 NIs / 1000 patient days (Figure3). The most common NIs in LBC was blood stream infection (BSI) (46%), followed by cardiovascular system infection (CVI) (25%), urinary tract infection (UTI) (17%), lower respiratory tract infection (LRI) (6%) and burn wound infection (BWI) (4%). There were 30 AB NIs in LBC during 2001-2009. The incidence was 0.43 NIs / 1000 patient days (Figure 4).

Seventeen patients including 12 males and 5 females developed 20 MDRAB NIs in LBC during 2001-2009. The incidence was 0.27 NIs / 1000 patient days (Figure 5). The most common MDRAB NIs in LBC was BSI (55%), followed by CVI (15%), UTI (15%), LRI (10%) and BWI (5%) (Table 2). The mean age of these 17 patients was 49.8 +/- 25.7 years old (range, 2-85). The mean interval of MDRAB NIs confirmed by culture after ICU admission was 19.1 +/- 14.9 days (range, 4-56). Causes of burn injury were 9 flame burns (53%), 5 scald burns (29%), and one chemical burn (6%). Mean TBSA was 39.3 +/- 30.7% (range, 3-100%). The mean length of hospital stay was 53.5 +/- 32.2 days (range, 21-154). Five (29%) patient expired, including 2 BSI, 2 BWI and one LRI. The detail clinical characteristics of 17 patients with MDRAB NIs are shown in Table 3.

Figure 1

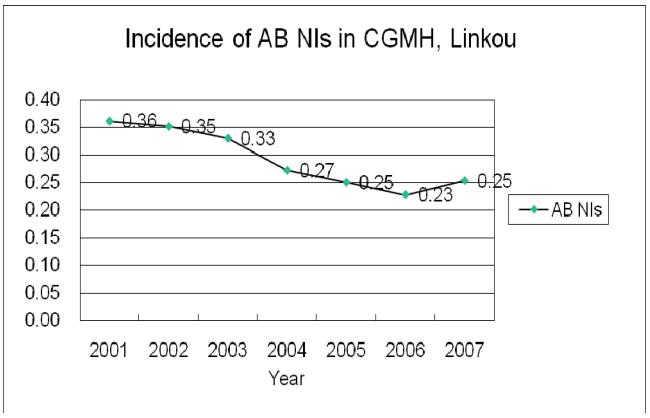

Figure 2

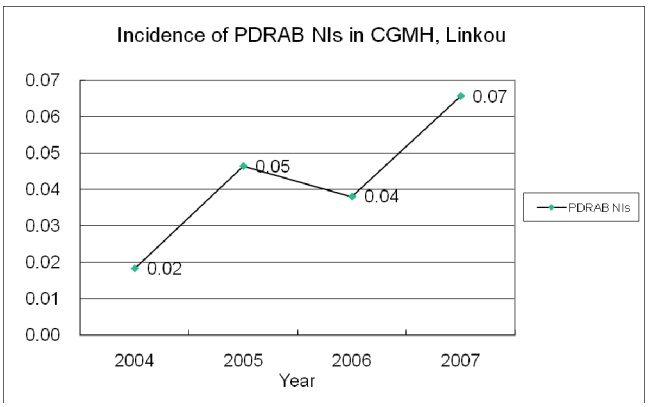

Figure 3

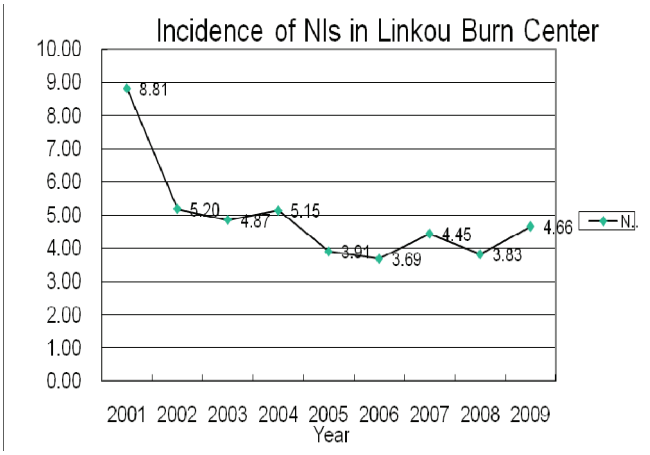

Figure 4

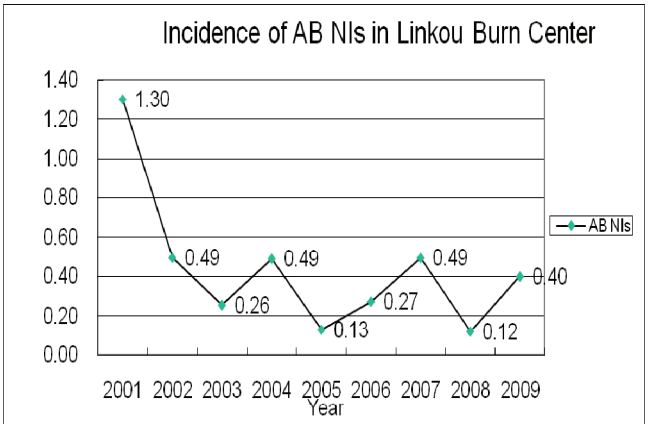

Figure 5

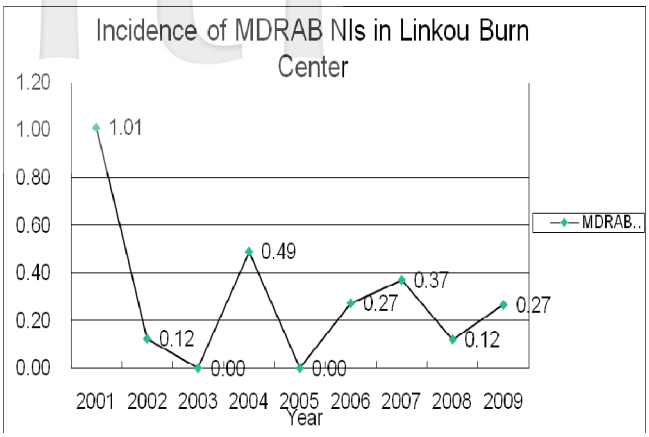

Table 1

NIs in Linkou burn center during 2001-2009						
	Total	BSI(%)	CVI(%)	UTI(%)	LRI(%)	BWI(%)
NIs	342	157(46)	84(25)	60(17)	20(6)	14(4)
NIs/1000 patient days	4.91	2.25	1.20	0.86	0.28	0.20

Abbreviations: BSI: blood stream infection; CVI: cardiovascular system infection; UTI: urinary tract infection; LRI: lower respiratory tract infection; BWI: burn wound infection

Table 2

MDRAB NIs in Linkou burn center during 2001-2007						
	Total	BSI(%)	CVI(%)	UTI(%)	LRI(%)	BWI(%)
NIs	20	11(55)	3(15)	3(15)	2(10)	1(5)
NIs/1000 patient days	0.27	0.15	0.04	0.04	0.03	0.01

Table 3

Clinical characteristics of 14 patients with MDRAB NIs								
Case No.	Age (y/o)	Gender	Injury mechanism	TBSA (%)	Interval of culture(+) after admission (day)	Infection site	Hospital stay (day)	Mortality
1	60	M	Flame burn	30	8	BSI	68	
2	76	M	Scald burn	30	21	UTI	53	
3	71	M	Flame burn	26	5	BSI	38	Mortality
4	2	M	Scald burn	3	10	BSI	39	
5	20	M	Flame burn	100	7	BSI	22	Mortality
6	85	F	Scald burn	15	10	BSI	31	
7	26	M	Scald burn	80	4	BSI	53	
8	37	M	Flame burn	25	8	CVI	48	
9	39	M	Flame burn	60	28	BWI	66	Mortality
					30	BSI		
10	56	M	Scald burn	10	16	LRI	21	Mortality
11	54	M	Chemical burn	5	13	BSI	32	
12	84	F	Flame burn	15	56	UTI	72	
					56	CVI		
13	30	F	Flame burn	60	34	BSI	89	
					34	BSI		
14	27	M	Flame burn	70	47	BSI	68	
15	79	F	Drug skin eruption	79	17	CVI	25	
16	74	F	Fornier's gangrene		28	LRI	60	
17	27	M	Flame burn	20	13	UTI	39	
Mean	49.8			39.3	19.1		53.5	
SD	25.7			30.7	14.9		32.2	

Abbreviations: M: male; F: female; TBSA: total body surface area; SD: standard deviation; BSI: blood stream infection; CVI: cardiovascular system infection; UTI: urinary tract infection; LRI: lower respiratory tract infection; BWI: burn wound infection.

Discussion

MDRAB is emerging as a major cause of nosocomial infection (NIs) worldwide, so does in Taiwan since the first hospital outbreaks 10 years ago.[7] It is difficult to control this microorganism because it is widely distributed in the hospital environment as mentioned before and it can withstand harsh environment such as disinfectant solutions,[14] dry[15] and iron-deficient conditions[16]. Besides, MDRAB has ability to accumulate diverse mechanisms of resistance to many commercially available antimicrobial agents and the lack of new antimicrobial agents in development.[17]

The main treatments for MDRAB NIs patients are antibiotics and infection control measures. Antibiotic choices for MDRAB NIs patients are limited. Colistin (Detergent: Polymyxin B, polymyxin E) is the most active agents in vitro.[18,19] However, it has nephrotoxicity and neurotoxicity and patients receive colistin treatment need careful monitering.[20] Tigecycline is a glycylcycline antibiotic and is active against some MDRAB. Unfortunately, development of resistance to tigecycline has been reported recently.[21]Because of the synergy or additive effects, rifampin or Sulbactam (beta-lactamase inhibitor) are often used to combine other antibiotics to treat MDRAB patient. In LBC, we use these antibiotics to treat MDRAB patients by the culture results and under infectious diseases physician's suggestion.

Infection control measures include strict isolate and cohort MDRAB patients, strict cohort nursing, strict hand hygiene and environmental cleaning. MDRAB NIs patients and carriers were placed in neighboring rooms and isolated in one section of the LBC until their culture results were negative for tree times. Cohort nurses were assigned to care only MDRAB carriers and patients. Physicians and nurses are asked to perform strict hand hygiene before and after patients care and the wearing of disposable gowns, shoe covers, and gloves before entering rooms. Materials contaminated with blood and body fluid were discarded or cleaned immediately. Surfaces in all rooms of the LBC were disinfected daily.

Patients with MDRAB infections may have longer lengths of hospital and ICU stay, higher mortality rate and greater medical cost.[22, 23, 24] Burn patients are prone to MDRAB nosocomial infection because they are often intubated due to inhalation injury and most of them have large burn wounds and need multiple invasive procedures such as debridement, frequent wound dressing, central venous catheter, arterial catheter and urinary indwelling catheter insertion. Stephen J. Wilson et al reported that MDRAB NIs in their burn unit was associated with significantly increased hospital costs.[24] Rebecca H. Sunenshine et al reported that patients with MDRAB infections have prolonged hospital and ICU length of stay compared with uninfected patients and those infected with drug-susceptible *Acinetobacter.*[22]In this study, the mean length of hospital stay of burn patient with MDRAB NIs was 56 days, much longer than the average length of hospital stay, 9.3 days, of LBC. The mortality rate of burn patient with MDRAB NI was 29%, compared with the mortality rate, 4.2% of LBC. Our results suggest a trend toward increased mortality rates and socio-economic loss among patients with MDRAB NIs. However, the difference was not statistically significant because it's difficult to control the multiple confounding risk factors among so many patients in LBC.

The incidence of MDRAB NIs in LBC was very high in 2001 then it lowered down in recent years. The high MDRAB NIs in LBC may correlate with the higher AB NI in CGMH in 2001. Many control effort in LBC stabilized the incidence, which includes strict infection control method, limiting the use of intravascular and urinary catheters, avoiding unnecessary prolongation of ventilation, restricting the use of broad-spectrum antibiotics, and antibiotics stewardship. Corbella et al reported that emergence of carbapenem resistant AB linked to the heavy use of broad-spectrum antibiotics and restricting the use of broad-spectrum antibiotics in addition to infection control measures reduce the incidence of CRAB infection.[6] In CGMH, we try to control antibiotics usage to avoid the development of antibiotics resistance by a computer controlled antibiotic prescribing system. If a physician wants to prescribe more than 2 kinds of antibiotics or broad-spectrum antibiotics to treat a patient, the

computer will notice and ask the physician to complete the infection consults sheet. If the physician doesn't complete the infection consults sheet, the computer will delete the prescribed antibiotics automatically. Infectious diseases physician will then review the infection consult sheet and give suggestions or discuss with the physician.

Conclusion

MDRAB Nis will persist and sporadic emerges in world, Taiwan, CGMH and LBC. The incidence is not high but the risks always exist. MDRAB may increase the morbidity, mortality, hospital stay and socioeconomic loss in burn unit. Proper antibiotic treatment, infection control, antibiotics stewardship and prevention measures can control or decrease the incidence.

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多重抗藥性鮑氏不動桿菌感染：林口長庚醫院燒燙傷中心的治療經驗

陳宏彰 楊瑞永 莊秀樹 楊士毅

背　景：

住院病患，特別是加護病房病患的多重抗藥性鮑氏不動桿菌（Multi-drug Resistant Acinetobacter Baubannii，以下簡稱 MDRAB 菌）感染，在最近幾年引起很大的重視。林口長庚醫院燒燙傷中心也面臨同樣的問題。因此，面對這隻病源菌，找出預防，感染控制與治療的方法是減少併發症，死亡率，與住院日數最好的方法。

目的及目標：

我們審查了林口長庚燒燙傷中心自 2001 年至 2009 年鮑氏不動桿菌（Acinetobacter Baubannii，以下簡稱 AB 菌）與 MDRAB 菌的院內感染發生率，並試圖從過去的經驗與文獻上的資料來找出控制 MDRAB 菌院內感染的方法。

材料及方法：

我們蒐集了所有林口長庚燒燙傷中心自 2001 年至 2009 年遭受 AB 菌與 MDRAB 菌院內感染的病患，這些病患的資料被統計與分析。

結　果：

林口長庚燒燙傷中心自 2001 年至 2009 年有十七個病患，包括 12 位男性與 5 位女性，總共發生 20 次 MDRAB 菌院內感染。MDRAB 菌院內感染發生率是 0.27（次數／1000 病患住院日）。最常見的 MDRAB 菌院內感染是血循感染 (55%)。病患的平均年齡是 49.8 +/- 25.7 歲 (2-85 歲)。這些病患在燒燙傷中心住院後平均 19.1 +/- 14.9 天 (4-56 天) 經細菌培養確認是 MDRAB 菌院內感染。這 17 位病患有 9 位是火焰灼傷 (53%)，5 位是燙傷 (29%)，1 位是化學性灼傷 (6%)。平均燒燙傷面積是 39.3 +/- 30.7% (3-100%)；平均住院日數是 53.5 +/- 32.2 天 (21-154 天)。有 5 位病患 (29%) 死亡，其中兩位死於 MDRAB 菌血循感染，兩位死於 MDRAB 菌傷口感染，1 位死於 MDRAB 菌呼吸道感染。

結　論：

MDRAB 菌院內感染會持續在世界，台灣，與林口長庚燒燙傷中心發生，雖然發生率不高，但感染的風險永遠存在。經由我們過去的經驗與文獻資料顯示 MDRAB 菌院內感染可能會增加併發症，死亡率，住院日數與社會經濟的損失。適當的抗生素治療，感染控制，抗生素使用管理可以控制並減少 MDRAB 菌院內感染的發生率。