Oral Clindamycin as Drug of Choice for Scabies Patients with Secondary Bacterial Infections in West Java, Indonesia

Hendra Gunawan, Unwati Sugiri, Nurhasanah, Kristina Makarti and Oki Suwarsa

Departement of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin Hospital, Bandung, Indonesia

Article history Received: 18-10-2017 Revised: 29-12-2017 Accepted: 09-01-2018

Corresponding Author: Hendra Gunawan Departement of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran– Dr. Hasan Sadikin Hospital, Bandung, Indonesia Email: h.gunawan2016@unpad.ac.id

Abstract: The aim of this study was to identify the causative secondary bacterial infection in scabies and its susceptibility against systemic antimicrobials. We performed a cross-sectional descriptive study of 34 scabies patients clinically diagnosed by investigators through consecutive sampling in one District Hospital in West Java, Indonesia from January to March 2017. The secondary bacterial infection was confirmed by Gram staining. Bacterial culture was derived from intact pustules, then identified using Vitek® 2 system, including its susceptibility against 30 systemic antimicrobials. The result of bacterial identification consisted of 48.89% Group A Beta-Hemolytic Streptococcus (GABHS), 44.44% Staphyloccocus aureus (S. aureus), 4.44% Staphylococcus epidermidis (S. epidermidis) and 2.22% Klebsiella pneumoniae (K. Pneumoniae). All bacterias were sensitive to carbapenem group, however resistant to cephradine and kanamycin. The overall percentages of GABHS sensitivity to the tested antibiotics were as follows: 95.45% for chloramphenicol and ceftriaxone, 90.91% for amoxicillin/clavulanate, 86.36% for clindamycin, cloxacillin, cefotaxime, 72.27% for ciprofloxacin and methicillin. Sensitivity of S. aureus to the antibiotics were as follows: 100.00% for methicillin, 95.00% for clindamycin and cloxacillin, 90.00% for ciprofloxacin and levofloxacin, 85.00% for cotrimoxazole and 75.00% for ceftriaxone. The sensitivity of S. epidermidis to clindamycin, amoxicillin/clavulanate and methicillin were 100.00%. All of K. pneumoniae (100.00%) were sensitive to ciprofloxacin, cotrimoxazole, ampicillin/sulbactam, cefazolin, ceftriaxone, ceftazidime and cefepime. The most common etiology of secondary infection in scabies were GABHS and S. aureus with varying sensitivity and oral clindamycin is a drug of choice which can be given to pediatric or adults patients.

Keywords: Antimicrobial Susceptibility, Secondary Infection, Scabies

Introduction

Bacterial skin infections or pyodermas are still common in most developing countries (Hay *et al.*, 2014). It is a superficial skin infection that primarily affects children. Mostly, adults acquire pyoderma through close contact with infected children (Halpern and Heymann, 2008). Pyoderma is classified into primary and secondary types. One study in 2012 reported that among the various diseases that were found to be associated with primary pyodermas, scabies was the most common, seen in 8.50% cases (Gandhi *et al.*, 2012). Most of pyodermas are caused by Gram positive bacteria,

especially either *S. aureus* or GABHS (Bowen *et al.*, 2015). *S. aureus* in pyoderma may cause serious complications, such as invading the bloodstream, producing bacteremia (Vanderkoo *et al.*, 2011) and infective endocarditis (Twele *et al.*, 2010). Meanwhile Acute Post-Streptococcal Glomerulonephritis (APSGN) in several studies (Streeton *et al.*, 1995; White *et al.*, 2001; Rodriguez-Iturbe and Haas, 2016), acute rheumatic heart disease (Edison *et al.*, 2015) and death (Wong and Stevens, 2013) may follow GABHS infections.

Brook (1995) reported that scabies was often accompanied by secondary bacterial infection. This secondary bacterial infection may develope to



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antimicrobial resistance. Bacterial resistance to antimicrobials may lead to inefficient treatment, cripple the ability to fight infectious disease and difficulty to eradicating the infection (CDCP, 2013). It is not always feasible to perform pus cultures and sensitivity tests before instituting antimicrobial therapy for pyodermas. Therefore, it becomes imperative to have periodic updates on the causative organisms, their strains and antimicrobial sensitivity patterns in any given local community. Hence, this study was undertaken to identify the causative microorganisms of secondary infection in scabies and their susceptibility againts systemic antimicrobials in one District Hospital in West Java, Indonesia on 2017.

Materials and Methods

Patients

The study was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia with ethical clearance. Thirty-four subjects were recruited and enrolled after informed consent was explained. Patients were further divided into two age groups 0-14 years and ≥ 14 years. All patients of scabies with secondary bacterial infection were enrolled in this study irrespective of any concomitant disease. Scabies patients were diagnosed clinically by the investigators. Clinical criteria for diagnoses were: (1) presence of papules, vesicles, nodules, or burrows at sites of predilection, (2) night itch and (3) involvement of at least another family member or companion. Patients with two of the above criteria were included in the study. Bacterial infection in scabies was marked by pustules at sites of predilection and was proved by Gram staining with the appearance of Gram-positive or Gram-negative cocci or rods. Subjects who had used systemic or topical antimicrobial agents in the preceding two weeks were excluded from the study.

Bacterial Culture and Antimicrobial Susceptibility Testing

Only one specimen was taken from every subject. The specimens were purulent material from intact pustules, obtained with 1 mL spuit after cleaning the surrounding skin with alcohol swab. Gram staining was conducted on the specimens which were sent to the laboratory incubated in tryptic soy broth transport medium, then cultured on both Blood agar and MacConkey agar. The plates were incubated aerobically at 37°C for 18 to 24 h. The time between specimen collection and inoculation to these agar plates never exceeded 72 h. Identification of bacteria and antimicrobial susceptibility testing using Vitek® 2 were further carried

out according to manufacturer's instructions. Vitek 2 uses an antimicrobial dilution according to Clinical and Laboratory Standards Institute (CLSI) (Pincus, 2006; Shetty *et al.*, 1998) to determine Minimal Inhibitory Concentrations (MIC). MIC results are either sensitive, intermediate, or resistant antimicrobials (Pincus, 2006).

Results

Of the 34 subjects, the number of female patients was similar to the number of male patients. Patient ages ranged from two months to 70 years old. The majority (82.35%) were children and a majority were students (55.88%) (Table 1).

From 34 specimens, 23 (67.65%) of the infections detected a single causative microorganism. GABHS accounted for 35.29% of these infection, followed by *S. aureus* (29.41%). Eleven (32.35%) specimens yielded mixed infection and were mostly caused by mixture of GABHS and *S. aureus* (26.47%) (Table 2).

Table 1: Characteristic of subjects

× · · ·	Number		
Variable	n=34	%	
Gender			
Female	18	52,94	
Male	16	47.06	
Age			
Children: 0-14 years old	28	82.35	
Teenager/adult: ≥14 years old	6	17.65	
Occupation			
Student	19	55.88	
Unemployee	13	38.23	
Housewife	1	2.94	
Farmer	1	2.94	

Table 2: Bacterial Culture Result

Number					
n = 34	%				
12	35.29				
10	29.41				
1	2.94				
9	26.47				
1	2.94				
1	2.94				
	Number n = 34 12 10 1 9 1 1 1				

Table 3:	Isolates	of Microe	organism	from	34	speciments
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	Number					
Bacterial						
culture result	n = 34	%				
GABHS	22	48.89				
S. aureus	20	44.44				
S.epidermidis	2	4.44				
K. pneumoniae	1	2.22				

The number of microorganisms that were isolated from 34 specimens recovered 4 isolated microorganisms. GABHS and *S. aureus* were the most common species. *S. epidermidis* recovered in two specimens and *K. pneumoniae* in one specimen (Table 3).

Sensitivity test of GABHS, S. aureus and S. epidermidis against various antimicrobials are

presented in Table 4. The highest sensitivity of these microorganisms was to imipenem and meropenem (each sensitivity 100.00%) and resistant to cephradine and kanamycin (sensitivity 0.00%). In addition, GABHS were resistant to doxycycline, erythromycin and azithromycin, whereas *S. epidermidis* were resistant to azithromycin.

Table 4: Antimicrobial Susceptibility Tests of GABHS, S. aureus and S. epidermidis

	GA	BHS $(n = 2)$	22)		<i>S. au</i>	ureus (n = 2	= 20)		S. epidermidis $(n = 2)$			
	Sen	sitive	Re	sistant	Sens	itive	Res	sistant	Se	nsitive	Res	sistant
Antimicrobial	n	%	n	%	n	%	n	%	 n	%	n	%
Imipenem	22	100.00	0	0.00	20	100.00	0	0.00	2	100.00	0	0.00
Meropenem	22	100.00	0	0.00	20	100.00	0	0.00	2	100.00	0	0.00
Ceftriaxone	21	95.45	1	4.55	15	75.00	5	25.00	1	50.00	1	50.00
Chloramphenicol	21	95.45	1	4.55	3	15.00	17	85.00	1	50.00	1	50.00
Amoxicillin/clavulanate	20	90.91	2	9.09	9	45.00	11	55.00	2	100.00	0	0.00
Cloxacillin	19	86.36	3	13.64	19	95.00	1	5.00	1	50.00	1	50.00
Cefotaxime	19	86.36	3	13.64	12	60.00	8	40.00	1	50.00	1	50.00
Clindamycin	19	86.36	3	13.64	19	95.00	1	5.00	2	100.00	0	0.00
Ciprofloxacin	17	77.27	5	22.73	18	90.00	2	10.00	1	50.00	1	50.00
Vankomycin	17	77.27	5	22.73	14	70.00	6	30.00	2	100.00	0	0.00
Methicillin	17	77.27	5	22.73	20	100.00	0	0.00	2	100.00	0	0.00
Levofloxacin	15	68.18	7	31.82	18	90.00	2	10.00	1	50.00	1	50.00
Amoxicillin	14	63.64	8	36.36	3	15.00	17	85.00	1	50.00	1	50.00
Ceftazidime	14	63.64	8	36.36	4	20.00	16	80.00	1	50.00	1	50.00
Sulfamethoxazole/trimethoprim	11	50.00	11	50.00	17	85.00	3	15.00	1	50.00	1	50.00
Gentamicin	8	36.36	14	63.64	10	50.00	10	50.00	2	100.00	0	0.00
Tetracycline	3	13.64	19	86.36	4	20.00	16	80.00	1	50.00	1	50.00
Amikacin	2	9.09	20	90.91	11	55.00	9	45.00	1	50.00	1	50.00
Ampicillin	2	9.09	20	90.91	2	10.00	18	90.00	1	50.00	1	50.00
Cephradine	0	0.00	22	100.00	0	0.00	20	100.00	0	0.00	2	100.00
Doxycycline	0	0.00	22	100.00	2	10.00	18	90.00	1	50.00	1	50.00
Kanamycin	0	0.00	22	100.00	0	0.00	20	100.00	0	0.00	2	100.00
Erythromycin	0	0.00	22	100.00	1	5.00	19	95.00	1	50.00	1	50.00
Azithromycin	0	0.00	22	100.00	3	15.00	17	85.00	0	0.00	2	100.00

Table 5: Antimicrobial susceptibility tests of K. pneumoniae

	Number $(n = 1)$								
	Sensiti	ve	Interme	diate	Resistant				
Antimicrobial	 n	%	 n	%	n	%			
Ampicillin/sulbactam	1	100.00	0	0.00	0	0.00			
Cefazolin	1	100.00	0	0.00	0	0.00			
Ceftriaxone	1	100.00	0	0.00	0	0.00			
Ceftazidime	1	100.00	0	0.00	0	0.00			
Aztreonam	1	100.00	0	0.00	0	0.00			
Cefepime	1	100.00	0	0.00	0	0.00			
Ertapenem	1	100.00	0	0.00	0	0.00			
Meropenem	1	100.00	0	0.00	0	0.00			
Amikacin	1	100.00	0	0.00	0	0.00			
Gentamicin	1	100.00	0	0.00	0	0.00			
Ciprofloxacin	1	100.00	0	0.00	0	0.00			
Tigecycline	1	100.00	0	0.00	0	0.00			
Sulfamethoxazole/trimethoprim	1	100.00	0	0.00	0	0.00			
Nitrofurantoin	0	0.00	1	100.00	0	0.00			
Ampicillin	0	0.00	0	0.00	1	100.00			

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	GABHS ((n=22)	S. aureus	s (n=20)	S. epidermidis (n=2)		
Antimicrobial	n	%	n	%	n	%	
Clindamycin	19	86.36	19	95.00	2	100.00	
Ciprofloxacin	17	77.27	18	90.00	1	50.00	
Levofloxacin	15	68.18	18	90.00	1	50.00	
Chloramphenicol	21	95.45	3	15.00	1	50.00	
Amoxicillin/clavulanate	20	90.91	9	45.00	2	100.00	
Sulfamethoxazole/trimethoprim	11	50.00	17	85.00	1	50.00	
Amoxicillin	14	63.64	3	15.00	1	50.00	
Tetracycline	3	13.64	4	20.00	1	50.00	
Ampicillin	2	9.09	2	10.00	1	50.00	
Azithromycin	0	0.00	3	15.00	0	0.00	
Doxycyclin	0	0.00	2	10.00	1	50.00	
Erythromycin	0	0.00	1	5.00	1	50.00	

In this study, there was only one sample recovered *K. pneumoniae* and it was resistant to ampicillin (sensitivity 0.00%) (Table 5). Sensitivity of GABHS, *S. aureus* and *S. epidermidis* against various oral antimicrobials were presented in Table 6. Clindamycin was an oral antimicrobial which had a sensitivity of more than 85.00% in all three bacteria.

Discussion

In this study, GABHS and S. aureus were the most common isolated microorganisms from secondary infection in scabies, with GABHS slightly more common than S. aureus. The occurance was similiar to the observations made by Currie and Carapetis (2000). Bacterial infection following scabies might be related to the deterioration of skin barrier as the outcome from repetitive scratching. An analysis of the skin lipid showed inhibitory effect of linolenic acid, an essential free fatty acid normally present on intact skin which is responsible for inhibition of Staphylococcus colonization and a potential bactericidal factor against Streptococcus pyogenes as well as against bacteria which are normally present in skin microflora (Bergsson et al., 2001). In addition, Streptococcus and Staphylococcus have the main components of adhesin that will bind to fibronectin, an adhesin receptor in the host. In non-intact skin, fibronectin binds easily to bacteria, allowing the bacterial colonization to occur on the skin (Craft, 2012).

Our study showed among all tested specimens, *S. epidermidis* accounted for 4.44%. This organism is a component of the normal cutaneous flora (Otto, 2009). However, if the number increases it can be an opportunistic pathogen (Otto, 2009).

Most pyodermas are caused by Gram positive bacteria (Craft, 2012), though it can be caused by Gram negative bacteria, such as *Pseudomonas aeruginosa* (*P. aeruginosa*), *Proteus vulgaris* (*P. vulgaris*), *Escherichia coli* (*E. coli*) and *K. pneumonie* (Kakar *et al.*, 1999). *K. pneumoniae* is one of the normal flora of the skin which is found most often in leg and buttock lesions (Grice and Segre, 2011; Pinto-Almeida *et al.*, 2012). It is suspected that the most probable sources of these organisms are the rectal and vaginal orifices, where they normally reside (Brook, 1995). *K. pneumoniae* was isolated in the present study in the co-infection with GABHS (2.94%). The other study by Brook (1995) have been reported 3.33% mixed infections due to GABHS and *K. pneumoniae* in scabies with secondary infection.

In the present study, the sensitivity of various bacteria to amoxicillin/clavulanate is varied, as the drug was widely used in the community. Besides as a treatment of bacterial infections on the skin, amoxicillin/clavulanate is also often prescribed by other clinicians to treat lower respiratory tract infections, urinary tract infections, otitis media, etc (Lammie and Hughes, 2016).

The sensitivity of GABHS and S. aureus to cloxacillin in our study was more than 86.36%, while only 50.00% sensitivity to S. epidermidis. All of the Gram possitive cocci in this study had a low sensitivity to amoxicillin and ampicillin (less than 63.64%). Likewise, the high resistance to these antimicrobials in the present study is in agreement with some other reports (Klevens et al., 2007; Seybold et al., 2006). This could also be due to indiscriminate usage of this antimicrobials in the community and the emerged of penicillinase producing strains (Gandhi et al., 2012). Group A betahemolytic Streptococcus, S. aureus and K. pneumoniae had high sensitivity to ciprofloxacin (greater than 77.27%) in this study, whereas sensitivity to levofloxacin was only high in S. aureus (90.00%). This study shows similar result to those earlier study which found the sensitivity of GABHS and S. aureus to ciprofloxacin more than 70.00% (El Kholy et al., 2003). The high sensitivity of fluoroquinolone in children due to their limited used, since this class of drugs should not be given if less than 18 years old (Choi et al., 2013). Group A beta-hemolytic Streptococcus, S. aureus and S. epidermidis have high

sensitivity to clindamycin (more than 85.00%) in this present study. Increased sensitivity of Gram-positive bacteria to clindamycin probably due to the decreasing in the prescription of this antibiotic for various diseases (Lewis and Jorgensen, 2005).

In this study, the most sensitive drugs for secondary bacterial infections in scabies caused by GABHS, *S. aureus*, *S. epidermidis* and *K. pneumoniae* were carbapenem class, because the drug is not widely used in the community. However, this drug was only available for intravenous administration, therefore it is not a treatment option for uncomplicated pyodermas.

Based on this study, antimicrobials that could be given for infections caused by GABHS and/or *S. aureus* were cloxacillin, clindamycin, ciprofloxacin, ceftriaxone and methicillin. However, only the first three antimicrobials mentioned were available in oral form in Indonesia. Clindamycin and cloxacilin can be used either for pediatric and adults (Chen *et al.*, 2011), unfortunately cloxacillin was not always available in many regions in Indonesia. Whereas ciprofloxacin can not be used for children because it may cause arthropathy (Choi *et al.*, 2013), tendon disorders and cartilage changes (Kim *et al.*, 2001).

According to our study result, antimicrobials choice for skin infection caused by S. epidermidis were amoxicillin/clavulanate, methicillin, clindamycin, vancomycin, gentamicin and however only amoxicillin/clavulanate and clindamycin were available in oral form. Antibiotics that could be given orally and still sensitive to K. pneumoniae were ciprofloxacin and sulfamethoxazole-trimethoprim, while other sensitive drugs only available intravenously, such as ampicillinsulbactam, cefazolin, ceftriaxone, ceftazidime, cefepime, amikacin, gentamicin, aztreonam, ertapenem, meropenem and tigecyclin.

The sensitivity of GABHS and *S. aureus* as the most common causes of secondary infection in scabies were low to amoxicillin, ampicillin, erythromycin, azithromycin, doxycycline, tetracycline, cephradine, amikacin, gentamicin, kanamycin and ceftazidime. This may be due to the widespread use of the drugs, without proper indication, inadequate dosage, long-term use and emerged of strains bacteria resistant to antimicrobials.

Conclusion

Oral clindamycin is a drug of choice which can be given to pediatric or adults patients for the treatment of secondary bacterial infection following scabies. The use of antimicrobials rationally can alter bacterial susceptibility patterns, resulting in changes of resistance pattern to antimicrobials. Therefore, antimicrobial susceptibility testing should be revised periodically.

Acknowledgment

This study was supported by Universitas Padjajaran, Bandung, West Java, Indonesia. (Grant No. 855/UN6.3.1/PL/2017).

Author's Contributions

Hendra Gunawan, Unwati Sugiri and Nurhasanah: All experiments.

Kristina Makarti: Manuscript preparation.

Oki Suwarsa: Design the research plan and organized the study.

Conflict of Interest Statement

We declare that we have no conflict of interest

Ethics

The study was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia with ethical clearance.

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