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Prophylactic effect of cefazolin on normal skin flora in patients harbored elective neurosurgery and surgery staffs

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Abstract

Introduction: Surgical site infection (SSI) is one of the most important and dangerous complications of surgery. The normal skin flora is the most common source of the infection.
Objectives: This study aimed to determine the prophylactic effect of cefazolin on normal skin flora in patients harbored elective neurosurgery and surgery staff.
Patients and Methods: This analytical-descriptive study was carried on the samples taken from the hands of 100 personnel of operation room and the skin of incision site of 100 neurosurgical patients through swab and then cultured in blood agar and EMB (eosin methylene blue) medium. The effective antibiotic on dominant flora of skin was specified by antibiogram test.
Results: *Staphylococcus* is consisted of 85.5% of strains grown in culture which included 80 cases methicillin resistance *Staphylococcus epidermidis* (MRSE) (40%), 11 cases *Staphylococcus aureus* (5.5%), 73 cases of *S. epidermidis* (36.5%), 7 cases *Staphylococcus saprophyticus* (3.5%) and 5 cases of methicillin resistance *S. aureus* (MRSA) (2.5%). The antibiotic resistance of the mentioned strains showed that 60% of MRSE strains, 100% of *S. aureus* strains and 67% of *S. epidermidis* strains were sensitive to cefazolin. Regarding ceftazidime, the sensitivity of gram-positive bacteria was 13% and 100% and 53.42% respectively.
Conclusion: SSI is one of the main concerns of surgeons. Skin flora of patient or personnel's hand are one of the main infectious sources, which are caused by *Staphylococcus* in 88% of cases because of not being full and sufficient sensitivity against cefazolin.

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Introduction

Surgical site infection (SSI) is one of the common complications after surgery and significantly increases morbidity, mortality and hospitalization. SSI is the second common infection after surgery (20-25% of infections) which happens at the site of surgery within 30 days after it or one year after implant surgery. Despite recent attempts on care of hospitalized patients, the control of infection in patients under surgical operation is still considered the main challenge (1).

Infection after surgical operation is one of the main side effects and complications of surgery which prevents to achieve the surgical operation aim. Although in most cases, the cause of infection is not well – understood. The influence of some factors such as unsterilized surgical instruments, extensive surgical site, long time surgical procedure, pollutant air of surgery room and unsterilized surgeon's hands on SSI have been detected. SSI without prophylactic antibiotic therapy in craniotomy surgeries is around 0.8%-5% and it is 5%-11% in cerebral spinal fluid shunt (2,3).

Among hospital infections; the urinary tract infection (42%), lower respiratory tract infection or pneumonia (15% to 20%) and infection of circulatory system (5%-10%) are more important (4,5). However, SSI is the most common infection in surgical patients which is about 24% of all nosocomial infections and 38% of surgical infections (4-6).

SSI usually happens due to microbial pollution of incision site at the time of surgery. The source of infection is usually the normal flora of patient. However, pathogenic factors can appear from exogenous sources like the environment or the hospitals staff. Factors which influence the microbial pollution of wound and lead to SSI include the number of inoculated bacteria (high number of bacteria increases the risk of infection), presence of foreign bodies in the wound (foreign object reduces bacterial dose required for infection) and the virulence of the infectious agent (7). Infection after operation especially neurosurgeries is one of the main problems since, it has influenced

Core tip
Since the main infectious source of skin flora – *Staphylococcus* – has not sufficient sensitivity against cefazolin, we suggest using vancomycin instead of cefazolin lonely and using another antibiotic to cover the gram negatives strains.

the surgery prognosis from a long time ago (8). Studies have shown that prescription of appropriate prophylactic antibiotic is effective in reducing SSI and the effects of infection after surgery. Concerning prophylactic antibiotics, most sources have recommended the IV type of cephalosporin, and in most cases, cefazolin has been mentioned as a proper drug for prophylaxes (9, 10).

Objectives

This study aims to determine the dominant flora of skin and investigate cefazolin prophylactic effect. Additionally, we aimed to evaluate the effect of other antibiotics on dominant flora of skin to find a proper antibiotic for prophylaxis.

Patients and Methods

Study design

This is a descriptive-analytical study, which was done in 2012 in Al-Zahra hospital, the medical and educational center of Isfahan University of medical sciences. The statistical sample of this study included elective neurosurgical patients and surgical personnel of this hospital.

The inclusion criteria of this study were lack of surgical operation within the last six months, no administration of antibiotic within the last two weeks and absence of injury in sampling site of the body.

Exposed site of patients gone under surgery and the hand of surgery personnel were rubbed by wet sterile swap with normal saline to be cultured on the culture medium. Then blood agar culture and eosin media were used to tracking the gram-positive and gram-negative bacteria. Plates were kept for 24 hours in 35°C incubator and then investigated for bacteria growth. In cases of bacteria growth, the effects of cefazolin and other antibiotics on skin dominant flora, the antibiogram test was conducted. To perform antibiogram test, agar Hinton media was used, where the grown bacteria were cultivated with standard code of half-MacFarland. Then related discs to each bacterium were placed on culture medium and maintained for 24 hours in 35°C incubator and then the diameter of halos was evaluated for resistance and sensitivity.

Ethical approval

The research followed the tenets of the Declaration of Helsinki and its later amendments. The design and objectives of the study were explained to all participants and written informed consent was obtained from the participants. This study was conducted as the medical doctorate at medical school of Isfahan University of Medical Sciences, Isfahan, Iran (thesis # 391429).

Data analysis

Data were presented as mean ± standard deviation (SD) for continuous variables. To analyze the findings of this study, SPSS 18 software was applied. *P* value of 0.05 or less was considered as the significance level. Quantitative variables were also compared with t test, Fisher's exact test and Mann-Whitney U test.

Results

In this study, 100 samples were taken from the skin of personnel and 100 others from the skin of patients and were cultured in microbial and antibiogram media. No bacteria grew in 16 taken samples. In 80 cases (40%) methicillin resistance *Staphylococcus epidermidis* (MRSE), in 11 cases (5.5%) *S. aureus*, in 73 cases (36.5%) *S. Epidermidis*, in 7 cases (3.5%) *Staphylococcus saprophyticus*, in 5 cases (2.5%) *Staphylococcus aureus* resistance to methicillin, in 2 cases (1%) *Micrococcus* and in 6 cases (3%) other cultivars such as 1 case of *Klebsiella pneumoniae*, 1 case of *Acinetobacter*, 1 *Micrococcus*, 1 *Bacillus*, 1 diphtheroid and 1 case of vancomycin resistance enterococci (VRE) were observed. In four cases were seen fungi grew which in three cases it was along with bacteria growth and in one sample, fungi growth was alone. Thus, concerning the obtained results, in our study just two strains of gram-negative bacteria were seen (1 case of *Klebsiella* and 1 case of *Acinetobacter*). *Klebsiella* sample was related to personnel and *Acinetobacter* sample was related to patients. In Table 1, the distribution of each type of bacteria has been shown according to patients and personnel. Based on this table, the most common bacterium grown in culture media among personnel was *S. epidermidis* with frequency of 43% and the most common bacterium grown in patients was *S.*

Table 1. The distribution of bacteria according to personnel and patient

Type of Bacteria	Personnel Number	Patient Number
No microorganism growth	5	11
MRSE	34	46
Staphylococcus aureus	8	3
Staphylococcus epidermidis	43	30
Staphylococcus saprophyticus	6	1
Micrococcus	1	1
Only fungi	1	0
Bacillus	1	0
Klebsiella	1	0
Acinetobacter	0	1
Diphtheroids	0	1
MRSA	0	5
VRE	0	1
Total	100	100

epidermidis resistance against methicillin with frequency of 46%. On the other hand, all cases of MRSA and just VRE sample were observed among patients. Furthermore, the only *Klebsiella* sample was related to personnel. In this study, the distribution of bacteria in patients and staff had a significant difference (Fisher's exact test; P= 0.01). In Figure 1, the frequency percentage of bacteria has been shown for patients and personnel.

The average numbers of bacteria in staff samples and patients' skin were 15147 ± 2148 and 24046 ± 3204, respectively. According to t test, the average number of bacteria in patients was significantly more than staff (P= 0.02). In Table 2, the frequency distribution of antibiotic resistance of strains grown in culture has been shown. Fisher's exact test on the mentioned data showed that the resistance of studied strains against clindamycin, gentamicin, and rifampin has no significant difference (P > 0.05). However, their resistance against ciprofloxacin, vancomycin, cotrimoxazole, cefoxitin, cefazolin, tetracycline and ceftazidime had significant difference (P < 0.05).

Among the samples, VRE was sensitive to ciprofloxacin, vancomycin, tetracycline, gentamicin and ampicillin versus susceptible to linezolid. Furthermore, we found a relative sensitivity against cefazolin among common gram-positive bacteria like *S. aureus, S. epidermidis* and MRSE. Around 60% of MRSE strains, 100% of *S. aureus* strains and 67% of *S. epidermidis* were sensitive to cefazolin. Furthermore, the sensitivity of common gram-positive bacteria to ceftazidime was less than cefazolin, while 12.5% of MRSE cases, 100% of *S. aureus* and 53.3% of *S. epidermidis* were sensitive to this antibiotic.

Table 3 shows the frequency distribution of antibiotic resistance of various strains, according to personnel and patients.

Fisher's exact test showed that the resistance to MRSE strain has a significant difference between personnel and patients (P = 0.007), however, the resistance of other strains has no meaningful difference between patients and personnel.

Discussion

The aim of this study was to determine the dominant microbial flora on the hand's skin of personnel and the skin of surgical incision site of our patients, and also to investigate the effect of cefazolin on the microbial flora. Additionally, we aimed to propose an appropriate prophylaxis protocol for neurosurgical patients.

According to the results of the study, the most common bacteria of skin flora in patients and personnel were *Staphylococcus*. Around 40% of cases include MRSE, 36.5% *S. epidermidis*, 5.5% *S. aureus*, 3.5% *Staphylococcus saprophyticus* and 2.5% MRSA. In 8% of cases there was not grown microorganism and only 4% includes gram-negative and other microbes. In the study by Khodadad et al, 87.5% of samples of personnel hands were pollutant. They found, the most common grown bacterium was *Staphylococcus epidermidis* with frequency of 79.4% (11).

Since every prophylactic antibiotic regimen should have a proper coverage on *Staphylococcus*, thus, first generation cephalosporin including cefazolin (12) leads to osmotic instability of the bacteria through inhibition of cell wall synthesis of gram-positive and gram-negative bacteria and has bactericidal effects (13).

In the present study, the sensitivity of *S. aureus* to cefazolin was 100%, however, the sensitivity of *S. epidermidis* was between 60 to 67%, while cefazolin has not full antibiotic coverage.

Sensitivity against gentamicin for *S. aureus* was 100% while it was 86% to 95% for *S. epidermidis*. Rifampin had an appropriate sensitivity of 97% to 100% with 2.5% resistance. Concerning the third generation cephalosporin, ceftazidime had good effect on *S. aureus*; however, its effect on *S. epidermidis* was not significant (12.5 to 53%).

In the study by Jalal-Pour et al conducted in Al-Zahra medical education centre, *S. aureus* and *S. epidermidis* were the most common bacteria from the hands of personnel. They found, 38% of separated samples were *S. epidermidis* while 21% of them were resistant against cefalotin (14). In another study which was carried out by Moezi et al in another hospital of Isfahan, 24% of samples

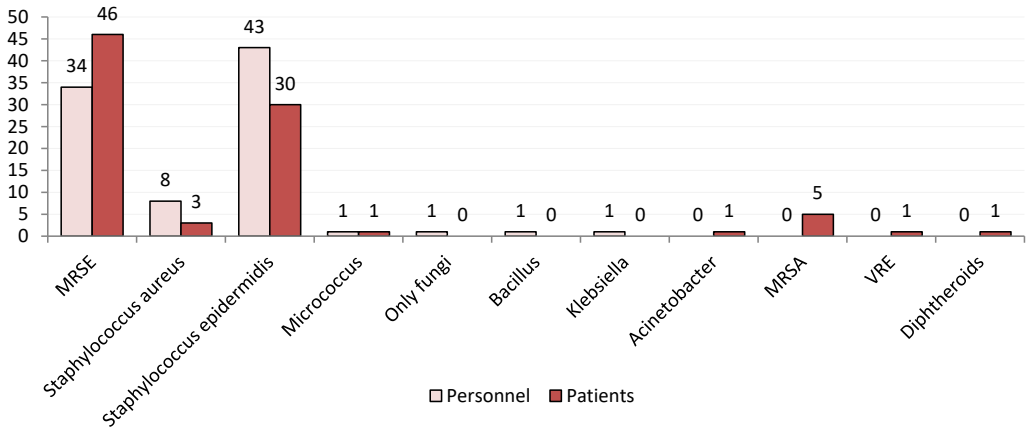

Figure 1. Absolute and relative frequency of grown bacteria in culture medium according to patient and personnel

Table 2. Frequency distribution of antibiotic resistance of grown strains in culture medium

Antibiotics	Bacterial resistance	MRSE	SA	SE	SS	Micrococcus	MRSA	Other	*P*
	Sensitive	49 (59.8)	9 (81.8)	52 (71.2)	5 (71.4)	1 (50)	3 (75)	2 (100)	
Clindamycin	Intermediate	3 (3.7)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (25)	0 (0)	0.41
	Resistant	30 (36.6)	2 (18.2)	20 (27.4)	2 (28.6)	1 (50)	0 (0)	0 (0)	
	Sensitive	63 (76.8)	11 (100)	72 (98.6)	6 (85.7)	2 (100)	4 (100)	0 (0)	
Ciprofloxacin	Intermediate	7 (8.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0.001
	Resistant	12 (14.6)	0 (0)	1 (1.4)	1 (14.3)	0 (0)	0 (0)	1 (50)	
	Sensitive	82 (100)	11 (100)	73 (100)	6 (85.7)	2 (100)	4 (100)	2 (66.7)	
Vancomycin	Intermediate	0 (0)	0 (0)	0 (0)	1 (14.3)	0 (0)	0 (0)	0 (0)	0.006
	Resistant	0 (0)	0 (0)	0 (0)	1 (14.3)	0 (0)	0 (0)	1 (33.3)	
	Sensitive	71 (86.6)	111 (100)	70 (95.9)	6 (85.7)	2 (100)	4 (100)	3 (100)	
Gentamycin	Intermediate	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.56
	Resistant	9 (11)	0 (0)	3 (4.1)	1 (14.3)	0 (0)	0 (0)	0 (0)	
	Sensitive	50 (61)	11 (100)	66 (90.4)	5 (71.4)	1 (50)	3 (75)	0 (0)	
Cotrimoxazol	Intermediate	0 (0)	0 (0)	0 (0)	1 (14.3)	0 (0)	0 (0)	0 (0)	<0.001
	Resistant	32 (39)	0 (0)	7 (9.6)	1 (14.3)	1 (50)	1 (25)	2 (100)	
	Sensitive	80 (97.6)	11 (100)	73 (100)	7 (100)	2 (100)	4 (100)	3 (100)	
Rifampin	Intermediate	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.64
	Resistant	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	Sensitive	1 (2.4)	10 (90.9)	71 (97.3)	5 (71.4)	1 (50)	0 (0)	0 (0)	
Cefoxitin	Intermediate	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	<0.001
	Resistant	80 (97.6)	1 (9.1)	2 (2.7)	2 (28.6)	1 (50)	4 (100)	2 (100)	
	Sensitive	27 (32.9)	11 (100)	38 (52.1)	6 (85.7)	2 (100)	1 (25)	0 (0)	
Tetracycline	Intermediate	4 (4.9)	0 (0)	1 (1.4)	0 (0)	0 (0)	0 (0)	0 (0)	<0.001
	Resistant	51 (62.2)	0 (0)	34 (46.6)	1 (14.3)	0 (0)	3 (75)	2 (100)	
	Sensitive	48 (60)	11 (100)	49 (67)	0 (0)	2 (100)	5 (100)	1 (50)	
Cefazolin	Intermediate	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.01
	Resistant	32 (40)	0 (0)	24 (33)	7 (100)	0 (0)	0 (0)	1 (50)	
	Sensitive	10 (12/5)	11 (100)	39 (53/42)	0 (0)	2 (100)	5 (100)	0 (0)	
Ceftazidime	Intermediate	27 (33/75)	0 (0)	5 (6/84)	0 (0)	0 (0)	0 (0)	0 (0)	<0.001
	Resistant	43 (53.75)	0 (0)	29 (39/74)	7 (100)	0 (0)	0 (0)	2 (100)	

MRSE: methicillin resistance *Staphylococcus epidermidis*, SA: *Staphylococcus aureus*, SE: *Staphylococcus epidermidis*, SS: *Staphylococcus saprophyticus*, MRSA: methicillin resistance *Staphylococcus aureus*.

from the hands of hospital personnel were *S. aureus* and *S. epidermidis* with the prevalence of 26% and 21.5%. In their study, 27% of *S. epidermidis* samples and 31% of *S. aureus* samples were resistant against cefazoline (15). In a study done in China by Jiang et al, the most common cause of SSI was gram negatives. In their study, vancomycin had an appropriate effect on *Staphylococcus* (16).

Various studies have shown that normal skin flora, especially *Staphylococcus*, are responsible for sporadic and epidemic infections. *Staphylococcus* is transferred through various routs including contact with infected people, asymptomatic carriers, polluted devices and spreading through air which leads to SSI in the patients under surgical operation(17). Furthermore, asymptomatic carriers who carry *Staphylococcus* in different sites including nose, skin, hair, nail, axilla and perineum may be infected with these bacteria (8, 9).

Moreover, the bacterial carrying rate in adults is estimated as 20-40% depending on seasonal and local epidemiologic factors (17). Based on the studies, about 30% of individuals are permanent carriers of bacterium, 50% are temperate carrier of bacteria and 20% have no role in bacterial transfer (14). Bacterium can be transferred from the nose of carrier individuals to their skin while the presence of some factors like trauma and superficial wounds are the way for entrance of bacterium and infecting underlying tissues (17). However, fortunately, most bacteria that are widely spread in hospitals are gram-positive bacteria, especially *Staphylococcus* which can be prevented with proper medical prophylaxis and common antibiotics like cefazolin. The causes of SSI in most studies are *S. aureus*, *S. epidermidis* and gram negatives, respectively (18-20). In these studies, various recommendations have been proposed for reducing SSI incidence such as selection of antibiotic, prescription time, local application of antibiotic in surgical site and improvement of sterilization methods or preserving sterilization principles in surgical room. In most of these studies, cefazolin has been evaluated as the main treatment and its effect has been compared with vancomycin and third generation cephalosporine.

Table 3. The frequency distribution of strain's antibiotic resistance according to patients and personnel

Antibiotics	Bacterial Resistance	MRSE	SA	SE	SS	Micrococcus	MRSA	Other
	Personnel	16 (57.1)	2 (25)	13 (30.2)	1 (16.7)	1 (100)	0 (0)	0 (0)
Clindamycin	Patient	12 (29.2)	0 (0)	7 (23.3)	1 (100)	0 (0)	0 (0)	0 (0)
	P	0.12	1	0.42	1	0.29	1	1
	Personnel	1 (2.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ciprofloxacin	Patient	11 (22.9)	0 (0)	1 (3.3)	1 (100)	0 (0)	0 (0)	1 (50)
	P	0.007	1	0.41	1	1	1	1
	Personnel	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
Vancomycin	Patient	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)
	P	1	1	1	1	1	1	1
	Personnel	3 (8.8)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	0 (0)
Gentamicin	Patient	6 (12.5)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
	P	0.56	1	0.26	1	1	1	1
	Personnel	10 (29.4)	0 (0)	4 (9.3)	0 (0)	1 (16.7)	0 (0)	0 (0)
Cotrimoxazol	Patient	21 (43.75)	0 (0)	3 (10)	1 (100)	0 (0)	1 (20)	2 (100)
	P	0.17	1	0.99	1	0.29	1	0.64
	Personnel	1 (2.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Rifampin	Patient	1 (2.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	P	1	1	1	1	1	1	1
	Personnel	32 (94.1)	1 (12.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cefoxitin	Patient	47 (97.9)	0 (0)	2 (6.7)	2 (33.3)	1 (100)	5 (100)	2 (100)
	P	0.99	0.64	0.17	0.64	1	0.99	0.64
	Personnel	24 (70.6)	0 (0)	23 (53.5)	0 (0)	0 (0)	0 (0)	0 (0)
Tetracycline	Patient	25 (73.5)	0 (0)	11 (36.7)	1 (16.7)	0 (0)	4 (80)	2 (100)
	P	0.47	1	0.19	1	1	1	1
	Personnel	11 (13.75)	0 (0)	10 (13.7)	0 (0)	0 (0)	0 (0)	0 (0)
Cefazolin	Patient	21 (26.25)	0 (0)	14 (19.18)	7 (100)	0 (0)	0 (0)	1 (50)
	P	0.32	1	0.32	0.14	1	1	0.99
	Personnel	35 (43.75)	0 (0)	19 (26)	0 (0)	0 (0)	0 (0)	0 (0)
Ceftazidim	Patient	8 (61.5)	0 (0)	10 (13.7)	7 (100)	0 (0)	0 (0)	2 (100)
	P	0.13	1	0.99	0.99	1	0.99	0.99

MRSE: methicillin resistance *Staphylococcus epidermidis*, SA: *Staphylococcus aureus*, SE: *Staphylococcus epidermidis*, SS: *Staphylococcus saprophyticus*, MRSA: methicillin resistance *Staphylococcus aureus*.

Administration of vancomycin powder in the surgical site at the end of surgery which in most reported studies reduces SSI (21, 22), although some others have not confirmed this finding (23). Based on Myung et al study, intravenous vancomycin is recommended to be used before surgery with regard to high incidence of SSI due to *Staphylococcus*, while the effectiveness of cefazolin as prophylaxis has been questioned (18). Moreover, the effectiveness of cefazolin has been compared with third generation cephalosporins including ceftriaxone which seems cefazolin has better efficiency (24). Other effective measure to reduce the SSI is antibiotic prescription time. The best time is one hour before incision for surgery (25). The role of sterilization principles in surgical room is so important that in some studies the prescription of any prophylaxis antibiotic have been excluded. In the study by Gozal et al the infection due to ventriculostomy without intravenous antibiotic has been reported as 2%, while its prevalence in most studies has been reported to be even 24% (26). After vancomycin therapy, gentamicin from aminoglycoside group and ofloxacine from quinolone group have been recommended (19).

Conclusion

SSI is one of the main concerns of surgeons. Skin flora of patient or personnel's hand are one of the main infectious sources, which are caused by *Staphylococcus* in 88% of cases because of not being full and sufficient sensitivity against cefazolin. Hence, reconsideration should be done about using prophylaxis with cefazolin alone and vancomycin is recommended instead of cefazolin lonely. Moreover, it is recommended to use vancomycin alongside another antibiotic to cover the gram negatives strains.

Limitations of the study

This is a single center study. A relatively small proportion of patients can be mentioned as the study's limitation. This study can be a pilot for larger investigations on this aspect.

Authors' contribution

HT, SR and MM contributed to study design, preparation of manuscript and final revision. HT and MM participated in data gathering. SR conducted data analysis and interpretation. All authors read and approved the paper.

Conflicts of interest

All authors declare no potential conflicts of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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