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Review

Nosocomial infections in intensive care and medical rehabilitation units, and evaluation of antibiotics prescription

Al-Shenqiti A.[1], Bahashwan S. A.[2], Ghanem S.[3,5], Manzoor N.[3,6] and El Shafey H. M.[4,7*]

[1]Physical Therapy Department, College of Medical Rehabilitation Sciences, Taibah University, Madinah, Saudi Arabia.
[2]Pharmacology and Toxicology Department, College of Pharmacy, Taibah University, Madinah, Saudi Arabia.
[3]Clinical Laboratory Sciences Department, College of Applied Medical Sciences, Taibah University, Madinah, Saudi Arabia.
[4]Respiratory Therapy Department, College of Medical Rehabilitation Sciences, Taibah University, Madinah, Saudi Arabia.
[5]Microbiology Department, Faculty of Science, Helwan University, Cairo, Egypt.
[6]Department of Biosciences, Jamia Millia Islamia, New Delhi-110025, India.
[7]Radiation Microbiology Department, National Center for Radiation Research and Technology, Cairo, Egypt.

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Although, nosocomial infections (NIs) are considered to be an important cause of mortality and prolonged stay in hospitals, there are only a few studies that are concerned with their prevention and reduction in rehabilitation units. This could be because most NI surveys have been carried out mainly in acute and long-stay in hospitals. As a result, limited information is available on prevention and reduction of NIs in rehabilitation units. The present study is a systematic review that draws attention to the significance of setting up specific means for infection control in hospital units concerned with critical cases, and stresses on the need to adapt to new infection control policies, training of healthcare professionals, educating patients regarding safety measures and fighting nosocomial infections. Furthermore, this study aims to show the obligations of following certain considerations while prescribing antimicrobial therapy so as to maximize the efficacy and reduce the adverse effects of conventional antibiotics. Systematic review survey methods were adopted throughout the study. Results of the study were debatable concerning the question of predominance of Gram positive or negative microorganisms as nosocomial etiological agents. Infection control measures such as continuous surveillance protocols, suitable prevention methods and appropriate therapeutic treatment strategies such as de-escalation and rotational antibiotic therapies might help reduce nosocomial infections. Much attention should be given in hospitals to the environmental conditions including quality of water and air. Patients with a suppressed immune system during their stay in hospitals are susceptible to levels of microorganisms that are considered safe for a healthy community. Hence, this study suggests that special safety levels should be set up regarding the levels of microorganisms in hospitals and these should be much lower than those used for a healthy community.

Key words: Nosocomial infections, rehabilitation units, antibiotics, immunocompromised patients.

INTRODUCTION

Extensive studies have been done on the fundamental aspects of rehabilitation sciences. Several strategies are

under extensive research such as the use of laser therapy and phototherapy (Al-Shenqiti and Oldham, 2009; Al-Shenqiti and Oldham, 2014). Unfortunately, except for discovering new compounds having antifungal properties (Bahashwan, 2011a, b), many other cross-subsidiary aspects are neglected. One of the most neglected aspect is nosocomial infections in rehabilitation units. Acute medical rehabilitation units (MRU) are located in hospitals under the supervision of a physiatrist, a physician who specializes in rehabilitation care. He assesses and monitors the patient's medical and rehab status daily and also gives instructions to the team of rehabilitation professionals, while the acute MRUs provide round-the-clock rehabilitative nursing. The sub-acute MRUs (Subacute Rehab) are less intense and less comprehensive and are supervised only once or twice a week. Nosocomial infections, also called hospital acquired infections or healthcare-associated infection (HAI), are those infections which patients acquire during their stay in a hospital for some other reason other than for which they were admitted (Ducel et al., 2002). It is alarming since the infection was not present in that person when he was admitted. He may show symptoms after he is discharged (Benenson, 1995). Nosocomial infections could also be defined as infections that occur within 48 h of the patient's admission to the hospital or those infections which are acquired within 3 days after discharge or within 1 month of an operation. Occupational infection among the hospital staff are also included (Benenson, 1995). About 10% of the patients admitted to a hospital can be affected due to these infections (Inweregbu et al., 2005). Nosocomial infections are considered as a major obstacle in hospital care and complications in both adults and children (Fanos and Cataldi, 2002).

The main aim of this study was to draw attention to the importance of setting up specific means of infection control in hospital units that are concerned with critical cases. There is need to prepare and adapt to new infection control policies, train healthcare professionals, develop safety measures for patients and educate them on fighting nosocomial infections. The present study also aims to show the absolute necessity of following certain considerations when prescribing antimicrobial therapy so that the prescribed antibiotics can have maximum efficacy and minimum adverse effects.

PREVALENCE OF NOSOCOMIAL INFECTIONS

Several studies have documented and confirmed the high prevalence of nosocomial infections in health care environments and ICUs. Vincent et al. (1995) reported that more than 20% of the patients had ICU-acquired infections (Vincent et al., 1995). In a survey of 827 neonatal ICU patients, Sohn et al (2001) showed that 11.4% patients had 116 NICU-acquired infections (Sohn et al., 2001). The incidence of nosocomial infections varies among different studies but reports suggest high prevalence in ICU patients, the incidence ranging between 6 and 25% in neonatal ICUs. This large variation depends mostly on the weight of the new born child and the treatment conditions (Ferguson and Gill, 1996; Sohn et al., 2001; Babazono et al., 2008). The severity of the matter calls for an urgent need for surveillance at national level and more effective preventive measures to be evolved.

ETIOLOGY OF NOSOCOMIAL INFECTIONS

Pathogenic fungi like various species of *Candida* and *Aspergillus fumigatus* are responsible for nosocomial pneumonia. Being opportunistic, these infections are not so common in immunocompetent patients (Krasinski et al., 1985; Loo et al., 1996; El-Ebiary et al., 1997) but can be seen in organ transplant or immunocompromised, neutropenic patients. Outbreaks of pneumonia have been reported and are likely due to viruses like influenza, parainfluenza, measles, adenoviruses and respiratory viruses. Cases of hospital acquired, ventilator-associated and health-care associated pneumonia are common (American Thoracic Society, Infectious Diseases Society of America, 2005; Mühlemann et al., 2004).

The most common cause of nosocomial infections are Gram-positive bacteria. *Staphylococcus aureus* has been reported to be the predominant pathogen. The other common pathogens associated with nosocomial infections in ICU patients include methicillin-resistant (MRSA) and methicillin-sensitive *S. aureus* (MSSA) (19). Methicillin-resistant *S. aureus* (MRSA) is the cause of up to 60% of nocosomial infections in ICUs (Graffunder and Venezia, 2002; Inweregbu et al., 2005). Vancomycin-resistant *enteroccocus* (VRE) and multidrug-resistant *Acinetobacter* species are also commonly associated bacterial species (National Nosocomial Infections Surveillance System, 2004).

In contrast to previous findings, Ahoyo et al. (2014) showed that 65% of isolated microorganisms from nosocomial infected patients were Gram-negative, while only 30% were Gram-positive (Ahoyo et al., 2014). According to Vincent et al (1995), the infection causing micro-organisms, seen to inhabit ICUs more frequently were Enterobacteriaceae, *S. aureus* and *Pseudomonas aeruginosa* with a percentage of about 30 to 35%, while coagulase-negative staphylococci and fungi were reported to be 19 and 17%, respectively (Vincent et al.,

*Corresponding author: E-mail: hatem.elshafey@laposte.net. Tel: +966 56 58 54 837.

1995). Upto 60% cases of *S. aureus* were resistant to methicillin. The most common pathogens in neonatal ICUs were coagulase-negative staphylococci and enterococci as reported by Sohn et al. (2001). Sometime later in 2006, Prashanth and Badrinath (2006) claimed that Acinetobacter species caused nosocomial infections and is of increasing concern in critically ill patients. Also, the risk factors are not well established. The studies reported so far are still not clear about the predominance of the type of microorganisms as nosocomial etiological agents, that is, whether they are Gram positive or negative.

Frequency of nosocomial infections

In a recent study conducted using the National Nosocomial Infections Surveillance System, it was shown that percentage of bloodstream infections was the highest with a percentage that was greater than 39% followed by surgical site infections with a percentage greater than 13%, while pneumonia (PNEUM) and urinary tract infections (UTI) were the lowest with percentages 2.5 and 3.1%, respectively (National Nosocomial Infections Surveillance System, 2004). The percentage infection contribution of the other sites of colonization was only 15.5%. Oskouie et al. (2013) reported that the frequencies of different types of nosocomial infections were as follows: bacteremia (68.9%), urinary tract infections (13.6), lower respiratory tract infections (9.7%) and wound infections (7.8%) (Oskouie et al., 2013).

In ICUs, the frequency of nosocomial infections was about 29.13% of which 30.1% were respiratory tract infections, 39.1% were urinary tract infections and 23.7% were blood stream infections. Other infections were identified to be skin, soft tissue, wound and gastrointestinal tract infections (Shaikh et al., 2008). According to another report, pneumonia at a frequency of 46.9% is the most frequent followed by lower respiratory tract and urinary tract infections at a frequency of around 18%. Bloodstream infections occur at a frequency of 12% (Vincent et al., 1995). On the other hand, Ahoyo et al. (2014) reported that the most recurrent nosocomial infections were UTIs (37.5%) followed by, intravascular catheter-associated (27%) and surgical site infections (19.2%). Lower respiratory tract infections or pneumonia was at 11.7%, while bloodstream infections were at 1.5%, and infections originating otherwise were about 3.1% (Ahoyo et al., 2014).

Sohn et al. (2001) studied 827 neonatal ICU patients in 2001 and reported that 11.4% of these patients had 116 nosocomial ICU-acquired infections of which 53% were bloodstream, 13% were lower respiratory tract and 8.6% were ear-nose-throat or urinary tract infections. Nosocomial infections in a neonatal ICU showed a prevalence of 17.5%. Here, the bloodstream infections, clinical sepsis and pneumonia each showed a frequency of around 5 to 6%. The UTIs and surgical site infections comprised only 0.7%. The rate of infection due to medical interventions were about 14% associated with central intravascular catheters, 16% with total parenteral nutrition, 18.6% with ventilator-associated pneumonia, 13.7% with surgeries and 17.3% with urinary catheters (Su et al., 2007).

Risk factors for nosocomial infections

Several risk factors have been identified for ICU-acquired infections such as long stays in the hospital ICUs, greater than 48 h, mechanical ventilation, trauma, catheterization of blood vessels, and stress ulcer prophylaxis (Vincent et al., 1995). Besides these, use of postnatal steroids and H2-blockers are considered modifiable risk factors for nosocomial infections in neonatal ICUs (Rojas et al., 2005). More recently, Akkoyunlu et al. (2013) highlighted the inclusion of advanced age, long hospital stays, prior infections, transfusion of blood products and prior antibiotic usage as risk factors for nosocomial pneumonia in ICUs (Akkoyunlu et al., 2013). Seasonal viral infections can also be considered as putative risk factors in pediatric nosocomial infections (Mühlemann et al., 2004). It has been demonstrated that the highest risk is due to the pre-formation of urinary catheterization (King et al., 2012). Hence, unnecessary urethral catheterization should be avoided to prevent nosocomial UTIs (Savas et al., 2006).

Nosocomial UTIs constitute 40 to 50% of all hospital acquired infections (Saint and Lipsky, 1999; Merle et al., 2002) and hence are one the most common community acquired infections. These infections are associated with urinary catheters in 80% of the cases (Mulhall et al., 1988). Although, antibiotics are available and used frequently to control UTIs, they are widespread in the human population (Savas et al., 2006). A high incidence of these infections is reported to be caused by *E. coli*, *Enterococcus faecalis* and *Proteous mirabilis* (Chaudhry et al., 2016). Very low birth weights, gestational age and length of central venous lines of neonates especially those undergoing interventions such as mechanical ventilation are at the greatest risk of neonatal nosocomial infections (Pawa et al., 1997; Kasim et al., 2014). Mulu et al. (2013) confirmed that the most likely risk factors for post-operative infections are old age, any underlying disease, extended pre-operative and post-operative stay in hospitals, long surgeries and appendectomy (Mulu et al., 2013). Treating patients with drugs like imipenem, vancomycin and piperacillin-tazobactam can be a cause of imipenem-resistant *P. aeruginosa* infections in hospitalized patients (Onguru et al., 2008). Previous studies have illustrated several putative nosocomial infections risk factors that have been listed in Table 1.

NOSOCOMIAL INFECTIONS IN REHABILITATION ENVIRONMENT

Even though nosocomial infections are important causes

Table 1. Risk factors for putative nosocomial infections.

Active reasons	Passive reasons
Longer lengths of stay (LOS) (> 48 h) in ICU	Advanced age
Mechanical ventilation	Prior infection e.g. viral infections
Diagnosis of trauma	Gestational age
Central venous catheterization	Underlying disease
Pulmonary artery catheterization (PAC)	Very low birth weights (VLBW)
Urinary catheterization	
Stress ulcer prophylaxis	
Longer duration of surgery	
Use of H2-blockers	
Transfusion of blood products	
Prior antibiotic usage	
Length of central venous line of neonates	
Extended preoperative and postoperative hospital stay	
Appendectomy	

Figure 1. Nosocomial infections strategies.

of morbidity and mortality in health care sector along with prolonged stay in hospitals and increasing treatment costs, incompetent (Fanos and Cataldi, 2002) surveys have been carried out to investigate this issue. As a result, scanty information is available regarding rehabilitation sectors in hospitals (Baldo et al., 2002). Only a few studies are available that throw some light on reduction and prevention of NIs in rehabilitation environments. A study conducted in 2003 by Lewis et al. illustrated some modifications for Disease Control and Prevention (CDC) contact precautions applicable to the rehabilitation environment. These were easy to understand, consistent and could be effectively implemented by the hospital staff. These modifications did help in the prevention of nosocomial transmission of epidemiologically important pathogens (Lewis et al., 2003). Later in 2008, Geyik et al. proposed that appropriate interventions, surveillance and constant monitoring are effective in reducing the rate of NIs along with educating the staff on infection control practices (Geyik et al., 2008).

NOCOSOMIAL INFECTION CONTROL

Controlling nosocomial infections may include three strategies: Surveillance, prevention and treatment (Figure 1).

These infections can be prevented to a large extent by instituting careful surveillance of bacterial infections, improving hand hygiene, and limiting antibiotics abuse and invasive procedures (Garner, 1996; Goldman et al.,

1996; Goldmann and Huskins, 1997; Boyce and Pittet, 2002; Cohen et al., 2003; Shiojima et al., 2003; Ledell et al., 2003). The infection control programs should pay particular attention on preventing infections in patients who are at higher risk of infection due to exposure to certain procedures and medical devices (Emori and Gaynes, 1993). According to a study conducted concerning nosocomial infection control (SENIC) measures, it was observed that about 33% of the nosocomial infections could be prevented by taking proper infection control measures like using different surveillance methods and programs designed for prevention and treatment (Haley et al., 1985). Recently, Sonmezer et al. (2016) also suggested that the rate of nosocomial infections can be limited to a large extent by meticulously applying contact measures (Sonmezer et al., 2016).

Surveillance

Surveillance is a continuous process of systematically collecting, analyzing and interpreting all the information related to a patient's health. This process has immense significance while planning, implementing and evaluating the health of patients and timely disseminating all information. The surveillance service basically aims to collect information and make a database for comparing various hospital-acquired infections. It intends to uplift the health of patients by decreasing the rates of nosocomial infections and help in improving clinical practices. The surveillance procedures include the monitoring infections that occur after a surgery, hospital acquired bacteraemia, urinary tract and lower respiratory tract infections. Incidentally, UTI and lower respiratory infections are the second most common source of nosocomial infections. The studies have estimated that two-thirds of bacteraemia is associated with intravascular devices like catheters which are supposed to be the most common source of hospital-acquired bacteraemia (Inweregbu et al., 2005). Establishment of a surveillance system that monitors a device-related infection seems to be the principal strategy. This plan of action can achieve reduction and prevention of nosocomial infections associated with implantable biomaterials (Guggenbichler et al., 2011).

Prevention

A study was conducted to determine prevalence of nosocomial infections in ICU of European hospitals (Vincent et al., 1995) that identified several predisposing factors for nosocomial infections. The factors can be categorized as those related to the following: (i) underlying health status of the patient e.g. old age, malnutrition, alcoholism, heavy smoking, chronic lung diseases, and diabetes (ii) any kind of acute disease or condition e.g. surgery, trauma and burns (iii) invasive procedures like endotracheal or nasal intubation, central venous catheterization, extracorporeal renal support (iv) treatment issues like blood transfusion, recent antimicrobial therapy, immunosuppressive treatments, stress-ulcer prophylaxis, recumbent position, parenteral nutrition and length of stay in hospitals. These infections can be reduced and prevented by smartly regulating use of suitable antiseptics in combination with medical devices (Guggenbichler et al., 2011).

Treatment

There is increasing evidence suggesting that early use of appropriate antibiotics reduces morbidity and mortality. Conventional antibiotics are classified into one of the following four classes according to their mode of action: (i) inhibitors of the fungal cell wall such as penicillin (e.g penicillin V and G), semi-synthetic penicillin (e.g ampicillin, amoxicillin); cephalosporins (e.g cefotaxime, cefradine, ceftazidime); monobactams (e.g aztreonam); carbapenems (e.g meropenem); β- lactamase inhibitors (e.g clavulanate); and glycopeptides (e.g vancomycin). (ii) Inhibitors of fungal cell membranes such as polyenes (e.g nystatin); imidazoles (e.g ketoconazole; and triazoles (e.g fluconazole) (iii) inhibitors of protein synthesis such as aminoglycoside (e.g gentamicin); macrolides (e.g erythromycin); oxaolidinines (e.g erythromycin; ketolides (e.g telithomycin); and streptogramins (e.g synercid. (iv) Inhibitors of nucleic acids such as fluoroquinonolones (e.g ciprofloxacin); nitro-imidazoles (e.g, metronidazole); rifampicin (e.g, sulphonamides) and folate inhibitors.

Appropriate antibiotics are selected for treating a specific infection on the basis of the results of microbiological tests performed on clinical specimens. Some antibiotics have a broad-spectrum effect while others affect either Gram positive or negative bacteria only. It is highly recommended that any drug policy or guidelines should have an objective to stop or at least minimize antibiotic abuse and ease the pressure on a particular antimicrobial agent, rather an alternative drug should be used to prevent resistance in microorganisms (Inweregbu et al., 2005).

Two therapeutic strategies are used frequently for elimination of microbial infections using different antibiotics, de-escalation and rotational antibiotic therapies. De-escalation strategy requires the initiation of broad-spectrum antibiotic therapy at an early stage in patients with suspected sepsis even before diagnosis. On the other hand, rotational antibiotic therapy is a strategy that helps in reducing resistance to a particular antibiotic by its simple withdrawal, or the withdrawal of the whole antibiotic class from the ICU for a short and specified time period. This will stabilize and even decrease the rate of resistance to some extent. There are certain considerations that have to be taken care of while giving

antimicrobial therapy. It is absolutely necessary to acquire an accurate infection diagnosis before prescribing antimicrobial therapy. A clear understanding of the difference between empiric and definitive therapy should be achieved. Instead of using broad spectrum antibiotics straightaway, oral narrow-spectrum antibiotics should be tried first for the shortest duration necessary. Besides reducing drug resistance, this strategy will also be cost effective. It is important to understand the specific characteristics of antimicrobial agents, for instance, their pharmacodynamics and efficacy at the site of infection. Those drug characteristics that influence the efficacy of antibiotics should be taken into account along with the recognition of adverse effects of antimicrobial agents on the host (Leekha et al., 2011).

In the case of a patient suffering from a serious infection, it is critical to rapidly initiate effective antibiotic therapy, followed by de-escalation and, when new information and details are available the therapy should be discontinued promptly. At the same time, antibiotic resistance can be controlled effectively by complementing the therapy with effective infection control measures. The effective implementation of these principles requires the development of multidisciplinary antimicrobial supervising programs that assure adherence (Deresinski et al., 2007). The indiscriminate use of antimicrobials in non-infected patients is dangerous and should be discontinued immediately (Ahoyo et al., 2014). Furthermore, the use of high generation antibiotic and branded prescriptions where there is no requirement, adds to the cost of the therapy (Jose et al., 2016).

The most effective antibiotics against Gram-negative bacteria were found to be imipenem and meropenem (Savas et al., 2006). Antimicrobial agents have several adverse reactions and side effects, one of which is antimicrobial allergy (Leekha et al., 2011). The adverse effects can be direct or indirect. The direct adverse effects include allergy to the drug, its toxicity or its interaction with other drugs and therapeutic failure. Indirect effects, on the other hand, are those adverse effects which can be observed on the commensals and the environmental flora (Leekha et al., 2011). Hence, much attention should be given in hospitals to air, water and other environmental conditions as immuno-compromised patients in hospitals are susceptible to microorganism levels considered safe for healthy people. Torii et al. (2003) emphasized that even low concentrations (10 times lower than safety level) of *Ligionella pneumophila* found in the water used for washing is pathogenic and can cause serious infections in immunocompromised patients (Torii et al., 2003). Furthermore, Legionnaires' disease is estimated to be present in 3 to 15% of community acquired pneumonia and 10 to 50% of nosocomial infections in European countries and the United States (Chang et al., 2011). It has been reported that about 36% of the water samples are contaminated with *L. pneumophila* (Yamamoto et al., 2003; Suzuki et al., 2000).

Reports reveal that *S. aureus* shows a high resistance to methicillin at a frequency of 52.5% but show a low resistance frequency to vancomycin (7.7%). On the other hand, enterococci is highly resistant to vancomycin with a frequency of 67.5%. Among Gram-negative isolates, the highest percentage of resistance is observed against ampicillin (86.4%), tetracycline (77.3%), amoxicillin/ clavulanic acid (72.8%) and trimethoprim/ sulfamethoxazole (64%). In the case of different serotypes of *Salmonella* species, no well-defined differences in antimicrobial susceptibilities were observed. Isolates of *P. aeruginosa* gave an extended beta-lactamase spectrum where most of them were resistant to all beta-lactams (Abd El-Mohdy and Ghanem, 2009), except imipenem. Only 22% were found to be susceptible to gentamicin and ciprofloxacin (Ahoyo et al., 2014). Studies recommend the prescription of the antibiotic imipenem (IMP) for the treatment of *Proteus* spp. infections. In conditions where there is sensitivity to imipenem, amikacin (AK) can be prescribed. Acute *Proteus* infections may require the prescription of imipenem and amikacin together as combined therapy giving a synergistic effect (Bahashwan and El Shafey, 2013).

Nosocomial infections, especially those associated with ICU reveal that drug resistance rate in bacteria has increased tremendously. A common method by which bacteria develop resistance is by acquiring genetic mutations and transformations. Prescribing antibiotics senselessly leads to the selection of resistant bacteria. The genes that encode drug resistance may get transferred to other bacterial strains. Vancomycin, a broad-spectrum antibiotic, is usually prescribed to treat methicillin-resistant *S. aureus* (MRSA). But unfortunately, use of this antibiotic leads to resistance in enterococci and sometimes in *S. aureus*. Hence, there is an urgent need to very critically scrutinize prescriptions that include antibiotics. Reports reveal that the usage of vancomycin, which was the first line treatment for diarrhea due to *Clostridium difficile* infection, has been discouraged now a days (Inweregbu et al., 2005). Oskouie et al. (2013) reported that the wards that keep neonates had the highest share of nosocomial infections followed by NICU and hematology wards. It was observed that the most common pathogenic organisms were *Staphylococcus* sp. (35%), *Klebsiella* sp. (20.4%), *Serattia* sp. (9.7%), *E. coli* (6.8%) and *Pseudomonas* sp. (5.8%) (Oskouie et al., 2013). Hence, specific measures have to be taken to keep infection under control in critically ill patients. Nosocomial infection rates have to be reduced for which new national infection control policies have to be implemented. All the people who are concerned with healthcare should be educated on patient safety and given adequate training to highlight awareness of the disease and the significance of healthcare. The excessive use and misuse of antimicrobials has to be regulated especially in people who are admitted to hospitals not for

any kind of infection but some other reasons (Ahoyo et al., 2014).

Conclusion and recommendation

A reduction in nosocomial infection, especially in the rehabilitation milieu is of utmost importance. Special attention should be given to immunocompromised patients. The health care sectors should adapt to infection control policies giving adequate and proper training to the hospital staff and other professionals. The patients should also be aware of suitable safety measures. Antimicrobial therapy should be given with care. The antibiotics prescribed must have maximum efficacy and the least adverse effects. Natural products have great therapeutic potential with little side effects. These products and their derivatives are now being highly researched as potential antimicrobial agents. Synergy of the conventional antibiotics with natural products is also investigated to reduce drug doses and increase efficacy.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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