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Overcoming Antimicrobial Resistance: New Strategies, Expections: Greater Hope

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Abstract

Health workers are constantly exposed to infectious materials and pathogens while they provide care to the patients. There are plenty of chances for health workers to get affected by infection, so infection control measures are most necessary for health workers. By practicing infection control techniques, the health workers can avoid spreading microorganisms. This can be possible when there is up gradation of knowledge and attitude of health workers regarding PPE. A pre-experimental one group, pre-test-post-test study was conducted to assess the effectiveness of planned teaching program regarding personal protective equipment use among the students of GNM1st year at Maharaja Agrasen College of Nursing, Hisar. The study was conducted amongst 30 students of GNM 1st year by using structured knowledge questionnaire. The study findings reveal that only 43% study subjects had previous knowledge regarding PPE. The mean difference between pre-test and post-test score was 5.07 and it is statistically significant at 0.05 level of significance. The standard deviation of mean difference is 3.28 for pre-test and 2.89 for post-test. The paired 't" test value calculated is 7.31. Planned teaching program was effective to improve knowledge regarding personal protective equipment use.

Keywords: Nanotechnology; Antimicrobial Resistance; Microorganisms

Introduction

The word antimicrobial has its origin from the Greek words: "anti", "mikros" and "bios", which mean: "against", "little" and "life", respectively. Hence, antimicrobial agents are generally known to be any substance or compound capable of killing (microbicidal) or inhibiting the growth (biostatic) of microorganisms [1]. The use of antimicrobial agents in the treatment of a wide range of infectious diseases have, been very effective, in the past decades. However, with the indiscriminate use of these antimicrobial agents, antimicrobial resistance has developed, by a broad strain of several microorganisms [2,3] and thus, it has become very difficult to manage several infectious diseases. Some popularly known microorganisms that have developed resistance to antibiotics include: *Mycobacterium tuberculosis*, Pseudomonas aeruginosa, *Streptococcus agalactiae*, Methicillin-resistant Staphylococcus aureus, Klebsiella pneumoniae, Methicillin-resistant Staphylococcus aureus, *Escherichia coli* and Salmonella typhi, amongst many others [4]. Antimicrobial resistance has led to an increased statistical value in the numbers of morbidities and mortalities caused by infectious diseases [5] and there is a disturbing economic impact on the medical and human cost [6]. The development of resistance to antimicrobial agents (antibiotics) by microorganism, cuts across all known classes of natural and synthetic compounds that are available for treating microbial infectious diseases.

The cost and complexities involved in the discovery of novel drugs have limited their synthesis and as a result, only a few new antibiotics have been produced since the emergence of antimicrobial

resistance [7]. A variety of mechanisms has been linked to the development of resistance to antibiotics by microorganisms [8]. The most common of all mechanisms, being the inactivation of antimicrobial agents via the enzymic degradation of the drug by hydrolysis, group transfer or redox mechanisms [9,10]. The global rise in drug resistance by disease-causing microorganisms has become a pressing subject, thereby, posing a very dangerous public health issue [11-13]. Therefore, it is paramount for new and more effective strategies to be developed by synthesizing new antimicrobial agents or modifying the already existing ones in order to enhance their antimicrobial activity [3]. This has been significantly achieved by employing new technologies, such as: nanotechnology, its implication in combating resistance faced with the use of conventional methodology is briefly summarized in this mini review.

Conventional Strategies

Prior to the year 1930, there was a remarkable breakthrough in the treatment of infectious diseases by using antimicrobials following the discovery of penicillin. Subsequently, other antibiotics, such as: cefixime, linezolid, gentamicin, carbapenem, methicillin, vancomycin and streptomycin, were discovered [14,15]. These antibiotics were extensively employed in treating microbial infectious diseases as a result of the numerous benefits associated with their usage. The mode of antimicrobial actions of these agents varies, based on their structural nature and the degree of their affinities to the sites of the intended targets in the cells of the microorganism (bacteria) [1]. Unfortunately, over the years, these drugs (antibiotics) as well as the method of drug delivery appeared to have failed due to the development of drug (antibiotic) resistance by these microorganisms [16]. Microorganisms, especially bacteria have developed ways such as inactivation of enzyme, reduction in cell permeability, alteration in target site/enzyme, protection of target site by the formation of biofilms as mechanisms to resist antimicrobial agents (antibiotics) [5]. Thus, the route of the conventional approach of treating infectious diseases, can be very difficult. Figure 1 below shows an estimated duration of the time of the discovery of these antimicrobial agents and the year they developed antimicrobial resistance.

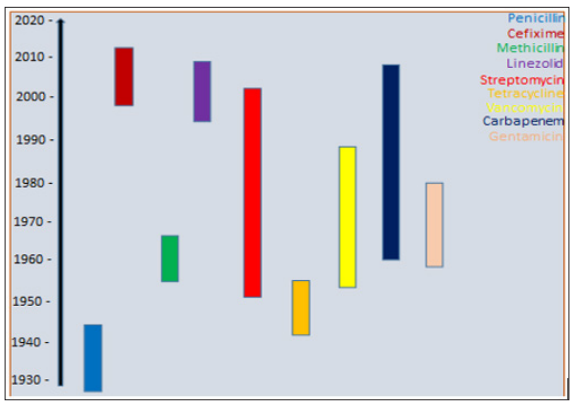

Figure 1: Some examples of antibiotics, year of discovery and year of antimicrobial resistance development.

Limitations: It has been observed that there is a concurrent exhibition of antimicrobial resistance by pathogenic microorganisms on most of the old and new antibiotics used in clinics and hospitals [17]. This has been associated with the limitations of the conventional dosage forms used in combating infectious diseases caused by microbes. Some of these limitations include, but are not restricted to, the following [18-20]:

a) Inadequate concentration at target infection sites

b) Poor penetration of the antibiotics

c) Exposure of antimicrobial agents to healthy sites

d) Unfavorable side effects

e) Poor patients' compliance

f) Ultimately, development of resistance by microorganisms

This implies that if these limitations are not overcome, antimicrobial resistance will inevitably; follow with the use of antibiotics [21]. Therefore, in order to avoid sliding back to the era of pre-antibiotic, a judicious modification of existing antimicrobials and the method of delivery must be developed.

New Strategies-Nanotechnology

Nanomedicine, which is a branch of nanotechnology, has experienced significant advancement in diagnosis, monitoring, drug delivery and control of diseases [4]. The limitations of conventional drugs and the methods employed for combating antimicrobial resistance, have prompted researchers from multidisciplinary fields worldwide, to explore the potential applications of nanotechnology in order to overcome antimicrobial resistance. This has led to the development of novel and more effective antimicrobial compounds as well as more effective strategies against antimicrobial resistance [22,23]. The advances made in recent years in the biomedical field, have offered new therapeutic agents and novel delivery systems that can target the infected site(s) [5]. The use of materials with nanosized (nanomaterials) is rapidly developing in order to overcome most of the antimicrobial resistant strain microorganisms. Some of these materials have inherent antimicrobial properties and can deliver antibiotics to targeted sites at the same time [5].

Nanoparticles, however, stand out as the mostly widely employed nanomaterial due to their interesting properties, such as enhanced drug stability and solubility [24], biocompatibility and ability to modulate their release via stimuli control [25], ease in the methods of synthesis [26] and possibility to functionalize them with different (bio) molecules. These features provide major advantages over the conventional therapies in the treatment of infectious diseases, caused by intracellular antimicrobial resistant pathogens [5]. Nanomaterials exhibit their antimicrobial activities by interacting with the cell wall of the bacterial directly, preventing the formation of biofilm, production of reactive oxygen species, triggering the immune response of the host as well as interacting with DNA and proteins [5,27-36]. Table 1 below summarizes some of the studies carried out on various strains of antimicrobial

resistant microorganisms. The various nanotechnology approaches above and even many more have shown promising potentials as alternate methods of circumventing antimicrobial resistance in microorganisms.

Table 1: Types of nanomaterials/antimicrobial agent used in combating antimicrobial resistance in different microorganisms.

Nanomaterials	Organism of targets	References
Silver nanoparticles	methicillin-resistant Staphyloccocus aureus (MRSA)	[37]
Pluronic-coated silver nanoprisms	methicillin-resistant Staphyloccocus aureus (MRSA)	[38]
Silver carbon complexes	Pseudomonas aeruginosa, Methicillin-resistant Staphylococcus aureus (MRSA) and Klebsiella pneumoniae.	[39]
Zinc oxide	methicillin-resistant S. epidermidis (MRSE), Klebsiella pneumoniae, Listeria monocytogenes, Salmonella enteritidis, Streptococcus mutans, Lactobacillus,	[40,41]
Gold	vancomycin-resistant enterococci, Methicillin-resistant Staphylococcus aureus, Staphylococcus aureus, *Escherichia coli*	[42-45]
Nitric oxide releasing nanoparticles	Klebsiella pneumoniae, Enteroccocus faecalis, Streptoccocus pyogenes, Escherichia coli and Pseudomonas aeruginosa	[46]
Silver nanoparticles	Pseudomonas aeruginosa, *Escherichia coli* and Klebsiella pneumonia	[47]
Chitosan	Pseudomonas aeruginosa	[48]
Silver nanoparticles	Pseudomonas aeruginosa, *Escherichia coli* and S. pyogenes	[49]
Copper Nanoparticles	B. subtilis	[50,51]
NO-releasing silane hydrogen-based NPs	**Methicillin-resistant Staphylococcus aureus (MRSA)**	**[52]**
NO-releasing silica NPs	Staphylococcus aureus and S. epidermidis, Pseudomonas aeruginosa, Escherichia coli, Candida albicans	[24]
Nanocarriers/Antimicrobial agents	**Microorganisms**	**References**
Polymeric Nanoparticles/Ampicillin	Salmonella typhimurium	[53]
Solid Lipid Nanoparticles/rifampicinisoniazid	Mycobacterium tuberculosis	[54]
Dendrimers/Sulfamethoxazole	*Escherichia coli.*	[55]
Liposome/Vancomycin	Methicillin-resistant Staphylococcus aureus (MRSA)	[56]

Conclusion

The development of antimicrobial resistance by microorganisms, has been linked to the difficulties encountered in treating infectious diseases. This has led to the development and application of nanotechnology approach in circumventing the limitations of the conventional drug dosage forms. Several *in-vitro* and *in-vivo* studies have shown to be very promising as reported in some of the references cited in this mini review. Therefore, it is highly anticipated and envisaged that in few years' time, the issue of antimicrobial resistance is expected to become a thing of the past because it is hoped that a far more efficient therapeutic method for combating antimicrobial resistance will be in the market. Although, these new approaches tend to be greatly promising, it is encouraged that further researches should still be undertaken by scientists from various fields in order to completely provide a long-lasting solution to antimicrobial resistance. This will indeed bring and restore a greater hope in eradicating antimicrobial resistance globally, thus leading to a probable longevity of human beings and a healthier community.

References

1. Bhaskar Das, Sanjukta Patra (2017) Chapter 1-Antimicrobials: Meeting the Challenges of Antibiotic Resistance through Nanotechnology in the book: Nanostructures for Antimicrobial Therapy: Micro and Nano Technologies. Philadelphia, USA.
2. Davies J, Davies D (2010) Origins and evolution of antibiotic resistance. Microbiol Mol Rev 74: 417-433.
3. FC Tenover (2006) Mechanisms of antimicrobial resistance in bacteria. Am J of Infect Control 34(5): 3-10.
4. Singh R, Smitha MS, Surinder PS (2014) The Role of nanotechnology in combating multi-drug resistant bacteria. J of Nanoscience & Nanotechnology 14: 1-12.
5. Baptista PV, Matthew PM, Andreia C, Daniela AF, Niamh MM, et al. (2018) Nano-strategies to fight multidrug resistant bacteria- A battle of the titans. Front in Microbiol 9: 1441.
6. McGowan, JE (2004) Minimizing Antimicrobial Resistance: The Key Role of the Infectious Diseases Physician, Clinical Infectious Diseases, volume 38(7): 939-942.
7. Projan SJ (2003) Why is big Pharma getting out of antibacterial drug discovery? Curr Opin Microbiol 6(5): 427-430.
8. Kalan L, Wright GD (2011) Antibiotic adjuvants: Multicomponent anti-infective strategies, Expert Rev. Mol. Med. vol. 13, e5.
9. Wyk, HV (2015): Antibiotic resistance. S Afr Pharm J 82: 20-23.
10. Dzidic S, Suskovic J, Kos B (2008) Antibiotic resistance mechanism in bacteria: Biochemical and genetic aspects. Food Technol Biotechnol 46: 11-21.

11. Meyer E, Schwab F, Schroeren Boersch B, Gastmeier P (2010) Dramatic increase of third-generation cephalosporin-resistant *E. coli* in German intensive care units: Secular trends in antibiotic drug use and bacterial resistance, 2001 to 2008. Crit Care 14(3): 113.
12. Rossolini GM, Mantengoli E, Docquier JD, Musmanno RA, Coratza G (2007) Epidemiology of infections caused by multiresistant Gram-negatives: ESBLs, MBLs, panresistant strains. New Microbiol 30: 332-339.
13. Spellberg B, Guidos R, Gilbert D, Bradley J, Boucher HW, Scheld WM, Bartlett JG, Edwards J (2008) Infectious Diseases Society of America. The epidemic of antibiotic-resistant infections: A call to action for the medical community from the infectious diseases society of America. Clinical Infectious Diseases 46, 155-164.
14. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, et al. (2010) Emergence of a new antibiotic resistance mechanism in India, Pakistan and the UK: A molecular, biological and epidemiological study. The Lancet Infectious Diseases 10(9): 597-602.
15. Clatworthy AE, Pierson E, Hung DT (2007) Targeting virulence: A new paradigm for antimicrobial therapy. Nat Chem Bio 3: 541-548.
16. Cantas L, Shah SQ, Cavaco LM, Manaia CM, Walsh F, et al. (2013) A brief multi-disciplinary review on antimicrobial resistance in medicine and its linkage to the global environmental microbiota. Front Microbiol 4: 96.
17. Levy SB (1998) The challenge of antibiotic resistance. Sci Am 278: 46-53.
18. Levison JH, Levison ME (2009) Pharmacokinetics and Pharmacodynamics of Antibacterial 1148 Agents. Infect Dis Clin North Am 23: 791-819.
19. Gao P, Nie X, Zou M, Shi Y, Cheng G (2011) Recent advances in materials for extended-release antibiotic delivery system. J Antibiot 64: 625-634.
20. Cheng G, Hao H, Xie S, Wang X, Dai M, et al. (2014) Antibiotic alternatives: The substitution of antibiotics in animal husbandr. Front Microbiol 5: 1-15.
21. Chang Ro L, Hwan C, Byeong CJ, Sang HL (2013) Strategies to Minimize Antibiotic Resistance. Int J Environ Res Public Health 10.
22. Metlay JP, Powers JH, Dudley MN, Christiansen K, Finch R (2006) Antimicrobial Drug Resistance, Regulation and Research. Emerg Infect Dis 12: 183.
23. Wise R (2006) Antimirobial Resistance: Paradox, Actions and Economics. J Antimicrob Chemother 57: 1024.
24. Huh AJ, Kwon YJ (2011) Nanoantibiotics: A new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era. J Control Release 156: 128-145.
25. Wang Z, Dong K, Liu Z, Zhang Y, Chen, Z, et al. (2017) Activation of biologically relevant levels of reactive oxygen species by Au/g-C3N4 hybrid nanozyme for bacteria killing and wound disinfection. Biomaterials 113: 145-157.
26. Gholipourmalekabadi M, Mobaraki M, Ghaffari M, Zarebkohan A, Omrani V, et al. (2017) Targeted drug delivery based on gold nanoparticle derivatives. Curr Pharm Des 23: 2918-2929.
27. Aderibigbe BA (2017) Metal-based nanoparticles for the treatment of infectious diseases. Molecules 22: 1370.
28. AlMatar M, Makky EA, Var I, Koksal F (2017) The role of nanoparticles in the inhibition of multidrug-resistant bacteria and biofilms. Curr Drug Deliv 15: 470-484.
29. Hemeg HA (2017) Nanomaterials for alternative antibacterial therapy. Int J Nanomed 12: 8211-8225.
30. Natan M, Banin, E (2017) From nano to micro: Using nanotechnology to combat microorganisms and their multidrug resistance. FEMS Microbiol Rev 41: 302-322.
31. Rai M, Ingle AP, Pandit R, Paralikar P, Gupta I, et al. (2017) Broadening the spectrum of small-molecule antibacterials by metallic nanoparticles to overcome microbial resistance. Int J Pharm 532: 139-148.
32. Slavin YN, Asnis J, Hafeli UO, Bach H (2017) Metal nanoparticles: understanding the mechanisms behind antibacterial activity. J Nanobiotechnology 15: 65.
33. Zaidi S, Misba L, Khan AU (2017) Nano-therapeutics: a revolution in infection control in post antibiotic era. Nanomed. Nanotechnol Biol Med 13: 2281-2301.
34. Bassegoda A, Ivanova K, Ramon E, Tzanov T (2018) Strategies to prevent the occurrence of resistance against antibiotics by using advanced materials. Appl Microbiol Biotechnol 102: 2075-2089.
35. Katva S, Das S, Moti HS, Jyoti A, Kaushik S (2018) Antibacterial synergy of silver nanoparticles with gentamicin and chloramphenicol against Enterococcus faecalis. Pharmacogn Mag 13: 828-833.
36. Siddiqi KS, Husen A, Rao RAK (2018) A review on biosynthesis of silver nanoparticles and their biocidal properties. J Nanobiotechnology 16:14.
37. Panacek A, Kvitek L, Prucek R, Kolar M, Vecerova R, et al. (2006) Silver colloid nanoparticles: synthesis, characterization and their antibacterial activity. J Phys Chem 110: 16248-16253.
38. Marta B, Jakab E, Potara M, Simon T, Imre Lucaci F, et al. (2014) Pluronic-coated silver nanoprisms: Synthesis, characterization and their antibacterial activity. Colloids Surf A 441: 77-83.
39. Leid JG, Ditto AJ, Knapp A, Shah PN, Wright BD, et al. (2012) *In-vitro* antimicrobial studies of silver carbene complexes: activity of free and nanoparticle carbene formulations against clinical isolates of pathogenic bacteria. J Antimicrob Chemother 67(1): 138-148.
40.
41. Byeth N, Houri Haddad Y, Domb A, Khan W, Hazan R (2015) Alternative antimicrobial approach: nano-antimicrobial materials. Evid. Based Complement. Altern Med 2015: 16.
42. Brayner R, Ferrari Iliou R, Brivois N, Djediat S, Benedetti MF, et al. (2006) Toxicological impact studies based on Escherichia coli bacteria in ultrafine ZnO nanoparticles colloidal medium. Nano Lett 6: 866-870.
43. Kuo WS (2009) Antimicrobial gold nanorods with dual-modality photodynamic inactivation and hyperthermia. Chem Commun 32: 4853-4855.
44. Pissuwan D, Cortie CH, Valenzuela SM, Cortie MB (2009) Functionalised gold nanoparticles for controlling pathogenic bacteria. Trends Biotechnol 28: 207-213.
45. Rai A, Prabhune A, Perry CC, (2010) Antibiotic mediated synthesis of gold nanoparticles with potent antimicrobial activity and their application in antimicrobial coatings. J Mater Chem 220: 6789-6798.
46. Grace NA, Pandian K (2007). Antibacterial efficacy of aminoglycosidic antibiotics protected gold nanoparticlesda brief study. Colloids Surf. A Physicochem. Eng Asp 297: 63-70.
47. Hajipour MJ, Fromm KM, Ashkarran AA, de Aberasturi DJ, de Larramendi IR, et al. (2012) Antibacterial properties of nanoparticles. Trends Biotechnol 30: 499-511.
48. Ninganagouda S, Rathod V, Jyoti H, Singh D, Prema K, Ul-Haq M (2013) Extracellular Biosynthesis of Silver nanoparticles by using Aspergillus Falvus and their antimicrobial activity against gram negative MDR strains. Int J Pharm Bio Sci 4: 222-229.
49. Tin S, Sakharkar KR, Lim CS, Sakharkar MK (2009) Activity of chitosans in combination with antibiotics in Pseudomonas aeruginosa. Int J Biol Sci 5: 153-160.
50. Lara HH, Ayala Nunez NV, Carmen LD, Ixtepan T, Cristina RP (2010) Lara HH, Ayala-Nuñez NV, Ixtepan-Turrent L, Rodriguez-Padilla C: Bactericidal

effect of silver nanoparticles against multidrug-resistant bacteria. World J of Microbiology & Biotechnol; 26: 615-621.

51. Ruparelia JP, Chatterijee AK, Duttagupta SP, Mukherji S (2008) Strain specificity in antimicrobial activity of silver and copper nanoparticles. Acta Biomater 4: 707-716.

52. Yoon KY, Hoon BJ, Park JH, Hwang J (2007) Susceptibility constants of Escherichia coli and Bacillus subtilis to silver and copper nanoparticles. Sci Total Environ 373: 572-575.

53. Martinez LR, Han G, Chacko M, Mihu MR, Jacobson M, et al. (2009) Antimicrobial and healing efficacy of sustained release nitric oxide nanoparticles against Staphylococcus aureus skin infection. J Invest Dermatol 129: 2463-2469.

54. Fettal E, Youssef M, Couvreur P, Andremont A (1989) Treatment of experimental salmonellosis in mice with ampicillin-bound nanoparticles. Antimicrob. Agents Chemother 33: 1540-1543.

55. Pandey R, Khuller GK (2005) Solid lipid particle-based inhalable sustained drug delivery system against experimental tuberculosis. Tuberc 85: 227-234.

56. Ma M, Cheng Y, Xu Z, Xu P, Qu H, et al. (2007) Evaluation of polyamidoamine (PAMAM) dendrimers as drug carriers of antibacterial drugs using Sulfamethoxazole (SMZ) as a model drug. Eur J Med Chem 42: 93-98.

57. Onyeji CO, Nightingale CH, Marangos MN (1994) Enhanced killing of methicillin-resistant Staphylococcus aureus in human macrophages by liposome-entrapped vancomycin and teicoplanin. Infection 22: 338-342.

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