



Review of Antibiotic Therapy Recommended for Sepsis Patients

Sarita Jangra Bhyan^{1*}, Dr. Ajay kumar², Abhishek Jain³, Divyanshi Rastogi³, Gourav Jain³, Raju singh³

1. Assistant Professor, Department of Pharmacy Practice, Teerthanker Mahaveer College of Pharmacy, TMU, Moradabad, UP, India.
2. Professor, Department of General Medicine, Teerthanker Mahaveer Medical College & Research Centre, TMU, Moradabad, UP, India.
3. Pharm D 5th Year, Department of Pharmacy Practice, Teerthanker Mahaveer College of Pharmacy, TMU, Moradabad, UP, India.

*Corresponding author's E-mail: sarita28787@gmail.com

Received: 03-09-2020; Revised: 21-11-2020; Accepted: 28-11-2020; Published on: 15-12-2020.

ABSTRACT

Sepsis is the life-threatening bloodstream infection caused by bacteria. With the use of antibiotics the mortality rate decreases. The objective of this review is to enhance the performance of the healthcare professionals. To preserve the antibiotic agents for future patients through appropriate antibiotic therapy. Broad spectrum antibiotics are active against all the microorganisms. The chances of mortality rate decrease with appropriate use of antibiotics. Antibiotic should be administered within the first hour after recognition of sepsis and septic shock. Studies have shown that any delay in initiation of therapy increases the risk of mortality. The drug must be given after considering patients factor, pathogen, resistance pattern, suspected source of infection.

Keywords: Bloodstream infection, sepsis, empiric antibiotic, gram positive, gram negative bacteria.

QUICK RESPONSE CODE →

DOI:
10.47583/ijpsrr.2020.v65i02.002



DOI link: <http://dx.doi.org/10.47583/ijpsrr.2020.v65i02.002>

DESCRIPTION OF THE CONDITION

Sepsis is a life threatening bloodstream infection caused by bacteria. Sepsis is defined as an acute organ dysfunction caused by a dysregulated host response to infection, with two or more suspected infection of: Hypotension (systolic pressure <100 mm Hg), Altered mental status (score < 14), Tachypnea (respiratory rate > 22 breaths / min).¹

Septic shock is defined as, sepsis induced with hypotension (>65mmHg) or serum lactate level exceeding 2mmol /L after adequate fluid reuscitation.

Every year there are around 3.15 million of cases of sepsis worldwide.² Sepsis is analysed by two criterias qSOFA and MODS.

quick Sequential Organ Failure assessment allows bedside analysis of patients, which includes systolic blood pressure of 100mmhg and respiratory rate of 22breaths /min³

Multiple Organ Dysfunction Failure shows the end stage condition of patients with organ dysfunction.

INTRODUCTION

Infectious microorganisms invade in humans and damage human tissues by their own or by their toxins. Antibiotics are used to treat these infections. Antibiotics has two

effects, bactericidal effect or bacteriostatic effect. Bactericidal antibiotics work by inhibiting the growth of microorganism whereas bacteriostatic antibiotics work by killing microorganism. Antibiotics targets nucleic acids synthesis, biological metabolic compound synthesis, protein synthesis, cell wall and cell membrane.⁵

Principles of Antibiotics

- Prophylactic

The prophylactic measure is used to prevent the chances of an infection.

- Preemptive

The pre-emptive measure is used to abort the infection.

- Empiric

The empiric measure is used in the absence of knowledge of its etiology to control the infection.

- Definitive

The definitive measure is used when the etiology is known, to cure the infection.^{6,7}

Classification of Antibiotics

- Penicillins
- Cephalosporins
- Vancomycin
- Aminoglycoside
- Tetracyclines
- Macrolides
- Linezolid
- Fluoroquinolones⁸



Impact of inappropriate use of Antibiotics

1. Poor Patient outcome i.e. antibiotic resistance, organ toxicity, increased mortality, adverse drug reactions, superinfections.

2. Excess costs i.e. prolonged hospital stays, drug acquisition costs.^{9,10}

The treatment of sepsis, septic shock requires an appropriate diagnosis measure, ventilator support and an accurate antibiotic therapy.

Antibiotic therapy is very successful against the bacterial infections, as they inhibit the growth or kill the microorganism. Antibiotic therapy is the life saving therapy for patients with sepsis and septic shock.¹¹

Antibiotics are the most commonly prescribed drugs in today's era. Almost 30% of in-patients receive antibiotic therapy.¹²

Administration of an empiric antibiotic therapy within the first few hours of sepsis recognition is recommended by current guidelines. These guidelines suggests early administration of antibiotic therapy should be broad spectrum antibiotics, because inappropriate use of antibiotics increase the chances of mortality of ill patients.⁶

General Principles for antibiotic therapy

Right Time:

Antibiotic must be initiated within the first hour after recognition of sepsis, as it increases the chances of survival of the patient. The chances of progression of severe sepsis to septic shock will be decreased.^{13, 14, 15}

Right antibiotic:

Right antibiotic therapy is important because inappropriate therapy increases the risk of resistance, failure of treatment^{16,17}. Antibiotic therapy is selected on the basis of organism(s) infecting and considering patient's factors.

Individual patient factors helps in identifying the risk progression of death and improvement. Individual patient

may have other co morbidities (renal disease, liver disease, etc) also which may affect drugs pharmacokinetics and pharmacodynamics parameters.

Infecting bacteria are of different types i.e. gram positive, gram negative, pseudomonas, etc. Patient could be affected either by gram positive, gram negative or pseudomonas.

Any patient full filling the criteria of sepsis and septic shock are treated with the broad spectrum antibiotic therapy.

Selected drugs must have adequate: pharmacokinetic and pharmacodynamic properties, have adequate tissue penetration activity at the suspected source of infection. However, some patients are resist with the drugs, their antibiotic regimen is selected on the basis of known resistant pathogens community.¹⁸⁻²¹

Multiple drug therapy and combination drug therapy:

Combination drug therapy increases the chances of initial therapy, as it covers larger area of infection. The therapy is suggested for the patients with septic shock.

Whereas multiple drug therapy includes multi drugs with different mechanisms, multiple drugs have high probability of killing the growth of the pathogen or inhibiting the growth of the pathogen.^{6, 22-24}

Table 1: Chosen Antibiotics and their Coverage.

	Gram +	Gram -
Vancomycin	X	
Ciprofloxacin	X	X
Meropenem	X	X
Linezolid	X	
Ceftriaxone	X	X
Piperacillin-tazobactam	X	X
Levofloxacin	X	X
Metronidazole		X

Pharmacodynamics of Different Antibiotics (Hydrophilic and Lipophilic)

Antibiotic class	Distribution volume	Plasma T/2	Vd increases with fluid changes?	TDM required?
Aminoglycosides	0.2 – 0.3	2-3	Yes	Yes
Linezolid	0.5 – 0.6	3.5 – 7	Yes	No
Meropenem	Variable	1	Yes	No

Pharmacokinetic of Different Antibiotics

Antibiotic class	Distribution volume	Plasma T/2	Normal Dose	Protein binding
Livofloxacin	0.92 – 1.36	6 – 8.9	500- 700mg	24 – 38%
Ciprofloxacin	1.2 – 2.7	2(4-5 h in elders)	400mg IV 8h	20- 40%



Right Dose:

Right dose means, dosage of antibiotics with accurate pharmacokinetic and pharmacodynamic properties. Broad spectrum antibiotics are effective against almost all the pathogens, so the presence of antibiotics at the site of infection should be sufficient for effective response. Therapeutic drug monitoring of antibiotics are necessary as it ensures its efficacy. Not every antibiotic have same PK and PD characteristics. There are lipid soluble antibiotics and water soluble antibiotics (Pharmacokinetics). As well as there are antibiotics which are either dose dependent or time dependent(pharmacodynamics).

In case of severe infection, concentration of antibiotic is affected by- Organ dysfunction, hypoproteinemia, tissue hypoperfusion.²⁵

Right Administration:**Oral and Parental**

Usually parental administration is suggested for severe sepsis. Intravenous route of administration is very convenient for unconscious patients as they are infused directly into the blood stream and are readily absorbed by the tissues, IV route is also safer for the patients who cannot take therapy orally.

Advantage: Review of the treatment can be done on the regular basis.

In the past, the bioavailability of the oral antibiotic drugs was poor. Now-a-days, various oral agents with proper penetration activity are available. Various studies have shown that these oral agents are as effective as those parental agents.

Advantage: The length of hospital stay is shorter and is cost effective²⁶

Duration of therapy:

Duration of antibiotic drug therapy varies with patients response to the treatment, severity of illness and site of infection.

SSC guidelines recommended a standard therapy of 7-10 days. Patients with rapid resolution of symptoms should be given therapy for shorter duration^{6, 25, 26}

Chances of resistance increases with longer duration of antibiotic therapy.

DISCUSSION

After studying various articles it has been observed that, antibiotic treatment should be initiated as soon as possible for both sepsis and septic shock as the development of sepsis to septic shock increases every hour. (Surviving Sepsis Campaign). The antibiotics are selected after considering patients factors, suspected pathogens. The drugs which covers both gram positive bacteria and gram negative bacteria should be given at the initiation of the therapy.

CONCLUSION

Broad spectrum antibiotic therapy is important as it covers all the pathogenic organisms and must be administered within the first hour after recognition of sepsis and septic shock. Studies have shown that any delay in the initiation of therapy increases the risk of mortality. The drug must be given after considering patient factors, suspected pathogen, resistance pattern, suspected source of infection.

REFERENCES

1. Mohanty L, Sahoo D, Panda S S, Patro S, Study of a prescribing pattern of empirical antibiotics in patients with sepsis in a tertiary care hospital of Eastern India, *PlumxMetrics*,11,2016,2039-2045. Doi:<https://ijmrr.medresearch.in/index.php/ijmrr/article/view/756/1367>.
2. Fleischmann C, Scherag A, Adhikari NK, Assessment of Global Incidence and Mortality of Hospital-Treated Sepsis: Current estimates and limitations. *American Journal of Respiratory and Critical Care Medicine*, 193(3), 2015, 259–272. Doi: <https://www.atsjournals.org/doi/10.1164/rccm.201504-0781OC>.
3. M S-H, Phillips, GS, ML L, Seymour CE. Liu VX, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock, *JAMA*,315(8),2016,775-787. Doi: 10.1001/jama.2016.0287; PMID:26903338.
4. Singer M, Deutscham CS, Seymour CW, Shankar HM, Annane D, V B M, et al, The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis – 3): *JAMA*, 315(8),2016,801-810. Doi:10.1001/jama.2016.0287 ; PMID:26903338.
5. Kirmusaoğlu S, Gareayaghi N, Kocazeybek BS, Introductory Chapter, The Action Mechanisms of Antibiotics and Antibiotic Resistance. 2019. Doi:10.5772/intechopen.85211.
6. Rhodes A, Evans LE, Alhazzani W, Surviving Sepsis Campaign, International Guidelines for Management of Sepsis and Septic Shock, *Intensive Care Med*, 43,2017,034- 377. Doi:10.1007/s00134-017-4683-6.
7. Dellinger RP, Schorr CA, Levy MM, A users' guide to the 2016 Surviving Sepsis Guidelines, *Intensive Care Med*,43,2017,299-303.Doi:10.1007/s00134-017-4681-8.
8. Paterson DL, Rice LB, Empirical antibiotic choice for the seriously ill patient: are minimization of selection of resistant organisms and maximization of individual outcome mutually exclusive, *Clin Infect Dis*,36,2003,1006-12.Doi: <https://doi.org/10.1086/374243>.
9. Deresinski S, Principles of antibiotic therapy in severe infections: optimizing the therapeutic approach by use of laboratory and clinical data. *Clin Infect Dis*,45,2007,5177-83.Doi:10.1086/519472.
10. Dupont H, Mentec H, Sollet JP, Bleichner G, Impact of appropriateness of initial antibiotic therapy on the outcome of ventilator-associated pneumonia, *Intensive Care Med*,27,2001,355–262.Doi: 10.1007/s001340000640.
11. Ibrahim EH, Sherman G, Ward S, The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting, *Chest*, 118,2000,146–155.Doi:10.1378/chest.118.1.146.
12. Kuti EL, Patel AA, Coleman CI, Impact of inappropriate antibiotic therapy on mortality in patients with ventilator-associated pneumonia and blood stream infection: A



- metaanalysis, J Crit Care,23,2008,91–100.Doi: 10.1016/j.jcrc.2007.08.007.
13. Kumar A, Ellis P, Arabi Y, et al, Initiation of inappropriate antimicrobial therapy results in a fivefold reduction of survival in human septic shock, Chest, 136,2009,1237–1248.Doi:10.1378/chest.09-0087.
14. Kumar A, Optimizing antimicrobial therapy in sepsis and septic shock, Crit Care Clin,25,2009,733–751.Doi: 10.1016/j.ccc.2009.08.004.
15. Craig WA, Pharmacokinetic/pharmacodynamic parameters: Rationale for antibacterial dosing of mice and men, Clin Infect Dis,3,1998,1–10.Doi: 10.1086/516284.
16. Mueller EW, Hanes SD, Croce MA, Effect from multiple episodes of inadequate empiric antibiotic therapy for ventilator-associated pneumonia on morbidity and mortality among critically ill trauma patients, J Trauma,58,2005,94–101.Doi: 10.3390/antibiotics2030339.
17. Luna CM, Vujacich P, Niederman MS, et al Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia, Chest,111,1997,676–685.Doi:10.1378/chest.111.3.676; PMID: 9118708.
18. Micek ST, Welch EC, Khan J, Empiric combination antibiotic therapy is associated with improved outcome against sepsis due to gram-negative bacteria: A retrospective analysis, Antimicrob Agents Chemother,54,2010,1742–1748.Doi:10.1128/AAC.01365-09; PMID:20160050.
19. Mouton JW, Combination therapy as a tool to prevent emergence of bacterial resistance, Infection,27,1999,524–528.Doi: 10.1007/BF02561666; PMID:10885823.
20. Klastersky J, Zinner SH. Synergistic combinations of anti- biotics in gram-negative bacillary infections, Rev Infect Dis,4,1982,294–30. Doi:10.1093/clinids/4.2.294; PMID:7051232.
21. Kumar A, Safdar N, Kethireddy S, Chateau DA survival benefit of combination antibiotic therapy for serious infections associated with sepsis and septic shock is contingent only on the risk of death: A meta-analytic/meta-regression study, Crit Care Med,38,2010,1651–1664. Doi:10.1097/CCM.0b013e3181e96b91; PMID:20562695.
22. Kalil AC, Metersky ML, Klompas M, Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society, Clin Infect Dis,63,2016,e61–e111.Doi: <https://www.thoracic.org/statements/resources/tb-opi/hap-vap-guidelines-2016.pdf>.
23. Angus DC, H MP, Poll TV, Severe Sepsis And Septic Shock: Critical care medicine, N Engl J Med,369,2013,840-51. Doi:10.1056/NEJMra1208623.
24. Zhou X, Su LX, Zhang JH, Liu DW, Long Y, Rules of Anti-infection Therapy for Sepsis and Septic Shock, Chinese Medical Journal, 132(5), 2019, 589-96. Doi: 10.1097/CM9.000000000000101; PMID: 30807357.
25. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al, Surviving Sepsis Campaign Guidelines for Mngement of Severe Sepsis and Septic Shock, Crit Care Med,32,2004,858–73. Doi: 10.1097/01.ccm.0000117317.18092.e4; PMID: 15090974.
26. Levy MM, Evans LE, Rhodes A, The Surviving Sepsis Campaign Bundle, Crit Care Med,46,2018,997–1000.Doi: 10.1007/s00134-018-5085-0; PMID:29675566.

Source of Support: None declared.

Conflict of Interest: None declared.

For any question relates to this article, please reach us at: editor@globalresearchonline.net

New manuscripts for publication can be submitted at: submit@globalresearchonline.net and submit_ijpsrr@rediffmail.com

