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Management of Patients with Infections Associated with Cancer Treatment

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ABSTRACT

The paper reviews the Management of Patients with Infections Associated with Cancer Treatment with either prostate, lung or breast cancer. The research approach is based on comparative analysis, observational methods and analytical approach. The sample size is based on 25 men and 25 women in all who have received chemotherapy with or without radiation therapy. Findings are based on patient's data available for the study of interest at this research centre within the last ten years who were diagnosed with either parasitic, fungal or viral bacterial infection with intermediate to low intensity during the period of treatment.

Introduction

Infections are a major complication in patients having a malignant disease. Various factors have been an influence on the cause of infections in increasing patient cancer population. Local factors include a tumour, certain deficiencies in the host defence mechanisms, defects in the host defence mechanism following the cancer chemotherapy, and specific malignant processes. Neutropenia is probably the most important factor that is predisposed to infection in cancer patients. Such patients are required to be treated with a prompt and broad-range antibiotic therapy in conditions where fever starts to develop. At present, the majority of the patient population is said to have suffered from infections that are caused by *gram-negative bacilli* and the rate of cure in these patients ranges in between 65 to 75 per cent. The most extrapolating and analytical factor involves whether or not the count of neutrophils recovers during infection. The likelihood of occurrence of fungal infections is comparable in higher frequency in neutropenic patients where an unknown origin of fevers is often presented among these patients.

In the recent practices, neutropenic patients are provided with antifungal agents as empiric therapy if the fever persists and if the response to antibacterial antibiotics fails. Diminution of the persisting malignant disease is the most critical element of recovery from fungal infection [1]. From previous literature, it is identified that infection is a major cause or risk factor that influences the rate of mortality and morbidity. The determination of risk is characterised by the type of cancer and the period and intensity of immunosuppressive chemotherapy. It is essential to identify the risks by determining both qualitative and quantitative immune defects and particular pathogens as the perspective of history, laboratory and radiological data and physical examination. Majority of the cancer patients with neutropenic fever have an occurred or established infection, but bacteremia is observed in a quarter of the patients. Following the procedure of chemotherapy, the clinical signs may be limited or constrained to only fever. It is essential to determine the important factors or symptoms of infection, that might be completely absent

or not apparent as a cause of immunosuppression in the clinical setting of febrile neutropenia. Therefore, in empiric therapy, prompt initiation of antibiotic is specified due to the prospective risk towards the development of severe sepsis [2].

Moreover, in other studies, the emphasis is diverted on other consequences of chemotherapy. It is identified that lung infections can be severe consequences of the chemotherapy-induced immune defects. Also, Aetiological causes of infections contain virus *(respiratory syncytial virus, parainfluenza virus, influenza virus A and B, and cytomegalovirus)*, fungi (*Aspergillus*, Fusarium, and *Mucorales species*, and *Pneumocystis jirovecii*), and Bacteria (*Pseudomonas aeruginosa, Stenotrophomonas maltophilia, and Nocardia species*). In the majority of the cases, it is identified that bacteria (specifically *Gram-negative*) is the main cause of infections. However, the virus is also recognised as an increasing factor in today's patient population. Treatment for patients specifically with fungal infections is most of the time unproductive, and the diagnosis is more time taking and problematic. It is suggested that the probable cure for cancer could be the anticancer drugs having minimal side effects on the immune system of a person [3].

Study Protocol

The individual study will be based on assessing male and female patients having prostate or breast cancer who have received Platinums or Taxanes in their history of chemotherapy and have also been diagnosed with vital bacterial or fungal infections during the course of chemotherapy. The fact will be verified whether calculated dose reduction or suspension for patients who experience a range of microbial infections leads to a decrease in disease of the patient, and if such patients face a risk of metastases. The sample size of the study will be based on picking up 25 men and 25 women randomly in the research centre whose last ten years data is available for the review of interest. Patients having prostate, lung or breast cancer who have received chemotherapy with or without radiation therapy will be considered, as well as patients with previous medical conditions will also be considered. The respondent will be a patient diagnosed with either, bacterial, fungal, viral or fungal infection with a low to intermediate intensity during the time of treatment. The respondent would have received prophylactic, ambulatory or oral therapy for the diseases. The respondents will be asked about the chemotherapy treatment and the risk of an increased rate of infections due to chemotherapy.

Moreover, the respondents will be asked about the side effects that are caused by the dose reduction and dose suspension in the patient. This procedure occurs once every three weeks. The patient receives the patient questionnaire once every three weeks because a complete treatment cycle is three weeks long. The data will be made available on the research site, this data will also be utilised to evaluate and determine the inclusive overall survival status and progressive survival status of the research subjects. Moreover, the data collection method will be unbiased. Data will be collected from both men and women equally, and the same analytical techniques will be used for both cohorts. The data will depict the results of all the patients who have previously received the treatment for cancer at the research centre for the last ten years. Methods of data collection for both cohorts would be equally implemented.

The protection of patient's demographics and other information will be kept protected. It will be made sure that the analyses, collection and publication of the collected data keep the patient's information secure. The protection of data collection will comply with the global data protection law of research subjects. The opportunistic infections of interest will be ear infections, lung infections, febrile neutropenia, skin infections, general immunodeficiency, viral and fungal infections, skin infections, and yeast infections but not limited to it. Also, the emphasis will be made on the following Diagnostic Methods to Determine Infection Load; Respiratory Sample Analyses, Blood Analyses (CBC, WBC, IG), Chest, Lung and Internal Organs at Risk Radiograph or CT Scan or MRI, Urinalysis, Creatinine analysis, Skin Biopsy of Suspected Areas, Treatment, Prevention and Infection Management will focus on the steps taken by the treatment centre to reduce the infectious disease load during the anticancer therapy; Empiric Therapy, Prophylaxis, Ambulatory Management; -Oral Therapy; Antibiotics, Antiviral, Antifungal and Antibacterial drugs, Hospitalization.

Inclusion and Exclusion Criteria

Data will be collected from the patients who are currently receiving or have received chemotherapy at the research centre within the past ten years only. For instance, the patients who have received or receiving treatment since 2008 will be included in the study. Patients with pre- existing medical conditions will be part of the sample. The results and findings of the study will also include patients who have been suffering from any previous medical conditions before their chemotherapy treatment. Also, patients must have received chemotherapy treatment either for breast, prostate or lung cancer with or without radiation therapy. The availability of the data will be inclusive of microscopic findings from blood culture, urine analysis and other suspected tissue analysis. Patients who have received or receiving chemotherapy at the research centre for more than ten years will not be included in the research criteria. For instance, patients who have received or are receiving chemotherapy before 2008 will not be part of the research criteria. In addition, patients must have been 18 years or older during the treatment period. In similar, those patients who have not received chemotherapy for either, prostate, and breast of lung cancer with or without radiation will be excluded from the research criteria. Patients whose data is not available to the requirements as mentioned above will not be part of the research criteria respectively.

General Research Questions

1. What is the major influence to the risk of microbial culture in patients who receive chemotherapy?
2. What are the most common side effects of chemotherapy?
3. How long does the side effects of chemotherapy last?
4. How vitamins affect chemotherapeutic drugs?
5. When should a patient call their cancer care team about the side effects from cancer therapy?
6. How do we successfully manage the side effects of chemotherapy?
7. What are the causes of fungal infection?
8. Why is fungal infection the most common infection among patients who receive chemotherapy?
9. What are the signs and symptoms of infections?
10. What should be the immediate aspects of diagnosis in infections caused by chemotherapy?

Sample Size

The total sample size for the collection of data is 50. Respondents are equally distributed on the basis of gender. 25 men and 25 women are selected to test the findings of the research questions. The sample size is kept small and precise as it is easy to evaluate the data and results. There is a likelihood that the chances of errors are reduced in small sample size and the results of the study are based on more accurate findings. Also, the sample size is kept low as it is easily managed and less time-consuming in comparison with a large sample size. In addition to these elements, most important subjects will relate to these statistics. The reason to choose a small sample size is that the criteria of the research are exact and statistical tests will be developed on the basis of samples and not the whole population. Large specimens are available in a survey model, but it consumes more time as the researcher has to draw subsamples before performing the statistical tests randomly. As this is a prospective study, it is necessary to collect only what is needed in specific.

An Overview of Previous Research Papers and Regulatory State of the Art

It has been observed from the available studies that the rate of mortality and morbidity has been increasing at a constant pace for a few years. However, the management process to improve these complications has been rapidly enhanced to overcome the fatality caused from cancer and its treatment specifically in the area of bacterial infection. Previous studies depict that nearly 800 acknowledged bacteraemias were observed in eight trails of therapy (I, II, III, IV, V, VI, VII, and VIII). The therapeutic session was performed by the International Antimicrobial Therapy Group of the European Organisation for Research and Treatment of Cancer (EORTCIATG) from 1978 to 1994. It was observed that the mortality rate of overall cancer patients declined from 21 percent to 7 percent. It was noted that the 30-day rate of mortality from an undefined cause in patients suffering from Gram-negative and Gram-positive bacteraemia reduced from 10 percent to 6 percent in all. The statistics depict an enormous improvement in the management of infection in cancer patients as compared to the previous classical studies that covered Gram-negative bacteraemias where the mortality rate rose to 90 percent in 1962.

However, the reasons behind the improvements in managing infections in cancer patients are multiple. The strategy to seek for the prompt organisation of *empirical, broad-spectrum* antibacterial therapy in overcoming the development of neutropenic fever has undoubtedly played a vital role in the management of infections in cancer patients.

Since the initiation of the EORTC-IATG, the organisation has worked commendably in setting the track record that is followed by a series of excellent articles published by various authors in various renowned scientific journals in the department of clinical research for the management of infectious complications in cancer patients. A standard has been set for managing Febrile Neutropenia in cancer patients according to the trials conducted by EORTC- IATG. However, it is argued that various problems are still pertinent to the improvement of anti- infective care of cancer patients and the issues still lack settlement [4]. However, in another research, it was suggested that the diagnosis of immunosuppressed patients have rapidly increased in recent years. Patient's diagnosis has made it evident that unusual yeasts are the cause of fungal infections in cancer patients. In a prospective study of 95 adult cancer patients having acute lymphoblastic leukaemia, 30 cases of fungal infections were diagnosed among a series of 190 episodes of febrile neutropenia. It is suggested that combination therapy is best suited to treat patients with cryptococcal meningitis; however, its use in the invasive fungal infections is not bright enough to conclude. In the case of a fungal infection (*candida endocarditis*), it is recommended that combination therapy is the best fit for the management of diseases in cancer patients. Although not enough data is present to find out the emerging opportunistic yeast infections, combination therapy in the referred case is recommended as salvage therapy [5].

Moreover, from the previous studies, evidence has been drawn to identify the factors of treatment that cause skin infections in cancer patients. It is found that patients who are treated with epidermal growth factor receptor inhibitors (EGFRIs) are more prone to dermatological toxic effects. However, the impact of the subjected effects on EGFRI dosing and the quality of life is described, but the effect of these effects on the physical health of a cancer patient has not been determined. At Kinases clinic, 221 patients were identified who

caught infections due to the treatment in the eye and skin reactions to inhibitors of EGFIR. Results were reviewed from a histopathologic assessment of biopsy samples, immunohistochemical staining of specimens of skin for viral pathogens and bacterial cultures extracted from the medical records of the patients. Fisher's exact test was applied in the study to determine the relationship between the demographics of the patient, the development of infections and characteristics of the treatment. It was evident from the results that 34 percent caught infections as a cause of dermatological toxic effects. 22.6 percent of the 221 patients had cultures positive for *Staphylococcus aureus*, and 5.4 percent of the 221 patients were observed as culture positive for methicillin-resistant *S aureus*. It was concluded from the findings of the study that patients who go through toxic dermatological treatment with EGFRI, are more prone to catching cutaneous infections. The possibility of bacterial infections due to the effects of dermatological toxic effects specifically with leukopenic patients is at greater risk [6]. The results of the above studies will be helpful in identifying the suitable therapies and causes of infections in cancer patients. It will be easier to determine the approach to be taken for effective management of infections in cancer patients.

Antibiotics, Antimicrobial Resistance and its Relation with Chemotherapy

The concept of antimicrobial resistance is a global phenomenon, depicting a public health challenge that has significantly accelerated due to antibiotics overuse. With the increased prevalence of antimicrobial resistance risks for infections, other health complications increased mortality rate and longer hospital stays. It has been determined that overprescribing in antibiotics is directly interrelated with the increased rates in risk for adverse effects, medicalization in conditions of self-limiting conditions, and frequent re-attendance [7]. Over prescription of antibiotics is amongst of the prominent issues in primary care, increasing the prevalence of most infections. Moreover, nearly 90% of entire antibiotic prescriptions are being issued by the general practitioners. However, respiratory tract infections remain the leading cause for prescribing [8]. The instruction of multifaceted interventions is accounted to show beneficial results by reducing the antibiotics overuse. Many researchers have debated that necessary interventions should be taken for encompassing the policy enforcement for prohibition of the antibiotics over- the-counter sale of, utilization of the antimicrobial stewardship approaches, clinicians active participation, incorporation of valid rapid point-of-care tests, implicit strategies for antibiotic prescription, use of informational aids for increasing communication skills in patients and finally the incorporation of the more pragmatic studies in order to accomplish primary care outcomes for the best interests of patient's long term health goals [9].

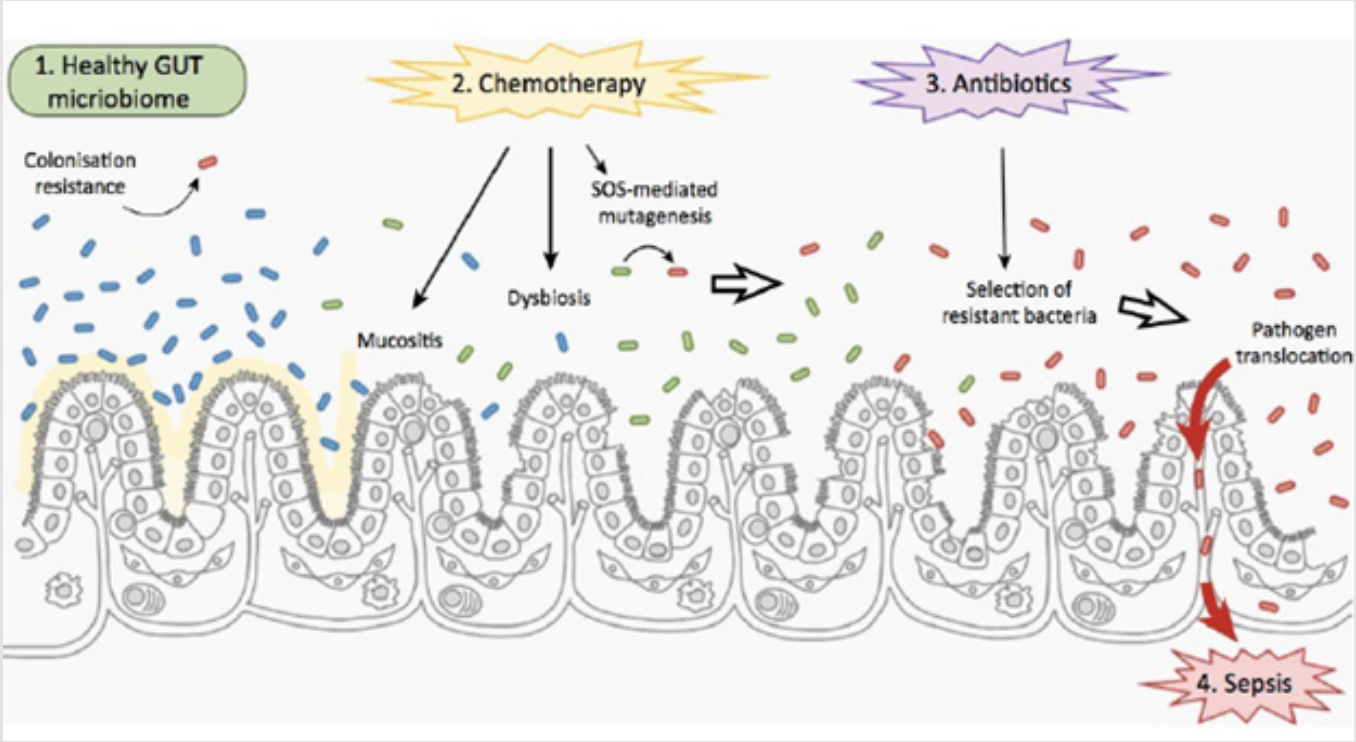


Figure 1: LeMieux, [27] Antibiotic-Resistance.

Chemotherapy and Antimicrobial Resistance

Cancer is amongst the leading cause of death on a global platform. However, one of the prominent factors which result in an increased mortality rate due to cancer is related to chemotherapy and the possible risks which are associated with chemotherapy. For most patients undergoing chemotherapy, the risk of bacterial infections is predominately higher mainly due to antibiotics, antimicrobial resistance [10]. Several researchers have presented that one of the forefront effects of chemotherapy includes the development of antibiotic resistant bacteria in the intestine of cancer patients. The bacteria further multiples and leak in the bloodstream due to the impaired gut lining. This, in turn, results in the development of antibiotic resistant bacteria, affecting the entire body an individual trough infected blood. It has been determined that the growth of antibiotic resistant bacteria is incredibly dangerous, which could potentially cause deadly [11]. A healthy intestine comprises of numerous bacteria (the microbiome), that are contributing integral roles in the maintenance of gut health, these bacteria are known as "commensal", no harm is caused to the body as long as these bacteria are present in the intestine. Additionally, these are involved in protecting the intestine from pathogenic bacteria (harmful bacteria) [12]. An abnormality arises when the system gets perturbed due to chemotherapy in cancer patients.

Initially, the intestinal wall is damaged by chemotherapy, termed as mucositis (as described in (Figure 1)). This further leads into the loss of cells and inflammation from the gut lining.

When this happens, the natural barrier that keeps the bacteria contained is broken down increasing the chance that bacteria slip through and enter the bloodstream. The effects of chemotherapy are devastating as it is toxic for the body cells and bacteria, which is one of the reasons why chemotherapy is more effective in cancer treatment. The chemotherapy activates the SOS response of the SOS response, resulting in the increase of DNA mutations (that is more bacterial mutants are present) [13]. Moreover, these increased new mutants have a probable property of straining bacteria making them antibiotic resistant. Additionally, the increased rate of antibiotic resistant bacteria due to chemotherapy can also cause bacteria to exchange their resistance property amongst each other, making the entire population of bacteria to become antibiotic resistant.

By making the whole population of bacteria into antibiotic resistant, it can be stated that chemotherapy is damaging the inner intestinal lining, also increasing the total number of antibiotic resistant bacteria present. Many researchers have proof that the options available for breaking or handling this cycle are relatively limited. Whereas, the primary consideration will be aimed at restoring the normal gut flora, as it has been deliberating as an effective approach for the treatment of "*Clostridium dificile infections*", where transplantation of normal fecal flora can be performed in patients. However, many researchers have provided that probiotic supplements are being studied to overcome the negative effects of chemotherapy, though presently there are barely any successful therapies for protecting the patients from receiving chemotherapy [14]. On the basis of this explanation, it can be stated that human bodies typically comprises of a network of interactions interconnected with one another. Hence ramification in one system affects the othersystems. Through developing an innate understanding of how these systems are interacting and interconnected, researchers will be able to identify innovative remedies in contrast with chemotherapy.

It has been identified that antibiotics are those medicines which are used for preventing as well as and treating the bacterial infections. Whereas the phenomena of antibiotic resistance occur in the case where bacteria change in turn of its response against medicines. Bacteria, not humans or animals, become antibiotic-resistant. Further, these infected bacteria are infecting the normal living of humans beings. Also, the infections are comparatively harder to treat as compared to those infections which are caused by the non-resistant bacteria [15]. In addition to this, the antibiotic resistance which is leading towards higher medical costs increased mortality, and prolonged hospital stays. It has been determined that the world is in urgent need of changing its usual ways for prescribes along with its uses for antibiotics [16]. In cases where new medicines are being developed without behaviour change, it is expected that antibiotic resistance will be a relatively major threat. In consideration of this, behavior changes should be included for carrying out further studies and reducing the spread of infections by using vaccination, practising safer sex, good food hygiene, and hand washing. It has been identified that the prevalence of antibiotic resistance has raised higher levels globally. Therefore, innovative resistance mechanisms are spreading and emerging globally, as to overcome the exiting prevalence of the threatening ratio of antibiotic resistance and interference in common infectious diseases. Similarly, in countries

without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-used by the public [17].

Mechanism of Action of Antimicrobial Drugs

The antibacterial action is usually made up of four relative sub-mechanisms, which comprise of; firstly regulation or inhibition of enzymes within the cell wall biosynthesis; secondly, the nucleic acid repair metabolism; thirdly, protein synthesis and fourthly, the mechanism involved in the membrane structure. Additionally, most of these cellular functions are usually the targeted antibiotics which are the most active and highly involved in the multiplication of cells. Due to the overlapping of these functions amongst the eukaryotic mammalian cells and prokaryotic bacterial cells, many researchers have debated that most of these antibiotics have been identified to be highly useful in terms of anticancer agents [18]. Moreover, one

of the vital qualities of antimicrobial drug is its selective toxicity, deliberating that it selectively inhibits or kills the growth of its targeted microbe by causing no or minimal harm to the host. In addition to this, many antimicrobial drugs are presently provided for clinical use due to their antibacterial properties, as it has been identified that prokaryotic cell is providing a greater range of the unique targets to perform its selective toxicity, in contrast with the parasites, viruses, and fungi [19]. Furthermore, every antibacterial drugs class possess a distinctive mode of action, which depicts the way in which a particular drug is affecting the microbes on the cellular level. (Figures 2 & 3) describe a summarized overview of antibacterial drugs.

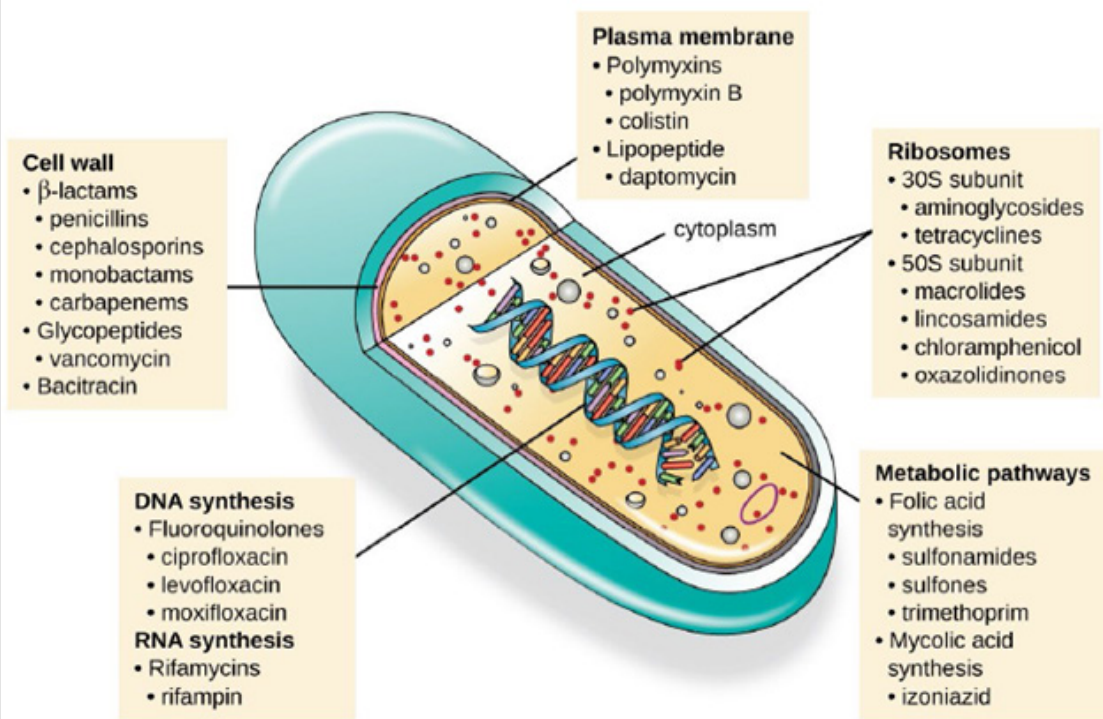


Figure 2: Antibacterial Compounds.

Mode of Action	Target	Drug Class
Inhibit cell wall biosynthesis	Penicillin-binding proteins	β-lactams: penicillins, cephalosporins, monobactams, carbapenems
	Peptidoglycan subunits	Glycopeptides
	Peptidoglycan subunit transport	Bacitracin
Inhibit biosynthesis of proteins	30S ribosomal subunit	Aminoglycosides, tetracyclines
	50S ribosomal subunit	Macrolides, lincosamides, chloramphenicol, oxazolidinones
Disrupt membranes	Lipopolysaccharide, inner and outer membranes	Polymyxin B, colistin, daptomycin
Inhibit nucleic acid synthesis	RNA	Rifamycin
	DNA	Fluoroquinolones
Antimetabolites	Folic acid synthesis enzyme	Sulfonamides, trimethoprim
	Mycolic acid synthesis enzyme	Isonicotinic acid hydrazide
Mycobacterial adenosine triphosphate (ATP) synthase inhibitor	Mycobacterial ATP synthase	Diarylquinoline

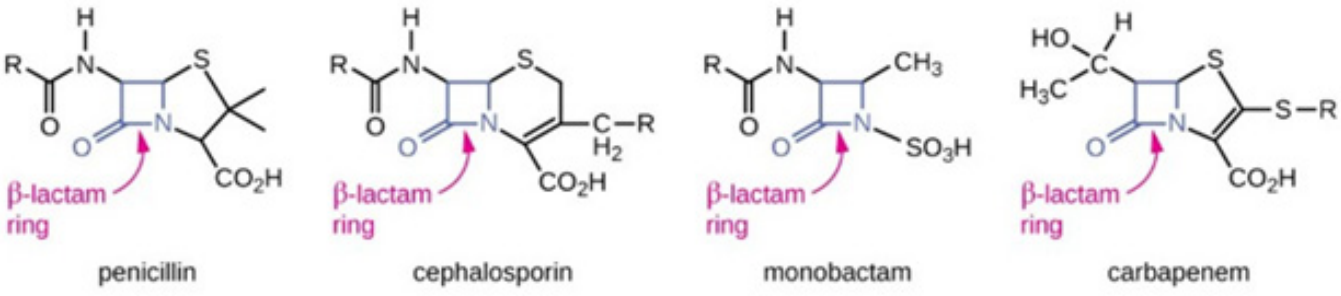
Figure 3: Common Antibacterial Drugs by Mode of Action.

Cell Wall Biosynthesis Inhibitors

There are multiple classes of antibacterial blocks which are taking part in the peptidoglycan biosynthesis; this makes cells relatively more susceptible towards osmotic lysis (as described in (Figure 4)). Hence, the antibacterials which are identified as the target cell wall in the process of biosynthesis are said to be bactericidal during their action. Furthermore, as the human cells are not making peptidoglycan, such mode of action has been deliberated as an excellent example for selective toxicity [20]. Additionally, the first discovered antibiotic was penicillin. Amongst several antibacterials which are termed as β-lactams, this group of molecular compounds is comprising of the penicillins, monobactams, carbapenems and cephalosporins [21]. Also, it is relatively characterized by the β-lactam ring presence which is depicted as the central drug molecule structure (as shown in (Figure 5)).

Mechanism of Action	Drug Class	Specific Drugs	Natural or Semisynthetic	Spectrum of Activity
Interact directly with PBPs and inhibit transpeptidase activity	Penicillins	Penicillin G, penicillin V	Natural	Narrow-spectrum against gram-positive and a few gram-negative bacteria
		Ampicillin, amoxicillin	Semisynthetic	Narrow-spectrum against gram-positive bacteria but with increased gram-negative spectrum
		Methicillin	Semisynthetic	Narrow-spectrum against gram-positive bacteria only, including strains producing penicillinase
	Cephalosporins	Cephalosporin C	Natural	Narrow-spectrum similar to penicillin but with increased gram-negative spectrum
		First-generation cephalosporins	Semisynthetic	Narrow-spectrum similar to cephalosporin C
		Second-generation cephalosporins	Semisynthetic	Narrow-spectrum but with increased gram-negative spectrum compared with first generation
		Third- and fourth-generation cephalosporins	Semisynthetic	Broad-spectrum against gram-positive and gram-negative bacteria, including some β-lactamase producers
		Fifth-generation cephalosporins	Semisynthetic	Broad-spectrum against gram-positive and gram-negative bacteria, including MRSA
	Monobactams	Aztreonam	Semisynthetic	Narrow-spectrum against gram-negative bacteria, including some β-lactamase producers
	Carbapenems	Imipenem, meropenem, doripenem	Semisynthetic	Broadest spectrum of the β-lactams against gram-positive and gram-negative bacteria, including many β-lactamase producers
Large molecules that bind to the peptide chain of peptidoglycan subunits, blocking transglycosylation and transpeptidation	Glycopeptides	Vancomycin	Natural	Narrow spectrum against gram-positive bacteria only, including multidrug-resistant strains
Block transport of peptidoglycan subunits across cytoplasmic membrane	Bacitracin	Bacitracin	Natural	Broad-spectrum against gram-positive and gram-negative bacteria

Figure 4: Drugs that Inhibit Bacterial Cell Wall Synthesis.



R group	$-CH_2-$	CH_2-O-	$-CH(NH_2)-$	$-CH(NH_2)-C_6H_4-OH$	CH_3O, CH_3O
Drug name	penicillin G	penicillin V	ampicillin	amoxicillin	methicillin
Spectrum of activity	G+ and a few G−	similar to penicillin G	G+ and more G− than penicillin	similar to ampicillin	G+ only, including β-lactamase producers
Route of administration	parenteral	oral	parenteral and oral	oral (better than ampicillin)	parenteral

Figure 5: Inhibitors of Cell Wall Biosynthesis.

Protein Biosynthesis Inhibitors

In animal cells (the 80S), cytoplasmic ribosomes are found comparatively and structurally distinct as compared to the bacterial cells (70S), which in turn makes the process of protein biosynthesis a suitable selective target that can be used by the antibacterial drugs [22]. Additionally, (Figure 6) describes multiple types of protein biosynthesis inhibitors discussed whereas (Figure 7) summarizes the protein synthesis inhibitors.

Membrane Function Inhibitors

For a better conceptualization, number (Figure 8) describes a small group of antibacterials that target the bacterial membrane along with their mode of action.

Nucleic Acid Synthesis Inhibitors

(Figure 9) describes a summarized overview of the certain antibacterial drugs which are working with nucleic acid synthesis inhibition.

Metabolic Pathways Inhibitors

(Figure 10) provides a brief description of few synthetic drugs which can control bacterial infections and are functioning in terms of competitive antimetabolites inhibitors against the bacterial metabolic enzymes. Additionally, the sulfa drugs (specifical sulfonamides) are considered as the oldest synthetic antibacterial agents, having "*structural analogues of para- aminobenzoic acid (PABA)*" [23], showing an early intermediate involvement in the folic acid synthesis (as described in (Figure 11)).

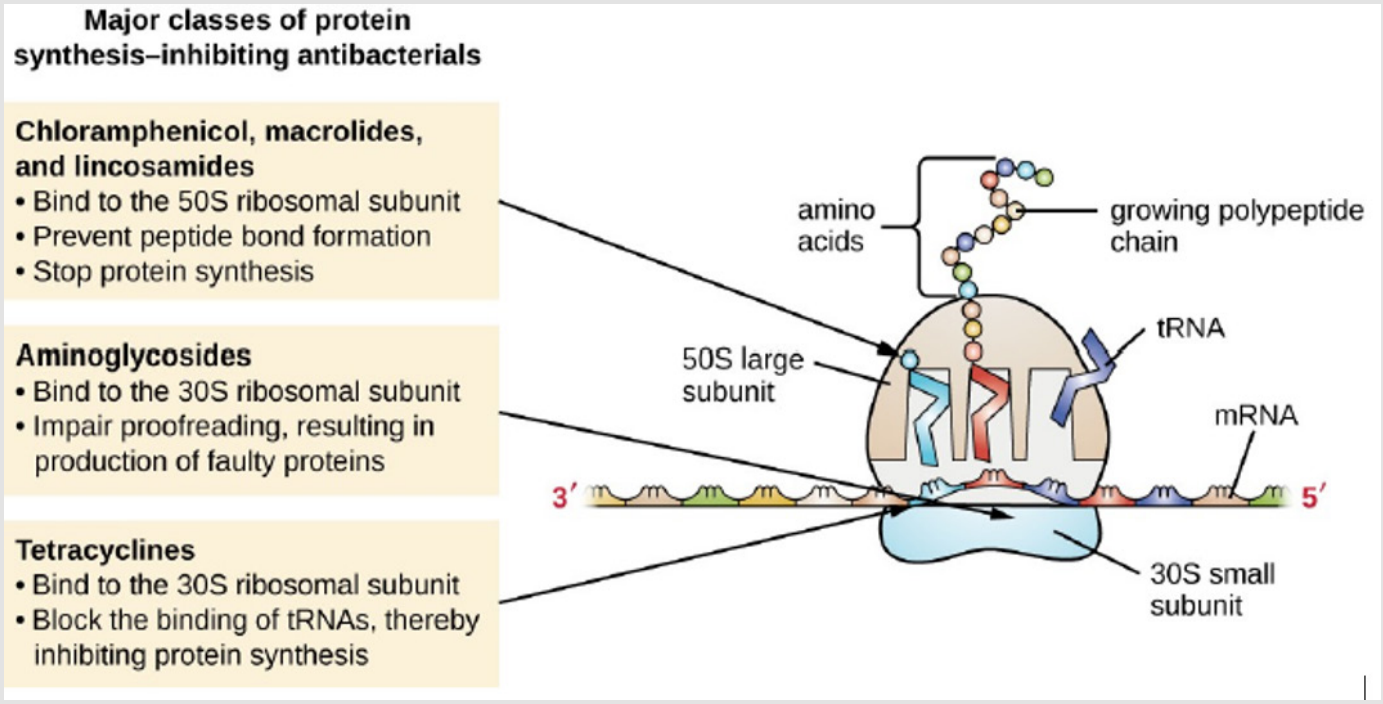


Figure 6: Multiple Types of Protein Biosynthesis Inhibitors.

Molecular Target	Mechanism of Action	Drug Class	Specific Drugs	Bacteriostatic or Bactericidal	Spectrum of Activity
30S subunit	Causes mismatches between codons and anticodons, leading to faulty proteins that insert into and disrupt cytoplasmic membrane	Aminoglycosides	Streptomycin, gentamicin, neomycin, kanamycin	Bactericidal	Broad spectrum
	Blocks association of tRNAs with ribosome	Tetracyclines	Tetracycline, doxycycline, tigecycline	Bacteriostatic	Broad spectrum
		Macrolides	Erythromycin, azithromycin, telithromycin	Bacteriostatic	Broad spectrum
50S subunit	Blocks peptide bond formation between amino acids	Lincosamides	Lincomycin, clindamycin	Bacteriostatic	Narrow spectrum
		Not applicable	Chloramphenicol	Bacteriostatic	Broad spectrum
	Interferes with the formation of the initiation complex between 50S and 30S subunits and other factors.	Oxazolidinones	Linezolid	Bacteriostatic	Broad spectrum

Figure 7: Drugs That Inhibit Bacterial Protein Synthesis.

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Mechanism of Action	Drug Class	Specific Drugs	Spectrum of Activity	Clinical Use
Interacts with lipopolysaccharide in the outer membrane of gram-negative bacteria, killing the cell through the eventual disruption of the outer membrane and cytoplasmic membrane	Polymyxins	Polymyxin B	Narrow spectrum against gram-negative bacteria, including multidrug-resistant strains	Topical preparations to prevent infections in wounds
		Polymyxin E (colistin)	Narrow spectrum against gram-negative bacteria, including multidrug-resistant strains	Oral dosing to decontaminate bowels to prevent infections in immunocompromised patients or patients undergoing invasive surgery/procedures.
				Intravenous dosing to treat serious systemic infections caused by multidrug-resistant pathogens
Inserts into the cytoplasmic membrane of gram-positive bacteria, disrupting the membrane and killing the cell	Lipopeptide	Daptomycin	Narrow spectrum against gram-positive bacteria, including multidrug-resistant strains	Complicated skin and skin-structure infections and bacteremia caused by gram-positive pathogens, including MRSA

Figure 8: Drugs That Inhibit Bacterial Membrane Function.

Mechanisms of Action	Drug Class	Specific Drugs	Spectrum of activity	Clinical Use
Inhibits bacterial RNA polymerase activity and blocks transcription, killing the cell	Rifamycin	Rifampin	Narrow spectrum with activity against gram-positive and limited numbers of gram-negative bacteria. Also active against *Mycobacterium tuberculosis*.	Combination therapy for treatment of tuberculosis
Inhibits the activity of DNA gyrase and blocks DNA replication, killing the cell	Fluoroquinolones	Ciprofloxacin, ofloxacin, moxifloxacin	Broad spectrum against gram-positive and gram-negative bacteria	Wide variety of skin and systemic infections

Figure 9: Drugs That Inhibit Bacterial Nucleic Acid Synthesis.

Metabolic Pathway Target	Mechanism of Action	Drug Class	Specific Drugs	Spectrum of Activity
Folic acid synthesis	Inhibits the enzyme involved in production of dihydrofolic acid	Sulfonamides	Sulfamethoxazole	Broad spectrum against gram-positive and gram-negative bacteria
		Sulfones	Dapsone	
	Inhibits the enzyme involved in the production of tetrahydrofolic acid	Not applicable	Trimethoprim	Broad spectrum against gram-positive and gram-negative bacteria
Mycolic acid synthesis	Interferes with the synthesis of mycolic acid	Not applicable	Isoniazid	Narrow spectrum against *Mycobacterium* spp., including *M. tuberculosis*

Figure 10: Antimetabolite Drugs.

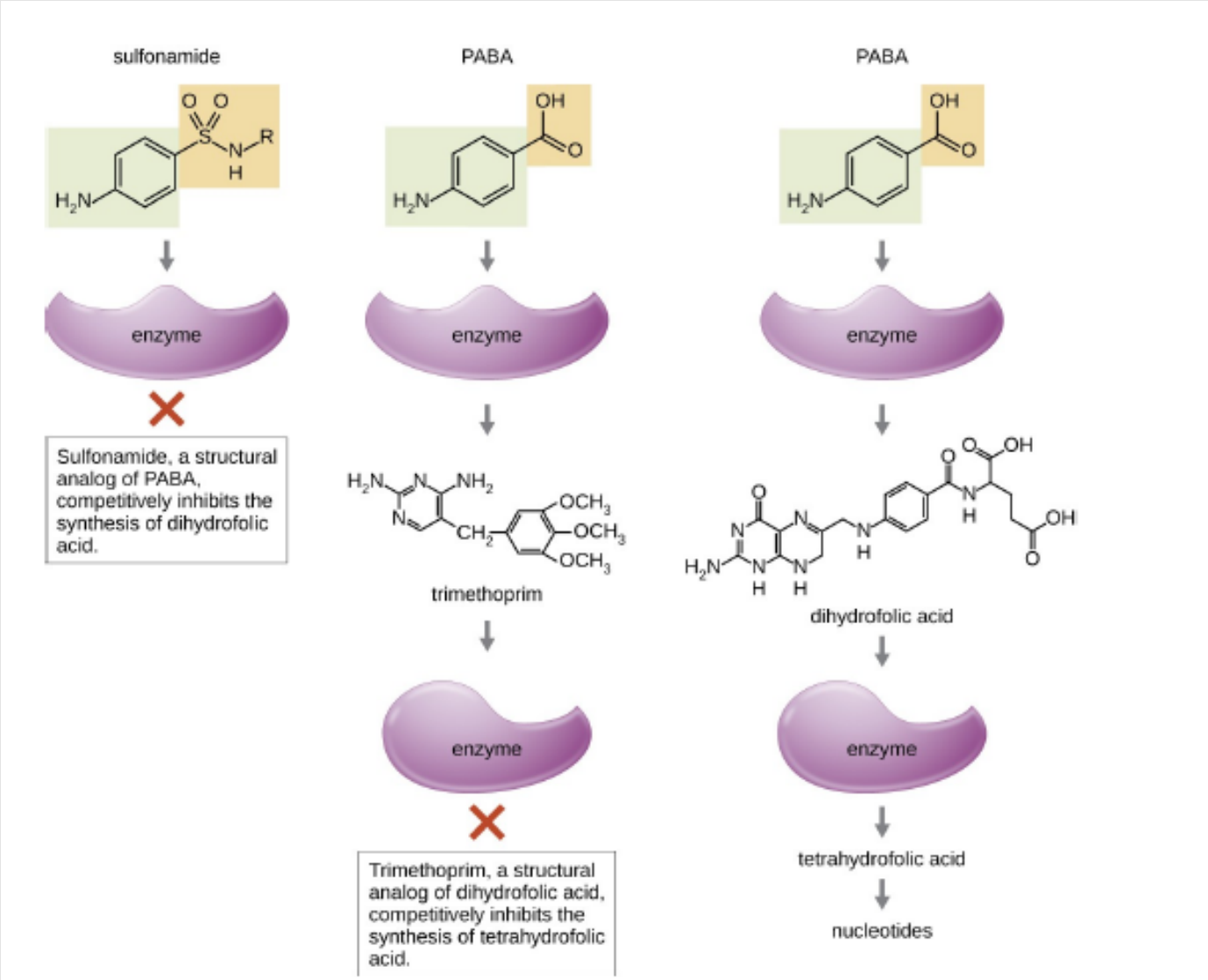

Figure 11: Sulfonamides and trimethoprim.

ATP Synthase Inhibitor

The "bedaquiline" has been represented as the synthetic antibacterial class in the diarylquinolones compounds which possess a unique mode of action that is specifically inhibiting the mycobacterial growth [24]. Devoid of of the fact that the specific mechanism is to be implicitly elucidated, the "diarylquinolones" compounds are interfering with the functioning of of ATP synthases, through interfering with the utilization of the hydrogen ion gradient that is used in ATP synthesis by means of carrying out the oxidative phosphorylation, which in turn further leads to reduced production of ATP [25]. Moreover, because of its apparent side effects, comprising of potentially lethal heart arrhythmia and hepatotoxicity, the uses of this compound are reserved for severe cases, predominately in most of the untreatable tuberculosis [26].

Innovative Techniques Involved in this Research

The following study has relatively used a unique approach to target one of the most common issues around the world related to the devastating effects of chemotherapy in cancer patients. By conducting a comparative analysis, this study will be able to target one of the crucial aspects in healthcare studies and explore such statistical information that has never been identified before [27-28]. This study will be embarking new research opportunities by utilizing observational methods and analytical approach in order to review the

aspects of chemotherapy in a diverse view. In addition to this, it has been determined that in comparison with the other studies that are carried out in the similar research area, this study possess a unique set of methodological approach which useful in obtaining those results which were not identified in the other studies. The uniqueness of this study can be determined from the fact that this study will be covering those elements in this research that are left undetermined in previous studies. The limitation which was identified in the previous studies is comparatively avoided in this research as to maintain authenticity and analyse crucial aspects. Moreover, with reference to the technicality of this research area, and the prevalence of the negative effects caused by the chemotherapy, this research is aiming to uncover those aspects which are barely touching or even discussed in the previous studies. The research has conducted a broad overview with multiple perceptions that is useful for future researches.

Conclusion

The research approach is based on comparative analysis, observational methods and analytical approach. Moreover, the emphasis of this research is diverted on other consequences of chemotherapy. The research also aims at exploring the treatment for patients specifically with fungal infections is most of the time unproductive, and the diagnosis is more time taking and problematic. The data collected will reflect the total duration of the anti-cancer therapy and the anti- infectious disease therapy and will also reflect the outcome of the methods used on the overall survival of the patients in question. Which will also be a huge contribution to the common assessment tools for identifying and preventing infection risks during chemotherapy. A sample size of the study will be based on picking up 25 men and 25 women in the research centre whose last ten years data is available for the study of interest. The results and findings of the study will be based on patients who have/have not been suffering from any previous medical conditions prior to their chemotherapy treatment.

Data will be collected from the patients who are currently receiving or have received chemotherapy at the research centre within the past ten years only. Patients who have received or receiving chemotherapy at the research Centre for less than ten years will not be included in the research criteria. The instruction of multifaceted interventions is accounted to show beneficial results by reducing the antibiotics overuse. The data collection will be arranged to take place about 2-3 times in a month, and the entire data collection timeline will cover a period of approximately 1-2 years. The analyses of this data will suggest a probable source of infection, its management and the final recommendation of the processes to the clinical expert.

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