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A Review on Evaluating Microbial Resistance Patterns in Chronic Wound Management Under Minimal Oral Antibiotic Use

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ABSTRACT

Chronic wounds pose a serious health problem due to their prolonged healing process, repeated infections, and potential complications. Chronic wounds can be inhabited by complicated microflora involving Gram-positive bacteria, Gram-negative bacteria, anaerobes, fungi, and multidrug-resistant pathogens. The problem of antimicrobial resistance has been raised significantly in the field of chronic wounds because of improper and unnecessary use of systemic antibiotics. One of the strategies that could mitigate this issue is minimal use of oral antibiotics, which only involves systemic antibiotics in the presence of clinically proven infections. The minimal use of oral antibiotics may lead to the low prevalence of multidrug-resistant microorganisms, maintenance of diversity of microflora, better susceptibility of microbes to antibiotics, and lesser adverse effects of drugs. Successful wound management requires efficient debridement, infection control, biofilm control, and antimicrobial use.

Keywords: Chronic wounds, antimicrobial resistance, minimal oral antibiotic use, wound infection, multidrug-resistant organisms, biofilms, antimicrobial stewardship, wound healing.

I. INTRODUCTION

Chronic wound care is a serious problem faced by healthcare services all over the world due to non-healing of wounds within the estimated period and their persistence up to weeks, months, or even years. Different examples of chronic wounds are diabetic foot ulcers, venous leg ulcers, pressure ulcers, and arterial ulcers. Due to the high prevalence of diabetes, obesity, vascular problems, and elderly population, the frequency of chronic wounds has increased significantly. Chronic wounds create considerable health issues and pose serious risks not only to patients but also to healthcare organizations because of prolonged healing, increased expenses, low quality of life, and possible infections.[1]

Microbial colonization is a natural occurrence during the wound-healing process, but when microbes grow in excess numbers and lead to infections, wound healing is greatly delayed. Chronic wounds are characterized by having microbial flora made up of both Gram-positive and Gram-negative bacteria, as well as fungi in certain circumstances. Some of the pathogens common in chronic wounds include S. aureus, Pseudomonas aeruginosa, Enterococcus spp., and E. coli. Microbes can also form something called biofilms, which are communities of microbes that attach themselves to the wound site and become resistant to the host's immune system defenses and antibiotics.[2]

For many decades now, oral antibiotics have been administered to treat infection in wounds and avoid complications that may arise. Though systemic antibiotics will always be needed in case of clinically infected wounds, overuse and misuse of antibiotics have resulted in antimicrobial resistance (AMR). These include MRSA, which is methicillin-resistant Staphylococcus aureus, as well as multidrug-resistant Pseudomonas aeruginosa and Enterobacteriaceae. The occurrence of AMR has brought about a major problem in the healthcare industry, leading to

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ineffective treatment, higher healthcare expenses, long periods of hospitalization, among others.[3]

Over the past years, there have been efforts by antimicrobial stewardship programs that have made healthcare workers become more prudent in their use of antibiotics with respect to minimal oral antibiotic usage wherever necessary. In this scenario, there is an emphasis on targeted antibiotic usage, wound assessment, proper wound debridement, the use of sophisticated dressings, and other infection control strategies as a way of minimizing unnecessary antibiotic usage. Microbial resistance patterns in situations where minimal oral antibiotic usage prevails need to be assessed.[4]

CHRONIC WOUNDS

A chronic wound is a wound that does not heal in accordance with the normal stages within the expected time frame. Such wounds do not heal within four to six weeks. Some characteristics of chronic wounds include persistent inflammation, infection, inability of the body tissues to regenerate, and microbial growth. Chronic wounds have an impact on the quality of life of patients and also pose financial burden on health systems. Some common types of chronic wounds include diabetic foot ulcers, venous leg ulcers, pressure ulcers, arterial ulcers, and post-operative non-healing ulcers.[5]

Types of Chronic Wounds

Diabetic Foot Ulcers : Diabetic foot ulcers are chronic wounds found in diabetic patients. They result from neuropathy, lack of adequate blood flow, and poor immunity among others. Patients suffer loss of protective sensation which predisposes them to unnoticed injuries leading to ulcers. The ulcers take longer to heal and can easily become infected leading to hospitalization and limb amputations.

Venous Leg Ulcers : Venous leg ulcers arise when there is venous insufficiency, leading to an elevation of blood pressure in the veins of the lower limbs. Tissue inflammation, swelling, tissue damage, and development of ulcers occur in the skin, especially in the area surrounding the ankles. Venous ulcers tend to be recurring and difficult to treat. Treatment includes compression therapy and wound care.

Pressure Ulcers : Pressure ulcers are also referred to as bedsores and develop because of the continuous pressure exerted on the skin and tissues, especially over areas that are prominent. Pressure ulcers are common in patients who are confined to their beds, elderly individuals, and those with limited mobility. Pressure ulcers develop because of restricted blood supply resulting in tissue death.

Arterial Ulcers : These types of ulcers develop as a result of peripheral arterial disease and are characterized by reduced blood supply to tissues. Poor oxygen and nutrients supply cause poor healing and tissue breakdown. Arterial ulcers are usually located in the feet, toes, and heels and may be painful.

Surgical Non-Healing Wounds : Non-healing surgical wounds are surgical wounds that do not heal as expected due to various complications. Causes like infection, poor vascularization, diabetes, malnutrition, obesity, and immunosuppression may affect healing. Inflammation and microorganisms worsen the problem, thus necessitating an accurate evaluation of the cause for effective treatment.[6,7]

CONTRIBUTING FACTORS FOR CHRONIC WOUNDS

Diabetes Mellitus : One of the major contributing factors in chronic wound formation is diabetes mellitus. The condition involves elevated levels of glucose in the body which interfere with circulation, immunity, synthesis of collagen, and cellular healing. Diabetic neuropathy limits sensations in affected individuals, hence reducing awareness of injuries. As a result, chronic wounds may occur as a complication, especially if there is an infection in poorly controlled diabetics.

Peripheral Vascular Disease : Peripheral vascular disease decreases blood flow to body tissues, thereby affecting the supply of oxygen and nutrients necessary for tissue repair. Lack of sufficient blood flow affects the functioning of cells, collagen formation, and immune response, thereby delaying the healing process. Those with peripheral arterial disease are prone to the development of chronic ulcers, particularly within the limbs.

Advanced Age : The ageing process leads to physiological changes that affect wound healing processes. The ageing process results in skin inelasticity, low production of collagen, ineffective immune responses, and poor cell regeneration. Conditions that come with aging include diabetes, heart problems, and malnutrition. These make it difficult for elderly people to recover from injuries sustained through accidents or during surgical procedures.[8]

Infection and Microbial Biofilms : Infections are a major causative factor in chronic wounds. The microbes present in the affected areas may grow to form biofilms, which are communities of microorganisms within an extracellular matrix that provides protection against host immune systems and antibiotics. The growth of microorganisms leads to

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inflammation, tissue damage, and non-healing of the wound, resulting in the creation of a chronic wound environment.

Malnutrition : Proper nutrition is vital for adequate wound healing. Insufficiency in protein, vitamins, minerals, and calories affects processes such as cell division, collagen formation, and immune response, leading to poor wound healing. Malnutrition is also characterized by the presence of poor wound healing and high levels of susceptibility to infections. Poor nutrition is very prevalent among elderly and chronically ill patients.

Obesity : The presence of obesity results in various conditions that facilitate the creation of chronic wounds. Some factors include inadequate perfusion, increased inflammation, and low oxygen supply to tissues. Additionally, obese patients have an excess amount of fat tissue, which may result in excessive pressure on the wound, hindering the wound healing process. Obesity is often correlated with diabetes, hypertension, and other diseases.

Immunosuppression : A suppressed immune system resulting from disease or medication can hinder wound healing. The compromised immune response would prevent efficient fighting against infection and regulation of inflammation within the body. As a result, wounds will become prone to infections due to the inability of the immune system to keep them at bay. The use of corticosteroids, chemotherapy, and immunosuppressants delays wound healing.

Repeated Trauma and Pressure : Chronic wounds can develop as a result of repeated injuries to tissues and continuous exposure to physical pressure. People with mobility problems are more prone to pressure injuries that can prevent normal wound healing due to sustained inflammation and tissue breakdown. Measures that should be taken into account include pressure redistribution techniques.[9]

WOUND HEALING PROCESS

Hemostasis

Hemostasis is one of the first processes that occur when there is a tissue injury. Its main function is the prevention of excessive blood loss from the body and the creation of a temporary barrier. Blood vessels contract, platelets aggregate and initiate the process of coagulation, resulting in the formation of a clot. The formed fibrin clot acts as an inflammatory mediator by providing the necessary environment for the growth factors and inflammatory cells.[10]

Inflammatory Phase

The inflammatory phase occurs almost right after the injury and usually lasts for several days. Neutrophils and macrophages gather at the wound to combat the presence of pathogens and clean up debris. Inflammation plays an important role in the process of wound healing because without it tissue regeneration cannot occur. At the same time, inflammation should be controlled since prolonged and excessive inflammation may hinder this process.[11]

Proliferative Phase

Proliferation phase refers to the creation of new tissues, and typically starts after a few days of wound. In proliferation phase, fibroblasts form new collagen fibers and other extracellular matrices to provide structural support for healing tissues. Angiogenesis results in formation of new blood vessels which ensures that healing tissue gets sufficient oxygen and nutrients. Formation of granulation tissues and migration of epithelial cells to close the gap formed by the wound takes place.[12]

Remodeling Phase

Remodeling phase is the last phase of healing process, and typically continues for months or even years in certain cases. Collagen fibers become reorganized, cross linked, and aligned in remodeling phase, resulting in greater strength of tissues. Activity of cells slows down in this phase due to the maturity of the tissue being formed. Although healed tissue becomes stronger than before, it does not achieve the same strength as before the injury.[13]

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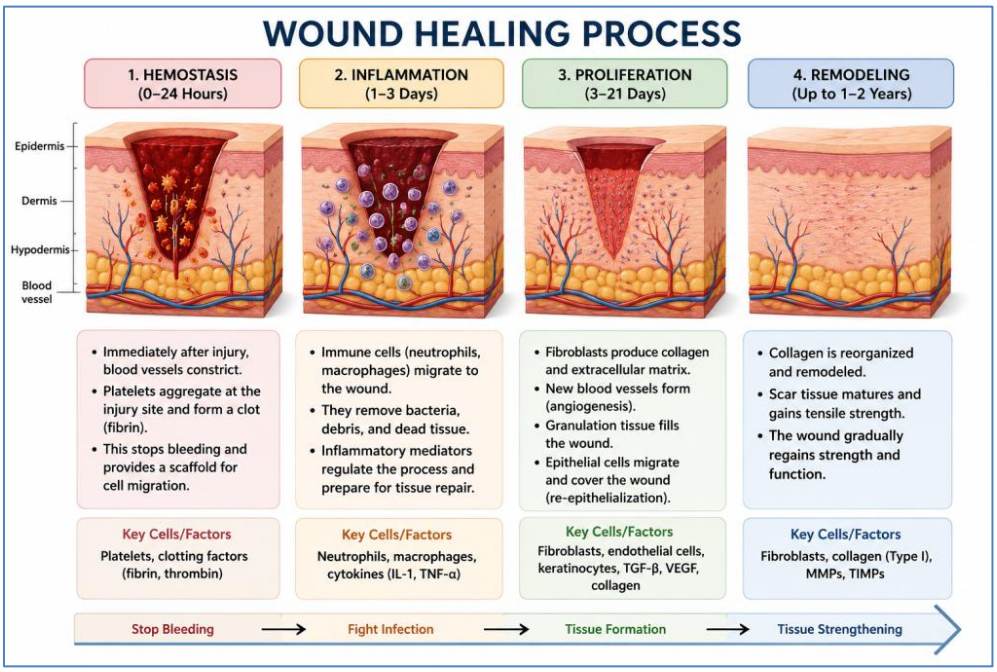

COMMON MICROORGANISMS ASSOCIATED WITH CHRONIC WOUNDS

Category	Microorganisms
Gram-Positive Bacteria	Staphylococcus aureus
	Methicillin-resistant Staphylococcus aureus (MRSA)
	Enterococcus faecalis
	Enterococcus faecium
Gram-Negative Bacteria	Pseudomonas aeruginosa
	Klebsiella pneumoniae
	Escherichia coli
	Acinetobacter baumannii
	Proteus mirabilis
	Proteus vulgaris
Anaerobic Organisms	Bacteroides fragilis
	Peptostreptococcus species
	Clostridium perfringens
	Prevotella species
Fungal Pathogens	Candida albicans
	Candida tropicalis
	Candida glabrata
	Aspergillus fumigatus
Emerging and Multidrug-Resistant Organisms	Methicillin-resistant Staphylococcus aureus (MRSA)
	Vancomycin-resistant Enterococcus (VRE)
	Extended-Spectrum β-Lactamase (ESBL)-producing Escherichia coli
	ESBL-producing Klebsiella pneumoniae
	Multidrug-resistant Pseudomonas aeruginosa
	Multidrug-resistant Acinetobacter baumannii
	Carbapenem-resistant Klebsiella pneumoniae (CRKP)[14]

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ANTIMICROBIAL RESISTANCE IN CHRONIC WOUNDS

Antimicrobial resistance (AMR) is defined as the survival and multiplication of microorganisms despite being exposed to antimicrobial drugs. AMR has become a serious global public health challenge. This situation is more pronounced when dealing with chronic wounds because of increased exposure to microorganisms and constant administration of antibiotics. It results in complicated cases of infections with higher morbidity and mortality rates.

Enzymatic Degradation of Antibiotics

The enzymatic breakdown of antibiotics is one of the most prevalent ways of bacterial resistance to antimicrobials. Enzymes produced by resistant organisms can break down or modify antibiotics so that they will not be able to reach the intended target sites. For instance, there is the production of β-lactamases, ESBLs, and carbapenemases. These enzymes break down β-lactam antibiotics such as cephalosporins, penicillins, and carbapenems. The presence of these enzymes leads to resistant bacteria in chronic wound infections such as Klebsiella pneumoniae, E. coli, and P. aeruginosa.[15]

Modification of Antibiotic Target Sites

Modification of the target site refers to the changes in the molecular structure that are made by the bacteria to decrease the effectiveness of antibiotics. The modifications may be due to genetic changes or due to the presence of resistance genes. One of the examples is that the methicillin-resistant strain of Staphylococcus aureus synthesizes a new form of penicillin-binding protein referred to as PBP2a, with lower binding capability towards the β-lactams. Modification of the target site makes pathogens resistant to macrolide and fluoroquinolone antibiotics.[16]

Reduced Membrane Permeability

Membrane impermeability is one form of resistance where the passage of antimicrobials into the bacterial cell is inhibited. Gram-negative bacteria have an outer membrane which contains channels called porins that control the transport of materials through the cell wall. Alterations in the presence or characteristics of these porins can result in decreased ability of the drugs to enter the bacteria. Organisms like Pseudomonas aeruginosa and Acinetobacter baumannii often show reduced permeability especially when exposed to β-lactam and hydrophilic antimicrobials. This prevents adequate amounts of the drugs from entering the bacteria, leading to survival within the body.[17]

Efflux Pump-Mediated Resistance

Efflux pumps are specific types of transport proteins found in bacterial cell walls which help in transporting antimicrobial substances out of the cell. Efflux pumps bring about a reduction in intracellular levels of antibiotics to levels that cannot effectively inhibit bacterial reproduction or kill cells. Efflux-based antibiotic resistance is known to occur in several different classes of antibiotics such as tetracyclines, fluoroquinolones, macrolides, and chloramphenicol. Several chronic wound-causing bacteria are endowed with effective efflux mechanisms that render them multidrug resistant.[18]

Horizontal Gene Transfer

HGT is one of the primary means that lead to quick transfer of antibiotic resistance among bacteria. HGT differs from vertical transfer that takes place during bacterial reproduction. Bacteria get resistant genes by direct acquisition from other bacteria by means of transformation, transduction, and conjugation. Several resistance determinants are encoded by plasmids, transposons, and integrons, and they spread quickly within polymicrobial chronic wound infections. Such gene transfer promotes the development of multidrug resistance. The presence of many different bacteria within chronic wound biofilms provides a good opportunity for transferring resistant genes horizontally.[19]

Biofilm-Mediated Resistance

Resistance due to biofilm formation is one of the biggest problems encountered in the treatment of chronic wounds. Biofilm refers to microbial colonies surrounded by an extracellular polymeric substance matrix produced by themselves and attached to the wound surface. The matrix is used as a barrier against antibiotics and prevents microorganisms from being attacked by the host's immune system. In addition, microbes inside the biofilm have different metabolic properties and lower multiplication rates than planktonic microbes, which makes them more resistant to antibacterial drugs that act on rapidly growing microorganisms.[20]

Genetic Mutations and Adaptive Resistance

Mutations within the DNA of the bacteria could be caused by spontaneous changes during the replication process of the bacteria and may result in resistance against certain antibiotics. The mutation

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may involve changing the target site, increasing efflux pump production, decreasing membrane permeability or enhancing enzymes activities. Exposure of the bacteria to antibiotics within the chronic wound leads to selection of mutated organisms that develop resistance. Moreover, there is the phenomenon of adaptive resistance where there is an alteration in physiology of the organism resulting from environmental conditions such as antibiotic exposure.[21]

ORAL ANTIBIOTIC USE IN CHRONIC WOUND MANAGEMENT

Antibiotics administered orally have played an essential role in the management of chronic wounds especially in those cases which show clear signs of infection. From the time antibiotics became available around mid-twentieth century, they have played a significant role in the reduction of infectious problems. In the management of chronic wounds, antibiotics administered orally have played an essential role in preventing any further progress of the infections, reducing the number of bacteria and thus promoting healing. The problem is, however, that at many times oral antibiotics are used routinely and even without necessity.

Antibiotics taken orally should be used only when there is strong clinical evidence of infection, not just colonization. Indications include the presence of pain, redness, inflammation, warmth, pus discharge, odor, cellulitis, and fever or any other sign of systemic infection. Examples of conditions that need systemic antibiotics are infected diabetic foot ulcers, infected venous leg ulcers, and infections following surgery. Ideally, antibiotic therapy should be based on culture and sensitivity results when available. The careful use of antibiotics helps to prevent infection and avoid the development of antimicrobial resistance.[22]

Common Oral Antibiotics Used in Chronic Wound Management

Antibiotic Class	Common Agents	Target Organisms / Use in Chronic Wounds
Penicillins	Amoxicillin, Amoxicillin-clavulanate	Streptococcus spp., MSSA, mixed infections
Cephalosporins	Cephalexin, Cefuroxime	MSSA, streptococcal skin and soft tissue infections
Tetracyclines	Doxycycline, Minocycline	MRSA, mild-moderate skin and soft tissue infections
Macrolides	Azithromycin, Clarithromycin	Gram-positive cocci, atypical infections (limited role)
Lincosamides	Clindamycin	MRSA, anaerobic coverage in polymicrobial wounds
Fluoroquinolones	Ciprofloxacin, Levofloxacin	Pseudomonas aeruginosa, Gram-negative infections
Sulfonamides	Trimethoprim-sulfamethoxazole (TMP-SMX)	MRSA, Gram-negative organisms
Oxazolidinones	Linezolid	MRSA, VRE (reserved for resistant infections)
Nitroimidazoles	Metronidazole	Anaerobic infections in deep or foul-smelling wounds

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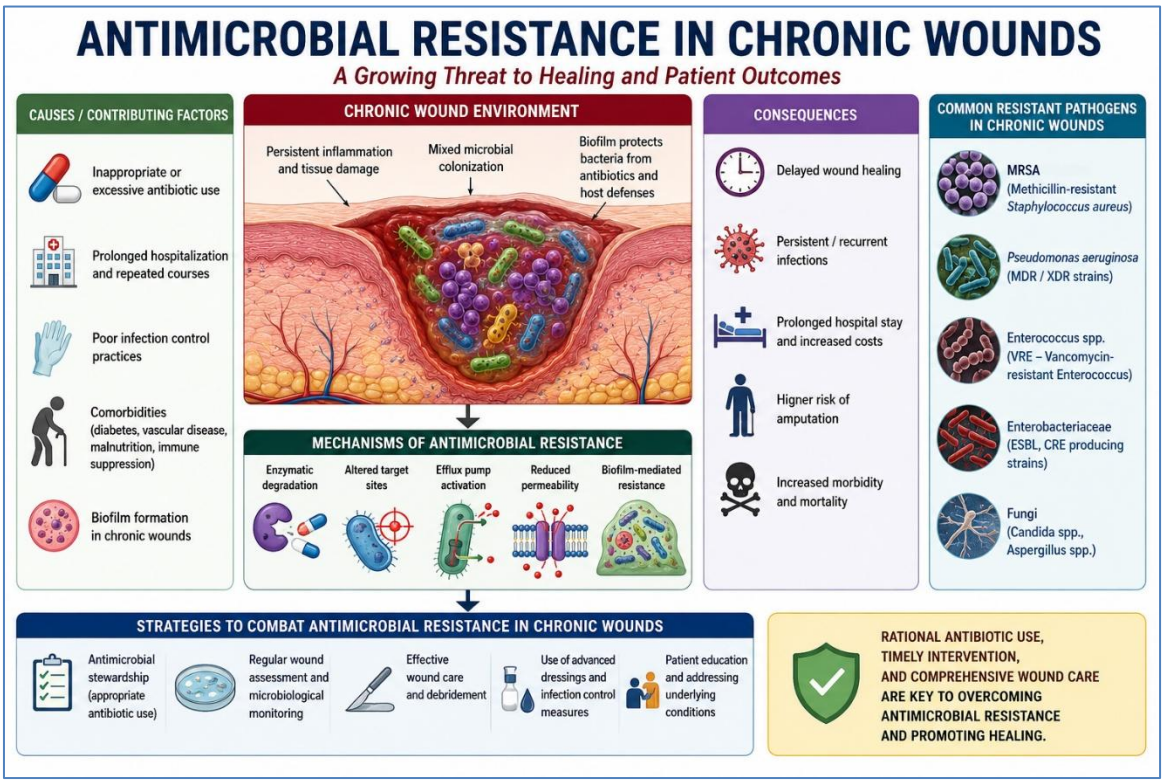
Carbapenems (oral equivalent limited/rare use)	Not commonly oral; step-down IV alternatives	Severe MDR infections (mostly IV use)[23]



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BENEFITS OF ORAL ANTIBIOTIC THERAPY IN CHRONIC WOUND MANAGEMENT

Infection Control and Reduction of Bacterial Load

Oral antibiotics play a role in control of infection through reduction in bacteria within the wound. It is especially beneficial in clinically infected chronic wounds like diabetic foot ulcers and venous ulcers. By controlling pathogenic bacteria, antibiotics minimize tissue damage and inflammation and facilitate progression of the wound into the healing phase.

Prevention of Systemic Spread of Infection

One of the biggest advantages of the use of oral antibiotics in chronic wound care is the ability to prevent the infection from spreading to systemic structures. Local bacteria could spread to deep tissues, including blood vessels, causing conditions such as cellulitis, sepsis, or even osteomyelitis. Oral antibiotic application helps to control the infection at the early stages of its development.[24]

Improved Wound Healing Outcomes

The use of oral antibiotics indirectly results in improved wound healing as they remove some of the obstacles to the process. By removing pathogens, antibiotics eliminate inflammation and improve blood flow to the injured area. Improved oxygenation leads to increased activity of fibroblasts and increased production of collagen and epithelial cells, allowing the wound to close.

Convenience and Patient Compliance

The use of oral antibiotics is a convenient method of administering medicine as they provide a painless mode of treatment that does not involve any surgical procedures. Since patients have easy access to these medicines and are not required to be admitted to a hospital for the treatment, they find compliance easier to achieve than if other methods of treatment had been involved.

Reduced Need for Hospitalization and Healthcare Costs

Since oral antibiotics can treat mild to moderately severe wound infections, they help in reducing the number of hospital stays and related expenses. Thus, they help reduce costs and make the process of treating such infections more convenient and economically feasible for patients.[25]

CHALLENGES ASSOCIATED WITH PROLONGED ORAL ANTIBIOTIC USE IN CHRONIC WOUND MANAGEMENT

Development of Antimicrobial Resistance

One of the primary reasons for the development of antimicrobial resistance among the pathogens that cause chronic wounds is their prolonged exposure to antibiotics through oral administration. Due to such exposure, there is selection pressure on resistant organisms to allow survival and proliferation of the bacteria in question. Consequently, such bacteria as MRSA, ESBL-positive Gram-negative organisms, and multidrug-resistant Pseudomonas aeruginosa become much more common.

Disruption of Normal Microbiota

Another problem that prolonged administration of antibiotics leads to is disruption of the microbiome balance in the human body. It especially concerns bacteria found in the intestines and on the skin surface. The shift towards a particular organism in such cases may facilitate the growth of opportunistic pathogens, like Candida spp. and Clostridioides difficile.[26]

Inappropriate Antibiotic Overuse

Another problem associated with wound management is the misapplication of antibiotics for treating colonized rather than infected wounds, leading to unnecessary drug use. This could interfere with wound healing procedures, including proper debridement, pressure offloading, and other therapeutic treatments. Misusing antibiotics poses an increased risk for developing resistance and hinders the implementation of the concepts of antimicrobial stewardship.

Adverse Drug Reactions and Toxicity

Prolonged antibiotic treatment by mouth enhances the potential for adverse reactions to medication. Depending on the type of drug prescribed, patients may suffer from different kinds of reactions, from nausea and diarrhea to more serious complications such as toxicities to liver and kidney functions. Adverse effects may lead to poor patient compliance with the treatment regime.

Increased Healthcare Costs and Treatment Burden

Long-term use of antibiotics results in higher healthcare costs due to longer periods of treatment, multiple visits, tests, and management of possible side effects. This is an additional cost that affects the patient as well. Also, high-frequency use of antibiotics will require the administration of more complicated treatment if antibiotic resistance occurs, resulting in higher costs.[27]

MINIMAL ORAL ANTIBIOTIC USE

The use of minimal systemic antibiotics in chronic wounds implies an evidence-based approach whereby the prescription of systemic antibiotics is

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done in cases where there is clinical, microbiological, or systemic evidence that infections exist. The approach does not advocate for the use of antibiotics in cases of wounds that are merely colonized but lack any form of infection. The approach takes into consideration culture sensitivity reports before administering the drugs.

Rationale for the clinical application of the protocol in question lies in the necessity of addressing the increasing problem of antimicrobial resistance. Chronic wounds tend to harbor various types of bacteria; however, their presence does not always necessitate the use of systemic medication. Uncontrolled administration of antibiotics leads to multidrug resistance, alters microbiome, and contributes to treatment failure. With the help of oral antibiotics restriction to infections only, clinicians manage to keep antibiotics for critical cases.

Furthermore, reduced antibiotic usage promotes the use of holistic approaches to wound care, including debridement, offloading, enhanced blood flow, and dressings. These measures deal with the actual cause of the wounds instead of simply concentrating on the microbial presence. As a result, this method produces better health results for patients, prevents adverse effects from drugs, saves money, and ensures sustainable infection control.[28]

CRITERIA FOR MINIMAL ANTIBIOTIC INTERVENTION IN CHRONIC WOUND MANAGEMENT

Clinical Signs of Active Infection

Indication of systemic antibiotics should occur only when there is obvious sign of infection in the wound. Such signs include increase in pain, redness, warmth, swelling, pus formation, foul smell, delayed wound healing with worsening condition. There is no indication for the use of systemic antibiotics even if there is colonization of the wound without such systemic signs.

Systemic Signs of Infection

The need to use very minimal amounts of antibiotics means consideration of involvement in the systemic process. Such involvement includes fever, chills, rapid heart rate, high white blood cell counts, elevated inflammatory markers, or signs of sepsis which signify that the infection is no longer local. In such situations, antibiotics may be administered systemically through oral or IV route.[29]

Depth and Severity of Wound Involvement

The degree and extent of involvement of the tissue are another major factor when selecting an antibiotic for treating wound infections. Superficial wound infections that are colonized without deep tissue infection do not require oral antibiotics. If there is deep infection or suspicion of bone infection or involvement of the fascia and muscles, then systemic antibiotics are needed. Proper imaging tests and physical examinations can help determine whether infection extends into deep tissues.

Microbiological Confirmation

The presence of bacterial cultures with susceptibility results are mandatory criteria for prescribing minimal antibiotics to manage wounds. When using systemic antibiotics, the choice and dose depend on the identified pathogens. Unless the condition of the wound gets worse very rapidly or becomes serious, it is always better to avoid empirical antibiotics for managing chronic wounds.

Failure of Local Wound Management

Antibiotics may only be prescribed when local wound management measures fail to heal the wound infection. This is the final step where a thorough evaluation of the debridement process, wound moisture balance, offloading of pressure from wounds, and dressings is completed. Only after evaluating these factors, one will get the idea of whether antibiotics are needed or not.[30]

CLINICAL OUTCOMES ASSOCIATED WITH MINIMAL ORAL ANTIBIOTIC USE IN CHRONIC WOUND MANAGEMENT

1. Improved Wound Healing Rates

The use of minimal oral antibiotics along with proper wound management may facilitate faster healing of chronic wounds. Since antibiotics are not used excessively, there will be less chances of dysbiosis in wounds, which will aid the process of faster healing. The proper infection management via selective therapy results in rapid granulation tissue formation and faster healing of wounds than the use of excessive and improper antibiotics.

2. Reduced Antimicrobial Resistance Development

Another important clinical effect of minimal antibiotics use is the prevention of antimicrobial resistance formation in bacteria. Using fewer systemic antibiotics will decrease selection pressure on pathogens, thus preventing them from becoming resistant bacteria such as MRSA, VRE, and ESBL.

3. Lower Infection Recurrence Rates

Patients who receive minimal doses of oral antibiotics exhibit a lower rate of re-infection in

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their wounds if there is proper local care. The use of minimal doses of antibiotics helps avoid the disturbance of the flora within the body, hence preventing the selection of resistant bacteria and infections resulting from re-infections. This practice promotes healthy microorganisms within the body.[31]

4. Decreased Hospitalization and Complications

The minimal dose antibiotic treatment methods help in reducing the number of admissions for patients suffering from chronic wound infections and the complications resulting from these infections. Patients are prevented from taking unnecessary systemic antibiotics; therefore, the chances of developing adverse effects and infections necessitating hospitalization are low. Proper management of the outpatients' wounds prevents them from developing infections like cellulitis, osteomyelitis, and sepsis.

5. Reduced Adverse Drug Reactions

There are several advantages associated with the decrease in side effects caused by antibiotics. With a limitation on the intake of oral antibiotics, there are no side effects, which include stomach problems, allergic reactions, liver toxicity, kidney damage, and secondary infections, including Clostridioides difficile. Patients will have fewer side effects during treatment and will be able to adhere to the wound care regimen.

6. Improved Microbial Balance in Wounds

Minimizing the use of antibiotics can preserve the healthy microbiome in wounds since the overgrowth of commensal microorganisms will not be disturbed. Such an environment will be less prone to pathogenic growth and will enable the immune system to function optimally due to fewer side effects.[32]

7. Cost-Effective Healthcare Outcomes

Economically, the minimal use of antibiotics orally would mean lower costs in terms of fewer prescription costs, fewer hospital admissions, and fewer cases of dealing with side effects of drugs. This is due to the lower cost of broad spectrum or last line antibiotics that are needed in treating resistant infections.

8. Enhanced Effectiveness of Targeted Therapy

If antibiotics are administered only in confirmed cases of infection, then there will be increased effectiveness of antibiotic therapy. With culture-directed therapy, the choice of an antibiotic is done in a more precise manner, resulting in better elimination of bacteria. This way, the probability of a successful management of infection in chronic wounds is increased.

9. Improved Patient Quality of Life

The patients have the advantage of receiving minimal doses of medication; as such, there are fewer side effects. This method also allows for faster recovery, thus reducing hospital visits, promoting outpatient treatment, and ultimately increasing the quality of life of the affected patients.

10. Support for Antimicrobial Stewardship Goals

Minimal use of oral antibiotics directly contributes to global efforts towards antimicrobial stewardship because it encourages rational drug prescription. This strategy minimizes needless use of antibiotics, keeps their effectiveness intact, and curtails the spread of resistance in hospital as well as community settings. In clinical practice, such a practice guarantees sustainable strategies for infections and wound treatment.[33]

EVALUATING MICROBIAL RESISTANCE PATTERNS

It is crucial to assess the microbial resistance patterns in chronic wound care when minimal use of oral antibiotics is used due to the issue of antimicrobial resistance. The chronic wounds harbor polymicrobial flora and are usually colonized rather than infected; however, antibiotics continue to be used unnecessarily in many cases. Using the minimal antibiotic approach can be helpful since it limits antibiotic use for the treatment of infections.

1. Baseline Microbial Profile Assessment

Initial microbial profile evaluation refers to the identification of microbes found within chronic wounds prior to the use of minimal antibiotics approaches. Culture and sensitivity tests will enable one to know the infecting and colonizing microbes and their resistance patterns. An initial microbial profile will help one understand the changes taking place with regards to microorganisms and the effects of the use of minimal antibiotic approaches.

2. Shifts in Microbial Diversity

The reduced usage of antibiotics orally affects microbial diversity in that there is reduced selection pressure on the susceptible microbes. The examination looks at the shift in species richness and dominance among the microorganisms found in chronic wounds. It is possible to have a balanced

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population of microorganisms in a scenario where the unnecessary use of antibiotics is minimized.

3. Antibiotic Susceptibility Trends

Resistance patterns of antibiotics are evaluated using culture sensitivity tests conducted regularly over some time. This helps determine whether the microorganisms become less or more resistant to the antibiotics due to low selection pressure. The reduction in antibiotic selection pressure can lead to the retention of the susceptibility pattern of the microorganisms to the antibiotics.[34]

4. Prevalence of Multidrug-Resistant Organisms

This evaluation assesses the prevalence of MDR organisms such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBLs) and carbapenem-resistant bacteria. Incidence, prevalence, and recurrence of these pathogens is assessed in the setting of minimal antibiotic exposure. A low incidence and prevalence of these MDR organisms would indicate optimal stewardship, whereas their continued presence could point to persistent resistance problems.

5. Biofilm Formation and Stability

The assessment of the biofilm becomes necessary since biofilms prevent the action of antibiotics and immunity against the microorganisms. In minimal usage of antibiotics in the mouth, the biofilm can be assessed by its density, structure, and durability in chronic wounds. Minimal application of antibiotics may minimize biofilm-promoting pressure, yet the biofilm may remain there even with less pressure.[35]

6. Horizontal Gene Transfer Dynamics

The horizontal gene transfer evaluation measures the rate at which the genes responsible for resistance are transferred from one bacterium to another in the wounds that are affected by chronic conditions. The processes involved include plasmids, transposons, and integrons carrying resistance determinants. Minimal use of antibiotics could lower the selective pressures needed to facilitate such exchanges.

7. Colonization versus Infection Ratio

The colonizations/infection evaluation assesses whether there is colonization or an actual infection in the case of chronic wound infections. It ensures that only the infections are treated since minimal use of antibiotics requires only clinically infected wounds to be treated with them. It prevents the unnecessary prescription of antibiotics when the colonization is at hand.[36]

8. Clinical Response to Treatment

The clinical response to treatment involves linking patterns of microbial resistance to the results of treatment in terms of wound healing, such as the size of the wound, pain relief, amount of exudates, and granulation of tissue. In the context of minimal use of antibiotics, positive results demonstrate that infections can be controlled via good local wound care practices.

9. Recurrence and Reinfection Rates

Rate of recurrence and reinfection serve as an essential measure of treatment efficacy in the long run. The measurement evaluates how many times chronic wounds become re-infected after they started improving. A lower rate of recurrence with minimal antibiotic use implies more balanced levels of microorganisms and less resistance pressure on them.

10. Antimicrobial Stewardship Outcome Correlation

Antimicrobial resistance is compared to the outcome of antimicrobial stewardship that may include consumption of antibiotics, resistance, and the healthcare burden. The study attempts to see if low oral antibiotic consumption leads to lower overall antibiotic consumption without compromising the efficacy of the intervention.[37]

CHALLENGES IN RESISTANCE MONITORING AND MANAGEMENT IN CHRONIC WOUNDS

1. Difficulty in Accurate Microbial Identification

Pathogen identification in patients suffering from chronic wounds is complicated by the presence of polymicrobial infection and biofilms. The conventional methods used in the identification of microbes may not be effective for the detection of all the pathogens, particularly those that cannot be cultured. In turn, proper resistance evaluation becomes impossible.

2. Biofilm-Associated Diagnostic Limitations

Microbes form biofilms that are very difficult to identify through common diagnostic procedures in laboratories. It has been noted that bacteria in a biofilm state have different resistance characteristics from those in the planktonic phase. Thus, it is hard to conduct accurate susceptibility analysis using common procedures.[38]

3. Inadequate Sampling Techniques

Poor sampling technique for wound infections could result in either contamination or inaccurate readings. The surface swab may not be an accurate reflection of the causative agent but of the colonizing organisms, while taking samples from deep tissues may prove too difficult in regular practice. Variation

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in the sample-taking procedure will compromise the quality of the resistance information obtained, making it hard to monitor trends in microbes within chronic wounds.

4. Variability in Laboratory Methods

Variation in laboratory practices used in culturing samples, identifying organisms, and testing susceptibilities could affect the quality of results. The lack of standardization across different labs will make comparison of resistance trends difficult. This variation undermines the reliability of resistance surveillance and its application in chronic wound management.

5. Antibiotic Overuse and Empirical Prescribing

Overreliance on empirical prescribing is another challenge facing clinicians today. This will undermine efforts towards accurate resistance surveillance and increase the prevalence of multidrug resistance organisms. It will also obscure the real picture of microbial trends in chronic wounds and make assessment of the impact of minimal oral antibiotic prescription strategy harder.

6. Resource and Infrastructure Constraints

The lack of adequate laboratories, sophisticated diagnostic equipment, and even finances affects efforts at conducting resistance monitoring, especially in resource-constrained settings. The use of molecular diagnosis approaches like PCR and sequencing is limited. Thus, the process of microbial identification and tracking the prevalence of resistance is impeded.

7. Lack of Standardized Guidelines for Monitoring

The lack of adequate laboratories, sophisticated diagnostic equipment, and even finances affects efforts at conducting resistance monitoring, especially in resource-constrained settings. The use of molecular diagnosis approaches like PCR and sequencing is limited. Thus, the process of microbial identification and tracking the prevalence of resistance is impeded.[39]

RECENT ADVANCES AND EMERGING TECHNOLOGIES IN CHRONIC WOUND MANAGEMENT AND ANTIMICROBIAL RESISTANCE CONTROL

1. Rapid Molecular Diagnostic Technologies

Fast molecular diagnostics systems have been crucial in facilitating the diagnosis of pathogens and resistance genes in chronic wounds. The technologies include polymerase chain reaction, multiplex PCR, and real-time PCR, among others, which give results faster compared to traditional culture testing. This has led to rapid diagnosis of resistant pathogens, targeted treatments, reduced misuse of antibiotics, and effective infection control in chronic wound patients.

2. Next-Generation Sequencing (NGS) and Metagenomics

The next generation sequencing method along with metagenomics enables full identification of wound microflora using methods other than cultivation. They include not only identification of bacteria, fungi, and viruses but also antibiotic resistance genes as well. Through gaining a better understanding of microbial diversity and resistance in wounds, NGS helps to improve the practice of precision medicine.[40]

3. Artificial Intelligence and Machine Learning Applications

The use of artificial intelligence (AI) and machine learning in predicting the outcomes of wound healing and infection risk along with detecting patterns of antibiotic resistance is rapidly increasing. The ability of the AI algorithms to utilize huge amounts of clinical data for better decision-making could greatly help in tailoring personalized wound care strategies.

4. Smart Wound Dressings and Biosensors

Wounds that have been dressed with smart bandages incorporating biosensors can be monitored continuously for changes in the condition of wounds, such as temperature, pH level, moisture content, and presence of bacteria. The smart bandages offer instant feedback regarding the state of the wound, as well as any infections that might develop.

5. Nanotechnology-Based Antimicrobial Therapies

Nanotechnology represents a new hope for treating resistant infections associated with wounds. Silver, gold, zinc oxide, and chitosan nanomaterials have antimicrobial capabilities, which help increase the delivery of drugs to the site of infection. Nanoparticles increase biofilm penetration, minimize bacterial colonization, and can become replacements or complementary therapies to existing antibiotics.[41]

6. Antimicrobial Peptides and Novel Biologics

Antimicrobial peptides (AMPs) are peptides that occur naturally and have broad-spectrum antimicrobial activity against bacteria, fungi, and viruses. Unlike conventional antibiotics, AMPs typically affect microbial membranes, making the emergence of resistance unlikely. Research into novel treatments using peptides and biological substances is ongoing in chronic wound infection treatment and biofilm resistance problems.

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7. Bacteriophage Therapy

In bacteriophage treatment, viruses that selectively attack bacteria causing infections are used. Bacteriophages can attack drug-resistant pathogens without affecting good microbes. Due to their ability to pass through biofilm and evolve along with the evolution of bacteria, they represent an alternative in combating multi-drug resistant chronic wound infections. They are still being studied in clinical trials.

8. Advanced Biofilm Disruption Technologies

A variety of techniques are under development to eliminate biofilms that cause persistent wound infections. Such techniques may involve enzymes, ultrasonic waves, electricity, and anti-biofilm substances. The use of these techniques breaks the biofilm structure, thus ensuring greater penetration by antimicrobial drugs.

9. CRISPR-Based Antimicrobial Strategies

The technology Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) provides an innovative means to target certain genes of pathogens, such as antimicrobial resistance determinants. The use of CRISPR-based antimicrobial therapies can allow clinicians to specifically destroy resistant pathogens or deactivate their genes without harming the beneficial microflora. Even though it is not widely implemented at present, CRISPR technology can be viewed as a promising approach to managing antimicrobial resistance in chronic wounds in the future.[42]

10. Personalized and Precision Wound Care

Tailored wound care takes into account microbiology results, personal features of the patient, genetics and resistance patterns to tailor a unique care program. Recent innovations in precision medicine help choose the most suitable treatments for patients. This strategy ensures effective treatment, reduces unnecessary use of antibiotics, leads to better healing and achieves goals of antimicrobial stewardship.

II. CONCLUSION

The problem of chronic wound continues to pose an important problem because of their persistent microbial contamination, recurrence of infections, slow wound healing process, and increased antimicrobial resistance. Over-reliance on systemic antibiotics in the treatment of chronic wounds contributes to the development of organisms that are resistant to multiple types of medications. In this regard, minimal oral antibiotic treatment is recommended by the administration of systemic antibiotics where the presence of infections has been clinically confirmed. This allows to avoid the selection pressure on the pathogens and follow the principle of antimicrobial stewardship. Proper treatment of chronic wounds also includes other approaches such as wound debridement and infection monitoring, among others.

Resistance patterns of microbes through monitoring under minimal oral antibiotic use can be very important for understanding how pathogens behave, how susceptible they are, and how resistant they become. It is believed that lowering the number of antibiotic doses used can help maintain microbial diversity, lower the occurrence of multidrug-resistant organisms, increase the efficacy of antibiotics, and prevent adverse effects associated with the use of drugs. There is potential in molecular diagnostics, artificial intelligence, nanotechnology, and biofilms therapy approaches. Research and standardization of monitoring methods along with antimicrobial stewardship programs are important for chronic wounds management.

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