

General Principles of Antimicrobial Drugs

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Superinfection

- Means 'Emergence of a New Infection while treating the present infection with Antimicrobial drugs'
- **(A) Causes of superinfections:-**
- **1) By Alteration in normal protective bacterial flora of the body :-**
- Normal microbial flora of the intestine are protective in nature by elaborating substances known as 'Bacteriocins' – which inhibits invasion of pathogenic organisms to the host cells → In **superinfection**, AMAs causes alteration of this protective bacterial flora of the body → resulting into loss of body's host defence system → giving rise to new infection by non-pathogenic organisms (eg. Candida)
- **2) Superinfection is commonly associated with Broad/ Extended spectrum antibiotics (Tetracyclines, Chloramphenicol, Ampicillin, Amoxycillin and Cephalosprins. It is least with narrow spectrum antibiotics like Penicillin, Macrolides & Aminoglycosides**

Superinfection (Contd...)

(B) Sites of Superinfections :- are

- Those which commonly harbours commensals :- eg.
 - 1) Oropharynx ,
 - 2) Intestinal Tract,
 - 3) Respiratory Tract
 - 4) Genitourinary Tract,
 - 5) Skin

(C) Organisms causing superinfections :- are

- (a) **Candida Albicans** :- Oral Candidiasis, Oral thrush, Monilial Diarrhoea and Vulvovaginitis. Treat with topical antifungal drugs like Nystatin or Clotrimazole.
- (b) **Resistant Staphylococcal Enteritis** :- Treat with Cloxacillin

Superinfection (Contd...)

- **(c) Clostridium Difficile :-** Produces Pseudomembranous Enterocolitis after colorectal surgery with the use of Clindamycin, Tetracyclines, Ampicillin, Aminoglycosides, Cotrimoxazole à Organism produces an Enterotoxin which damages gut mucosa forming plaques à Treat with Metronidazole and / or Vancomycin orally.
- **(d) Proteus :-** Produces Urinary Tract Infection and Enteritis à Treat with Cephalosporins and Gentamicin
- **(e) Pseudomonas :-** Produces Urinary Tract Infection, Enteritis à Treat with Carbenicillin, Piperacillin Or Gentamicin.

Superinfection (Contd...)

(D) Conditions Predisposing to Superinfection:-

(1) Immuno-compromised patients :- such as –

(i) AIDS –Patients (Acquired Immuno – Deficiency Syndrome)

(ii) Cancer Patients suffering from Leukaemias (Blood cancer) and other malignancies and treated with anti-cancer drugs and having low WBC counts & Leukopenia

(iii) Patients on Prolonged Corticosteroid Therapy

(2) Patients with Agranulocytosis

(3) Diabetic patients

(4) Patients with Disseminated Lupus Erythematosus (DLE)

Superinfection (Contd...)

- **(E) Measures To Minimize Superinfections :-**
- (i) Use of specific **Narrow spectrum antibiotics**
- (ii) **Restrict/Avoid use of antibiotics in viral infections, self-limiting or untreatable infections or trival infections**
- (iii) **Avoid unjudicious and prolong use of antibiotics**

Antimicrobial Drug Combinations

- **(I) Objectives of AMAs combinations :-**
 - (1) For specific purpose**
 - (2) For better results**
 - (3) For better patient compliance**
 - (4) To broaden antibacterial spectrum**
 - (5) To improve drug tolerability**
 - (6) to minimize development of drug resistance**
 - (7) To reduce or minimize chances of adverse drug reactions**

Antimicrobial Drug Combinations

- **(II) Advantages of AMAs combinations :-**
- **(1) To Broaden Antibacterial spectrum :-**
- **(a) Required to treat mixed infection :-**
- **Aerobic & anaerobic organisms produce mixed infections of Peritoneal cavity, Abdominal cavity, Urinary Tract, Genitourinary tract, Diabetic foot ulcers, Bed sores, Brain abscesses, Bronchial tract.**
- **Examples : Ciprofloxacin + Tinidazole**
- **Cephalosporins + Clindamycin**
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Antimicrobial Drug Combinations

- **(b) Treatment of severe infections :**
- To start empirical treatment in severe infections, till the blood/culture reports are awaited.
- **Examples :-**
- **Penicillin + Streptomycin**
- **Cephalosporin + Gentamicin + Clindamycin /metronidazole**
- **(C) Topically :-**
- For local effect on burns, wound, boils, cuts & surgical dressings
Combination of drugs can be used topically as ointment or dusting powders.
- **Examples :- Bacitracin + Neomycin + Polymyxin B**

Antimicrobial Drug Combinations

- **(2) To reduce incidence of adverse effects:-**
- Needed for AMAS with low safety margin
- **Examples :-**
- **(1) Amphotericin B + Rifampicin / Minocycline à**
Later drugs enhances the effect of Amphotericin B ,
thereby reduces its adverse effects
- **(2) Streptomycin + Penicillin G for SABE due to**
Strep. Faecalis à Combination reduces toxicity of
streptomycin

Antimicrobial Drug Combinations

- **(3) To Prevent Emergence of Resistance :-**
- **Combination of two or three AMAs for chronic infections needing prolonged therapy, reduces the incidence of development of resistance to individual drug .**
- **Examples :-**
- **(1) Rifampicin + Isoniazid + Pyrazinamide in Tuberculosis**
- **(2) Rifampicin + Ofloxacin + Minocycline in Leprosy**
- **(3) Omeprazole + Clarithromycin + Tinidazole for H. Pylori eradication in Peptic ulcers**
- **(4) Triple regimens in AIDS patients**

Antimicrobial Drug Combinations

(4) To achieve synergism :-

Synergism in terms of supra-additive effect, additive effect, indifference or antagonism can be achieved by combining two AMAs from different class

- **Synergistic effect :-** If MIC of each AMAs is reduced by 25%
- **Additive effect :-** If MIC of each is reduced by 25 – 50%
- **Antagonism effect :-** If MIC of each AMAs is reduced by more than 50%.

- Synergistic drug combination sensitizes the organisms & produce more lethal action than individual drugs.

- **Example :-**
- **Beta-lactum (Penicillin / Cephalosporin + Aminoglycosides)**

Antimicrobial Drug Combinations

(a) Two Bacteriostatic drugs combination :- are

Additive and not Synergistic

Examples :- Tetracycline + Chloramphenicol; Tetracycline + Erythromycin

However, two individual bacteriostatic drug produces supra-additive effect.

Example :- Sulfamethoxazole + Trimethoprim

Individually , these drugs are bacteriostatic, but when given in fixed dose combination they are bacteriocidal.

Example :- Amoxicillin + Clavulanic acid; Ampicillin + Salbactam

Clavulanic acid & Salbactam are Beta-lactamase inhibitors combined with Beta-lactum antibiotics Amoxicillin & Ampicillin are supra-additive against Beta-lactamase producing H. influenzae, N. Gonorrhoea

Antimicrobial Drug Combinations

(b) Two Bactericidal AMAs combination :- is Additive or sometime Synergistic, if organism is sensitive to both

- **Examples :-**
- **(i) Penicillin + Aminoglycosides (gentamicin) → Enterococcal SABC. Penicillin enhances penetration of aminoglycosides into the bacteria.**
- **(ii) Vancomycin + Gentamicin → Enterococcal SABC.**
- **(iii) Carbenecillin/Ticarcillin + Gentamicin → Pseudomonas infection in neutropenic patients**
- **(iv) Ceftazidime + Ciprofloxacin → Pseudomonas infections in orthopedic patients**
- **(v) Rifampicin + Isoniazid → in Tuberculosis**

Antimicrobial Drug Combinations

- (c) Combination of Bactericidal + Bacteriostatic :-
- May be Antagonistic or Synergistic, based on the organisms
- **Examples of Antagonism :-**
- **(i) Penicillin + Tetracycline/Chloramphenicol** in Pneumococcal infections. Penicillin being bacteriocidal, it acts on rapidly multiplying bacteria, while tetracycline/chloramphenicol being bacteriostatic retards multiplication.
- **(ii) Penicillin + Erythromycin** for Group A streptococci are antagonistic
- **(iii) Nalidixic acid + Nitrofurantoin** for E.coli are antagonistic

Antimicrobial Drug Combinations

- **Examples of drug synergism :-**
- **(i) Penicillin + Sulfonamides** for Actinomycosis
- **(ii) Streptomycin + Tetracycline** for Brucellosis
- **(iii) Sterptomycin + Chloramphenicol** for K. Pneumoniae
- **(iv) Rifampicin + Dapsone** for Leprosy
- **In above cases,** organisms have low sensitivity for bacteriocidal drugs, **hence synergism.**

Antimicrobial Drug Combinations

- **(III) Disadvantages of AMAs Combination Therapy :-**
- **1) Increase cost of therapy**
- **2) Increase incidence of adverse effects** due to enhancement of toxicity of one drug by another drug.
- **Example :- Vancomycin + Tobramycin produces nephrotoxicity**
- **3) Increase risk of contracting superinfections**
- **4) Resistance may be produced with inadequate use of non-synergistic drugs**