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Recommendations for Medical and Surgical Chemoprophylaxis

KEYWORDS

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ABSTRACT *Chemoprophylaxis is an approach towards prevention or suppression of a disease/ infection by administration of antimicrobials before clinical manifestation of disease/infection. A disease targeted chemoprophylaxis recommends prescribing antimicrobials in various settings e.g. post-exposure prophylaxis to prevent infection in patients with animal bites; whereas sometimes prophylaxis is directed towards prevention of any untoward infection in at risk patients. There is always a need for chemoprophylaxis before any major/minor surgery to prevent contracting any infection before, during or after surgery. Therefore present review emphasizes the use of specific and narrow spectrum antimicrobial, in appropriate dose and duration, for chemoprophylaxis so as to prevent super infections and development of resistance.*

Introduction:
Chemoprophylaxis is the practice of administering an antimicrobial agent for preventing an infection or for suppressing contacted infection before the clinical manifestations. Chemoprophylaxis is highly effective in some clinical settings. In others, it accounts for some of the most flagrant misuses of antimicrobials, is totally without value, and may be deleterious. Use of antimicrobial compounds to prevent infections remains controversial in numerous situations. In general, if a single, effective, nontoxic drug is used to prevent infection by a specific microorganism or to eradicate an early infection, then chemoprophylaxis frequently is successful. On the other hand, if the aim of prophylaxis is to prevent colonization or infection by any or all microorganisms present in the environment of a patient, then prophylaxis often fails (Katzung, 2009). Broadly chemoprophylaxis is of two types: (i) causal prophylaxis: complete prevention of infection by early elimination of invading or migrating causal agent e.g. no causal prophylaxis available against malaria. (ii) Clinical prophylaxis: implies the prevention of clinical symptoms, but does not necessarily mean elimination of infection. Chemoprophylaxis is influenced by host factors (like age, renal and hepatic function, local factors (pus or secretions at the site, haematomas), type of micro-organism and its sensitivity pattern, spectrum of activity of drug, type of activity (bactericidal/bacteristatic) and relative toxicity of drug meant for chemoprophylaxis (Murray, 2009; Cohen, 2004). The ideal antibiotic selected for chemoprophylaxis should be: Narrow spectrum single dose, cheap, with minimum adverse drug effects and toxicity. Alternatively chemoprophylaxis can also be categorized as disease targeted, post exposure or surgical (shown in table no. 1) (Wilson, 1995; Finberg, 2004; WHO, 2005; Welliver, 2001; WHO, 2006).

Table No. 1: Disease targeted and post- exposure prophylaxis

Disease	Indication(s)	Chemoprophylaxis
Rheumatic fever (Group A streptococci)	H/o of rheumatic fever or known rheumatic heart disease	• Oral Penicillin V 250mg BD daily • Erythromycin 250mg BD • Inj. Benzathine Penicillin 1.2L IM 4 weekly
Endocarditis	Dental, oral or upper respiratory tract procedures in at risk* patients.	A.Standard oral regimen 1. Amoxicillin 2.0 g PO 1 h before procedure B. Inability to take oral medication 1. Ampicillin 2.0 g IV or IM within 1 h before procedure C. Penicillin allergy 1. Cephalexin 2.0 g PO 1 h before procedure 2. Clindamycin 600 mg PO 1 h before procedure D. Penicillin allergy, inability to take oral medication 1. Cefazolin or ceftriaxone1.0 g IV or IM 30 min before procedure 2. Clindamycin 600 mg IV or IM 1 h before procedure
Malaria	• Travelers to areas endemic for chloroquine susceptible disease. • Travelers to areas endemic for chloroquine resistant disease.	Chloroquine sensitive Tab. Chloroquine 500mg base once weekly. Start 2 weeks prior & continue for 4weeks after travel.. Chloroquine resistant Atovaquone+Proguanil (Malarone) daily Mefloquine 250mg weekly
Tuberculosis	• Persons with +ve tuberculin tests and one or more of the following: HIV infection • Close contacts with newly diagnosed disease • Medical conditions with risk of acquiring tuberculosis.	Treatment of latent infection, Regimens INH 300mg daily for 9 months Or INH +Rifampicin daily for 6months Or Rifampicin for 4 months Rifampicin +Pyrazinamide for 2 months.
Influenza A and B	For contacts, unvaccinated geriatric patients, immunocompromised hosts, travelers, health care workers during outbreaks.	For Influenza A: M2 Ion Channel inhibitors: Amantadine (100mg b.d for 2 weeks) or Rimentadine. For Influenza B: Neuraminidase inhibitors: oseltamivir and zanamivir
Meningococcal Meningitis	Close contacts of case	Sulphadiazine for 4 days (only if strain is non-resistant) for household and close contacts. Start immunization in all cases (for serogroups A and C)

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Pneumococcal Meningitis (streptococcus pneumonia)	School going children, close contacts.	Penicillin : 2 doses of benzathine penicillin administered 1 month apart.(< 2years age) or Oral azithromycin prophylaxis (250 mg weekly for 2 weeks) or chemoprophylaxis with rifampicin (20 mg/kg, twice daily for 2 days) and clindamycin (25–30 mg/kg/day) or Ciprofloxacin (adult and child ≥12 years) 500 mg orally, as a single dose or Extended-spectrum cephalosporin, Trimethoprim-sulfamethoxazole.
Diphtheria	Unimmunized contacts, Household contacts and other close contacts of patient.	Single dose of i/m Penicillin (600,000 U) for persons < 6years. Penicillin (1.2MU) for persons >6 years. Or Oral erythromycin (30-50mg/kg; maximum 2gm/day) × 10 days.
HIV	Developing foetus of HIV + mother Health care workers exposed to blood after needle stick injury.	Two drug regime for low risk Zidovudine +Lamivudine Zidovudine+Lamivudine+Indinavir Three drug regime for high risk HIV Prophylaxis against opportunistic infections
Anthrax	Suspected exposure	–Oral Ciprofloxacin at the dose of 500 mg, 2x daily for 60 days – Oral Amoxicillin 500 mg, 3x daily for 60 days (prophylaxis in children)
H1N1 (Swine flu)	Household contacts, health care personnel, immunocompromised individuals, travelers, pregnant, children <5 years.	oseltamivir (>40kg body weight,75mg capsule o.d); <15kg, (30mg o.d),15-23kg(45mg o.d), 24-40kg (60mg o.d) All regimens for 10 days from the time of contact; Infants (6-11 months) 20mg o.d X 10 days. Not recommended for <3months.
Urinary Tract Infection (UTI)	Recurrent Infection	Trimethoprim- sulphamethoxazole

Prevention of infection in high risk situations: Few high risk conditions for chemoprophylaxis are: (a) Dental extractions, tonsillectomy, endoscopies can lead to endocarditis in patients with valvular defects by causing damage to mucosa harboring bacteria. (b) Before instrumentation or catheterization. (c) Chronic obstructive lung disease, chronic bronchitis. (d) Immunocompromised patients (receiving corticosteroids or antineoplastic agents, neutropenic patients).

Surgical Prophylaxis: Certain guidelines need to be taken care of before surgical prophylaxis: (1) history of anaphylaxis, hypotension, local swelling, urticaria or pruritic rash after use of penicillin. Always recommend an alternative for patients with allergy to penicillins or cephalosporins. (2) Another issue is over-diagnosis of an allergy, resulting in failure to use a beta-lactam when it would have been suitable. (3) The duration of prophylactic antibiotic therapy should be single dose except in instances of prolonged surgery or major blood-loss to prevent overprescribing of antibiotics and to prevent emergence of drug resistance. (4) The antibiotics selected for prophylaxis must cover the expected pathogens for that operative site. Recommended antibiotics in various types of surgical chemoprophylaxis have been shown in table no. 2 and 3.

Recommended antibiotics in clean surgical wounds: For major cardiothoracic, orthopedic or neurosurgeries most common organism involved are S. aureus, pseudomonas or gram –ve bacilli and cefazolin 1 g i/v is recommended as chemoprophylaxis dose. For Ophthalmic surgeries (S. aureus, gram-ve bacilli) Vancomycin (1g i/v); Gentamicin+neomycin+polymyxin eye drops are recommended at intervals up to 1st 24 hours (Katzung, 2009; Gilman, 2009).

Table No 2: Recommended antibiotics in Clean- Contaminated Wound (Harvey, 2009; Gilman, 2009; Kaplan, 2004)

Nature of surgery	Probable causative micro-organism	Recommended drug & dose(adult)	Time of administration
Head & Neck surgery	S.aureus and oral anaerobes	Cefazolin (1gm i/v) Clindamycin (600mg i/v) ±Gentamycin (1.5mg/kg i/v)	Induction of anaesthesia
Abdominal cholecystectomy		Cefazolin 91gm i/v)	Induction of anaesthesia
Abdominal appendecetomy		Cefoxitin or Cefotetan (1gm i/v)	Induction of anaesthesia
Colorectal		Electrolyte solution (4-5 lit)	Pre-operative day
Oral chemoprophylaxis		Erythromycin (1gm p.o) or metronidazole (500mg p.o) + neomycin 91gm p.o)	Pre-operative day and half hour before surgery
Par-enteral chemoprophylaxis	Enteric aerobes (E.coli, Klebsiella) Enteric anaerobes (B.fragilis, clostridium)	Cefotetan (1gm 12hrly, 2 doses) (P/E chemoprophylaxis required only if no lavage or oral antibiotics given pre-operatively)	
Obstetrics and gynecological			
Abdominal/vaginal hysterectomy		Ceftizoxime (1gm 12hrly , 2doses)	
Cesarean section following ROM	Aerobic & anaerobic streptococci from oral and cutaneous flora, Pasteurella multocida from animal bites	Cefoxitin (1gm 8hrly i/v, 3 doses); Ceftizoxime (1gm 12hrly i/v) 2doses) Clindamycin (600mg i/v)+ Gentamicin (1.5mg/kg i/v) for 3-5 days.	At induction of anesthesia or post cord clamp
High risk abortion		Cefazolin (1gm i/v)	
Urinary Tract Infections		Penicillin G (2 MU i/v); Doxycycline (300mg p.o); Cefazolin (1gm i/v)	

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Table No 3: Recommended antibiotics in Contaminated & Traumatic Injury (Harvey, 2009; Katzung, 2009; Gilman, 2009; Paul, 2004; Kaplan, 2004)

Nature of surgery	Probable causative micro-organism	Recommended drug, dose and duration
Orthopaedic	Staphylococci, Group A streptococci, clostridia	Cefazolin (1gm 8hrly i/v)
Bowel surgery, rupture viscus	Staphylococci, Group A streptococci, clostridia	V ancomycin* (1gm 12hrly i/v); Cefoxitin (1gm 8hrly i/v , 3 doses); Ceftizoxime (1gm 12hrly i/v) 2doses); Clindamycin (600mg i/v)+ Gentamicin (1.5mg/kg i/v) for 3-5 days.
Bites (Human & animals)	Aerobic and anaerobic streptococci from skin and oral flora. Pasteurella multocida in animal bites.	Amoxycillin+clavulanic acid (750+125mg b.d X 5days p.o; Alternative Doxycycline 100mg b.d X 5days p.o

i/v, Intravenous p.o, Per-oral
*Recommended for infections caused by methicillin resistant staphylococci or sensitivity to β- lactams.

Drawbacks of Chemoprophylaxis: All individuals who receive antibiotics for longer duration than recommended undergo alterations in the normal microbial flora of the intestine, upper respiratory and genitourinary tracts leading to emergence of super infection. Super infection is defined as the appearance of new infection during the chemotherapy due to removal of the inhibitory influence of the normal flora, which produces antibacterial substances and also presumably competes for essential nutrients, leading to dangerous consequences by appearance of drug resistant strains of infective bacteria i.e. enterobacteriaceae, Pseudomonas, and Candida or other fungi. The broader the antibacterial spectrum and the longer the period of antibiotic treatment, the greater is the alteration in the normal micro flora, and the greater is the possibility that a single, typically drug-resistant microorganism will become predominant, invade the host, and produce infection. Therefore it is recommended to use most specific and narrowest spectrum antibiotic whenever feasible. The fact that harmful effects may follow the therapeutic or prophylactic use of anti-infective agents should not discourage the physician from their administration in any situation in which they are definitely indicated. However, the clinician should use restraint in prescribing antimicrobial drugs in instances where evidence of infection is entirely lacking or, at most, only suggestive (Bennett, 2003).

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