DGAFMS Medical Memorandum No. 112

SEPTICAEMIAS

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SEPTICAEMIAS

Introduction

1. Septicaemia constitutes an important medical emergency. Septic shock is characterised by inadequate tissue perfusion, following bacteraemia most frequently with gram-negative enteric bacilli. In gram-negative bacteraemia, the shock syndrome is not due to bloodstream invasion with bacteria per se but is related to toxins from the organisms.

2. Gram-negative bacteraemia and septic shock occur primarily in hospitalised patients who usually have underlying diseases which render them susceptible to bloodstream invasion. Predisposing factors include diabetes mellitus, cirrhosis, leukemia, lymphoma or disseminated carcinoma ; cancer chemotherapy and immunosuppressive drugs ; and a variety of surgical procedures and antecedent infections in the urinary, biliary or gastrointestinal tracts. Particularly at risk are neonates, childbearing women, and elderly men with prostatic obstruction.

Diagnosis

3. The diagnosis of septic shock is not difficult in the presence of chills, fever, hypotension, oliguria, tachycardia, tachypnoea and an overt focus of infection. However, none of the obvious clues may be present. Elderly debilitated patients, in particular, may have severe infections in the absence offever. Unexplained hypotension, confusion, disorientation and hyperventilation without abnormal chest X-rays should call the diagnosis to mind.

Complications

4. Important complications determining prognosis in septicaemias are as under :—

(a) *Shock*. There are various stages of septic shock, from hyperventilation, respiratory alkalosis, vasodilation and high or normal cardiac output in early

shock, to perfusion failure characterised by high grade lactic acidaemia, metabolic acidosis, low cardiac output and small AV oxygen difference in irreversible, late shock. Moreover, in some patients there is little correlation between the outcome and the haemodynamic abnormalities.

(b) *Coagulation defects.* Usually result in disseminated intravascular coagulation. Unless there is bleeding, the coagulopathy requires no therapy and disappears as shock is treated.

(c) *Respiratory failure.* Respiratory failure is the most important cause of death in patients of shock, particularly after the haemodynamic aberrations have been corrected. Ths acute respiratory distress syndrome (ARDS) is characterised by pulmonary oedema, hemorrhage, atelectasis, hyaline membrane formation and formation of capillary thrombi.

(d) *Renal failure.* Oliguria occurs early in shock and is probably due to low intravascular volume and inadequate renal perfusion. If renal perfusion remains inadequate, acute tubular necrosis develops.

(e) *Cardiac failure.* Many patients with septic shock develop myocardial failure even though they were free of heart disease before development of shock.

Treatment

5. Where possible these patients should be treated in intensive care units in hospitals that have laboratories available for measurement of arterial pH, blood gases, blood lactate, renal function and electrolytes. Rational treatment of septic shock depends upon careful monitoring of patients. Specifically four basic indexes need to be monitored at the bedside.

(a) *Status of pulmonary circulation.* This should be measured by Swan-Ganz catheter or in its absence CVP should be measured.

(b) The *pulse pressure* serves as an estimate of stroke volume.

(c) *Cutaneous Vasoconstriction* provides a clue to peripheral resistance.

(d) *Hourly Urine output* should be used to monitor splanchnic blood flow and visceral perfusion.

Support of respiration

6. It is essential to establish an airway at the outset and to administer oxygen. Ventilatory support with a respirator should be employed early to avoid acidosis and hypoxia.

Volume Replacement

7. Blood volume should be made up with blood transfusion (if anaemia is present), plasma or other colloids ; and appropriate electrolyte solutions, primarily Isotonic dextrose saline and $7\frac{1}{2}\%$ sodium bicarbonate solution should be used. Bicarbonate should be given to increase the blood pH to about 7.2 to 7.3 and correct the acidosis. The quantity of fluid required in some cases may amount to 8 to 12 litres in a few hours.

Antibiotics

8. Blood cultures and cultures of relevant body fluids or exudates should be taken before instituting antimicrobial therapy. When the results of cultures and sensitivities are known, therapy should be adjusted appropriately. Drugs should be given intravenously and bactericidal agents should be used.

9. Clinical clues often guide the choice of antimicrobial to be used for example, a young woman with dysuria, chills, flank pain and shock is likely to have E. coli bacteraemia. Gram-negative sepsis in a burn patient is probably caused by Pseudomonas. When the cause of septic shock is unknown, therapy should be initiated with both Gentamicin (or Tobramycin) and a Cephalosporin or a penicillinase resistant penicillin. If Bacteroides is suspected, Chloramphenicol, Metronidazole, Clindamycin or Carbenicillin should be used. Metronidazole is effective in the treatment of serious anaerobic infections and is able to penetrate abcesses. Dosage and

spectrum of different antibiotics are given at Table I and II respectively.

Surgical intervention

10. Where required surgical intervention should be carried out, even if the patient is desperately ill. Operation should not be postponed "to get the patient in shape", because the condition will continue to deteriorate unless the septic focus is removed or drained.

Vasoactive drugs

11. Beta receptor stimulants dopamine/dobutamine) should be used. Dopamine hydrochloride should be started at 2 to 5 ug/kg/minute and the dose increased until urine flow and blood pressure respond.

Diuretics and digitalis

12. Once the volume status of the patient is repaired, furosemide should be given to keep the hourly urine output at a level higher than 30 to 40 mL/h. Digoxin may be beneficial in a patient who remains hypotensive despite an elevated CVP, but should be given cautiously.

Steroids

13. As soon as shock is recognised, use of methylprednisolone (30 mg/kg) or dexamethasone (3 mg/kg) is likely to be beneficial. Therapy is repeated after 4—6h interval in very serious cases, upto 24—48h

Failure of Therapy

14. The effect of antibiotic therapy on prognosis in Septicaemia may not be as great as might be expected. General condition and the presence or absence of shock are very important factors. If a patient remains febrile and sick after 48 hours of therapy, a total reassessment should be made. Most important is a complete physical examination looking for infectious foci. New blood cultures and culture of other material should be obtained. Any antibiotic therapy should be

appropriately changed according to the results of blood culture. If the original blood culture was positive and the organism was sensitive to the antibiotic in use ; the cause of lack of response is probably undrained pus somewhere. If the original blood cultures were negative and the patient remains febrile, antibiotics should be substituted with new ones. In a compromised host, other infections (fungi, viruses etc.), and other causes of fever like malignancies may be kept in mind. Some drug reactions may result in continued fever.

Pevention

15. The overall mortality rate of septic shock remains very high. Poor results are due to failure to institute therapy sufficiently early. Septic shock usually is recognised too late, after irreversible changes have taken place. A large number of patients who develop septic shock are in hospital before signs and symptoms of shock appear. It is essential to watch such patients for development of shock assiduously, to treat their infections vigorously and early, and to perform appropriate surgery before catastrophic complications set in. It is important to watch for infected venous and urinary catheters which may act as portals of entry for the organisims that cause gram-negative sepsis, and to remove them from all patients, as soon as possible. There is some evidence that early therapy of septic shock improves the ultimate outcome.

New Delhi

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LT GEN

DIRECTOR GENERAL ARMED FORCES

MEDICAL SERVICES

TABLE I

ANTIBIOTIC DOSAGE

Srl No	Antibiotic	Total Daily Dose		Interval between doses
		Child	Adult	
1	Penicillin G	200,000 units/kg/day	20 Million unit/day	2 to 4 hrly
2	Ampicillin	100 to 200 mg/kg/day	6 to 12 g/day	4 hrly
3	Amoxycillin	50 to 100 mg/kg/day	1.5 g/day	8 hrly
4	Cloxacillin	50 to 100 mg/kg /day	2 to 4 g/day	6 hrly
5	Carbenicillin	600 mg/kg/day	20 g/day	6 hrly
6	Ticarcillin	200 to 300 mg/kg/day	8 to 18 g/day	4 hrly
7	Azlocillin	300 mg/kg/day	8 to 18 g/day	4 hrly
8	Piperacillin	—	8 to 18 g/day	4 hrly
9	Cefazolin	—	4 to 6 g/day	6 hrly
10	Cefotaxime	200 mg/kg/day	12 g/day	4 hrly
11	Cefoperazone	150 mg/kg/day	8 to 12 g/day	6 to 8 hrly
12	Chloramphenicol	100 mg/kg/day	2 g/day	6 hrly
13	Gentamicin	2 to 2.5 mg/kg/day	3 to 5 mg/kg/day	8 hrly
14	Tobramycin	2 to 2.5 mg/kg/day	3 to 5 mg/kg/day	8 hrly
15	Amikacin	15 mg/kg/day	15 mg/kg /day	8 hrly
16	Metronidazole	30 mg/kg/day	1.5 g/day	8 hrly

NOTE :—

1. For patients with normal renal and hepatic functions.
2. Child doses should not exceed adult dose.
3. Neonatal dose is 30 to 50% reduced from child's dose.
4. Azlocillin not to be used in newborn.

ANTIBIOTIC AND ITS SPECTRUM	REMARKS
I. PENICILLINS	
(a) *Natural Pencillins—Penicillin G*	
Streptococcus species, Neisseria sp, Many anaerobes including Bacteroides and Fusobacterium, spirochaetes.	*Treatment of Choice* for Penumococcal and Meningococcal Meningitis and Strept. viridans endocarditis. Ineffective against most Staph. aureus.
(b) *Penicillinase Resistant Penicillins—Oxacillin, Cloxacillin, Naficillin*	
Staph, aureus, Strept. Pyogenes, Strept. penumoniae	*Drugs of choice for Penicillinase* producing Sta phylococci. Ineffective against enterococcus (S. faecalis) Naficillin :—more intrinsic activity against Staph. and Strept. Not substitutes for Penicillin G in the treatment of infections amenable to it.
(c) *Aminopenicillins—Ampicillin, Amoxicillin*	
Similar to Penicillin G, plus H. influenza Proteus mirabillis, E. coli Salmonella, Shingella.	Activity extended to include gram-negative organisms.
(d) *Carboxy penicillins—Carbenicillin, Ticarcillin*	
Spectrum of aminopenicillins plus Pseudomonas species, Enterobacter species and Proteus (indole positive)	Used in serious gram-negative infections. May precipitate Congestive Heart Failure due to excessive Sodium content in large doses. Hypokalemia and impairment of platelet aggregation are other side effects. Ticarcillin :—Four fold more active than Carbenicillin.
(e) *Ureido penicillins—Azlocillin, Piperacillin*	
Pseudomonas species. Pseudomonas Enterobacter, many Klebsiella.	Azlocillin :—10 times more active than Carbenicillin against Pseudomonas aervginose. Safer in renal failure. Piperacillin :—most active Penicillin against Pseudomonas and active against Klebsiella.

ANTIBIOTIC AND ITS SPECTRUM	REMARKS
II. CEPHALOSPORINS	
(a) *Ist generation—Cephalothin, Cefazolin, Cephalexin*	
Streptococci, Staph. aureus & epidermidis, E. coli, Kleb. pneumoniae, Proteus. mirabilis.	Good activity against gram positive bacteria and modest against gram-negative bctearia.
	Cephalothin :—given I/V only.
	Cefazolin :—parenteral, adjust dose in renal failure.
	Cephalexin :—Orally absorbed less active against Staph. aureus.
(b) *2nd generation—Cefamandole*	
As above, but more active against E. coli, Klebsiella, H. influenzae and indole positive proteus.	Increased activity against gram-negative organisms.
	Cefamandole :—parenteral, does not cross blood brain barrier.
(c) *3rd generation—Cefotaxime*	
Excellent against Streptococci (except S. faecalis), S. pneumoniae, H. influenzae, N. meningitidis, N. gonorrhoea, E. coli, Klebsiella.	Less active than 1st generation against gram positive cocci, more active than 2nd generation against gram negative micro organisms.
	Cefotaxime :—Parenteral, useful in meningitis.
(d) *3rd generation with good activity against Pseudomonas—Cefoperazone*	
Gram positive organisms, Enterobacteriaceae, and Pseudomonas aeruginosa.	*Most active against Pseudomonas* can cause bleeding due to hypoprothrombinemia.
III. AMINOGLYCOSIDES	
Gentamicin, Tobramycin, Amikacin	
Aerobic gram-negative bacilli, i.e. Enterobacteriaceae (E. coli, Klebsiella, Serratia, Euterobacter)	Nephrotoxicity and Ototoxicity are the common adverse effects.
Pseudomonas aeruginosa, some strains of proteus	Gentamicin :—1st line agent against gram-negative infection. More nephro toxic than other agents. Lease expensive.
Activity against gram positive bacteria is limited.	Tobramycin :—More active against pseudomonas, less nephrotoxic

ANTIBIOTIC AND ITS SPECTRUM	REMARKS
	Amikacin :—Broadest antimicrobial spectrum. Use if Gentamicin resistance is suspected.
IV. CHLORAMPHENICOL	
H. influenzae, N. meningitidis, N. gonorrhoeae, S. typhi, Brucella, Bordetalla, Most anaerobic bacteriae including gram positive cocci, clostridia, Bacteroides fragilis, Also against Rickettsia, Chlamydiae, Mycoplasma, Spirochaetes, Variable against *Entero-bacteriaea*	Bone marrow depression is the most important adverse affect and is dose related and sometimes due to idiosyncracy. Contraindicated in neonates who develop the "gray baby syndrome"
	I/M route is NOT recommended as absorption is unpredictable.
	Use :
	Therapy to be limited to infections where benefit outweighs the risk namely:—Typhoid fever, Bacterial meningitis (excellent in H. influenzae, alternate drug in N. meningitidis +S. pheumonia), Anaerobic infections specially originating in bowel, pelvis & in brain abscesses.
V. METRONIDAZOLE	
Bactericidal against B. fragilis, Fusobacterium, Clostridia.	Dose unchanged in renal failure to be reduced in hepatic disease.
Anaerobic gram positive cocci may be less susceptible.	Rare but important side effects are Neurotoxic reactions including ataxia, seizures, encephalopathy and peripheral neuropathy. The drug should be stopped if CNS complications occur.
Anti parasitic activity against E. histolytica, T. vaginalis, G. lamblia.	Not recommended in pregnancy. Effective in anaerobic infections especially intraabdominal, bacteremia, osteomyelitis and head and neck infections. Not very effective in aspiration pneumonia.

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