

# MANAGEMENT OF SEPTICAEMIA

*Lt. Col. Dr. S. B. Bajracharya M.D.*

*Head of Dept. of Medicine*

*Shree Birendra Hospital*

## INTRODUCTION

In spite of better critical care and new generation of antibiotic. Sepsis and septic shock are still big challenges to medical profession. Even in the best centres the mortality is in excess of 30%. Though in the western countries the increased incidence of sepsis is due to excessive use of IV catheter, urinary catheter, increase in use of cytotoxic immunosuppressive drugs and increase in antibiotic resistant infection, the scenario in our country is different.

We have more cases either due to late or none use of antibiotic.

## DEFINITION

**Sepsis:** Septicemia associated with a systemic response to infection including 2 or more tachypnoea, hypocapnia, tachycardia, hypothermia, hyperthermia, leucocytosis, and leucopenia,

**Sepsis syndrome:** Symptoms of sepsis accompanied by failure of one or more organs.

**Septic Shock:** Sepsis syndrome and hypotension, hypoperfusion without hypovolemia (hypotension unresponsive to IV fluid).

**Systemic inflammatory response syndrome (SIRS):** Systemic inflammatory response to a variety of service clinical insults including 2 or more features associated with sepsis.

*We had 8 cases of septic shock during last 2 years. The sites of infection were follow:-*

1. Genital tract infection following septic abortion	3
2. GI tract infection	1
3. Acute tonsillitis	1
4. Abscess of thigh	1
5. Chest infection	1
6. Subclavian catheter	1

Early diagnosis and treatment can reduce mortality considerably. We followed following line of management. Our mortality rate was 50%

## **ESSENTIALS IN THE MANAGEMENT OF SEPTICAEMIA ARE:**

1. To cut off inflow of organisms to the blood stream.
2. To kill or inhibit those already there.
3. Restore the perfusion of vital organs

All other considerations are secondary, & time should not be wasted on them initially.

Bleeding, Delirium, Pulmonary & Renal Failure will Take Care of themselves if the essentials have been achieved.

### **Operationally – The initial steps are:**

1. The removal or drainage of the source of sepsis if that is possible.
2. The selection of a suitable antibiotic or antibiotics.
3. The infusion of large quantities of fluid intravenously.

**CLINICAL ASSESSMENT**

1. Assess the severity of the patient's state.
2. The bedside chart – shows the height of fever & the speed of its rise.
3. Pulse Rate & BP are measured if not charted. Ideally they should be charted.
4. Look at the patient from foot end of the bed. You may see
  - Apathy
  - Clouding of consciousness
  - Tachypnoea
5. Other associated findings include
  - Skin Rashes or – jaundice
6. A rapid research for the source of injection follows.
7. Septicaemia in a patient from the Community look for signs of :-
  - Cutaneous ulcers
  - Pneumonia
  - Local or generalized peritonitis
  - Pyelonephritis
  - Pelvic Inflammatory disease
8. Septicaemia in a hospitalized patient look for:-
  - Intravascular Catheters
  - Monitoring Devices
  - Urinary Catheters
  - Surgical wounds
  - Deep infections of recent operation sites,
  - Pneumonia
  - Decubitus ulcer
9. This rapid assessment should take no more than 30 minutes.
10. A Tentative Diagnosis is made together with a guess at the responsible organism.
11. The most useful diagnostic specimens are taken & treatment instituted immediately.
12. X-rays, sonograms, CT scans & other time consuming investigators should be deferred until patient's condition stabilizes.

**LABORATORY INVESTIGATIONS**

- Certain lab parameters are deranged.
  - These include – I Blood & Urine Examination.
1. *In early stages of septicaemia*
    - a) Leukocytosis with a shift to the left.
    - b) Thrombocyto paenia
    - c) Hyperbili rubinaemia
    - d) Proteinurea
    - e) Lenkopaemia may occur. At times TLC is normal
    - f) The neutrophils may contain toxic granulations, Dohle bodies, or cytoplasmic vacuoli



- a. Early diagnosis & treatment which has been discussed.
  - b. Antibiotics & infection control.
  - c. IV fluid therapy, haemodynamic monitoring & cardiovascular support.
  - d. Interruption of pathogenetic sequence by inhibition of sepsis mediators.
  - e. Therapy of metabolic & other complications.
- b. Antibiotics & Infection Control**
- Treatment of the underlying infection is essential to treat septicaemia.
  - It is important to trace the source of sepsis to drain abscesses, pus collections & initiate appropriate antimicrobial therapy.
  - In dwelling IV catheters, may be the source & should be removed.
  - Urinary catheters should be checked & replaced if necessary.
  - Prompt & appropriate institution of antibiotic improve survival & decrease incidence of shock in septicaemia.
  - Relevant blood cultures should be taken before starting antibiotics but therapy should not be delayed just to obtain cultures.
  - Choose antibiotics based on source of infection. If no source is identified, give broad spectrum cover.
  - Therapy can be modified based on results of blood culture.
  - The drugs chosen should be:-
    - a) Bactericidal
    - b) Given IV
    - c) Dosage should be maximum recommended.
  - The choice of initial antibiotic combination should be based on the local bacteriologic pattern.
  - As many cases of septicaemia occur in hospital setting & organisms are often resistant to common antibiotics, more aggressive therapy may be required.
  - Each hospital should have its own antibiotic policy.
  - A guideline is shown as follows.

**Table**

S.No.	Source of infection	Antibiotic Choice
1.	Intrabdominal infection (Gram-ve anaerobes)	Ampicillin Metronidazole Gentamycin
2.	UTI (Gram negative)	Ampicillin Gentamycin or Cephalosporin (ceftazidime)
3.	Pneumonia Gram positive in healthy Community acquired Gram negative in nosocomial or immunocompromised	Penicillin + Gentamicin or cloxacillin + Gentamicin Ceftazidime
4.	Infected IV catheter (Usually staphylococci)	Vancomycin + Gentamicin
5.	No obvious Source	Vancomycin + Metronidazole Gentamicin Or Ceftazidime + Gentamicin
6.	For Pseudomonas	Ceftazidime
7.	Skin infection (Usually staphylococcus)	Cloxacillin or Vancomycin

## C. IV fluid therapy, haemodynamic

## Monitoring &amp; Cardio Vascular Support

- **A large bore IV line to be inserted soon**
  - **Give fluid till patient improves or there is evidence of fluid overload.**
  - **In milder cases, this can be monitored by regular pulse, BP, & respiratory rate measurements.**
  - Watch JVP & listen regularly for basal creps.
  - Give 1 liter ringer's lactate in first hour. If marked hypotension is present, it can be given rapidly & followed by a second litre – then reassess the patient.
  - If BP rises to normal, pulse slows, respiration is no faster, patient is alert & oriented urine outflow adequate – well good.
  - Slow IV fluid administration to 1 litre every 6 hours & wait events.
  - If patient fails to respond to simple management, or is desperately ill (? Septic shock), full resources of an ICU should be available.
  - Restore adequate O<sub>2</sub> & substrate delivery to the tissues.
  - Monitor Pulmonary capillary wedge pressor or CVP is ideal in this setting. To avoid Pulmonary edema – PCWP should be between 12 to 15 mm Hg or the CVP between 10 & 12 cm of H<sub>2</sub>O.
  - Urine output should be kept above 30 ml/hour by continuing fluid administration. A diuretic such as frusemide may be used if needed.
  - In about 1/3 rd of patients – hypotension responds to fluid resuscitation.
  - A reasonable goal is to maintain mean arterial pressure (MAD) > 60 mmHg & systolic pressure. 90 mmHg.
  - Pressor agents should be considered when patient has failed to respond to maximum fluid repletion.
  - Dopamine is the most widely used pressor agent. When given in low doses (5-10 µg/kg/min it has β<sub>1</sub> adrenergic effects, increase in Urine output & BP. At this dose it increases flow to vital area by stimulating dopaminergic receptors; caution is necessary as doses > 20 µg/kg/min stimulate & adrenergic receptors & can cause peripheral vaso constriction with ischaemia & gangrene.
  - Because of its β<sub>1</sub> stimulatory effect, more epinephrine (10-15 µg/kg/min) should be carefully titrated to achieve a mean BP of at least 60 mm Hg, this agent is used in patients who are hypotensive despite dopamine therapy.
- Low dose Dopamine (1-4 µg/kg/min) may be combined with norepinephrine for adequate renal & intestinal perfusion & achieve maximal pressor support.
- Ventilator therapy is indicated for progressive hypoxemia, hypercapnia, neurologic deterioration of respiratory muscle failure.
- Intubation is often done to ensure adequate oxygenation, divert blood from the muscles of respiration & reduce cardiac overload.
- Blood of packed cells transfusion is indicated if oxygen delivery is compromised by a low Hb level.

## D. Interruption of Pathogenetic sequence by inhibition of Sepsis Mediators.

- Despite improvement in the management of septicaemia, the mortality of severe septicaemia (Sepsic shock) remains 50-75%.
- This has led to the manipulation of exogenous & endogenous factors that seem to mediate tissue damage & endogenous factors that seem to mediate tissue damage & are important factors in pathogenesis of septic shock.



## AGENTS USED

1. Anti endotoxin agents
  - Lipid – A component of bacterial endotoxin is responsible for severe septicaemia leading to septic shock.
  - Antibodies to lipid A have been developed to neutralize its effects.
  - These antibodies which have been used clinically in trials include:-
- a. Murine 1 gm anti-lipid A monoconal antibody designated E5 was used. Dosage – 2 mg/kg E% hours apart. There was significant benefit in pts/with gram negative infection but not in shock. No benefit to its with gram-ve infection who were in shock.
- b. Antibody to endotoxin glycolipid, (HA-IA) was used. If pts, with gram-ve bacteraemia it reduced mortality from 49% in placebo treated patients to 30% in HA-IA recipients. HA-IA was protective in bacteremic patients who were in shock at presentation.
2. Anti – Mediator Agents
  - a. High dose corticosteroids 2 large scale randomized clinical trials of high dose methyl prednisolone therapy in patients with sepsis indicated that the regimens used did not prevent death or reverse septic shock. Therefore high dose glucocorticoid therapy is not recommended.
  - b. Tumor necrosis factor (TNF) & Inter Leukin – 1 (IL-1)
    - Cytokines TNF & IL-1 are both increased in the circulation of animals & humans who have received endotoxin or have septic shock.
    - Potential advantage in making TNF a target for intervention rather than endotoxin is the possibility that TNF might play a role in the pathogenesis of shock due to gram+ve bacteria.
    - In animal experiments, anti TNF antibody has been shown to prevent mortality both after shock induced by E. coli & St. aureus.
    - Another innovative method is the use of soluble receptors for TNF which could bind the cytokine in vivo, thus, inactivating it.
    - Other therapeutic measure in developmental stage includes the use of IL-1 receptor antagonist.
- E. Therapy of Metabolic & other Complications
  - Sodium bicarbonate is sometimes administered for reverse metabolic acidosis (Arterial pH < 7.2) Efficacy is not established.
  - DIC if complicated by major bleeding should be treated with transfusion of Fresh frozen plasma & Platelets.
  - Successful treatment of the underlying infection is necessary to reverse both acidosis & DIC.
  - ARDS & Acute renal failure are other complications which need energetic treatment.

## PROGNOSIS

1. General condition of the patient is the most important single factor. The mortality rises with age.
2. Species of the organism – Pseudomonas aeruginosa causes very high mortality is lower.
3. Infection at primary site may lead to such debilitation that patient dies of diseases of the bedridden bedsores. Pulmonary emboli & broncho pneumonia (e.g. extensive pneumonia, meningitis widespread intraperitoneal infection)
4. Presence of shock is associated with increased mortality.
5. A normal or subnormal temperature in septicaemia is a bad prognostic sign.
6. Appropriate use of antibiotics improves survival in septicaemia.

## FUTURE TRENDS

### 1. Future markers of sepsis

- As present no readily available markers allow rapid indication of sepsis.
- Recent studies show that in patients with sepsis, the level of endotoxin, il-1b, TNF & il-6 are elevated.
- In future, the rapid lab measurements of cytokines responsible for the inflammatory mediator systems may provide an early diagnosis in patients prone to develop sepsis.

### 2. Anti mediator agents

Apart from agents already covered other investigational compounds include.

- Platelet aggregating factor (PAF) antagonists
- Nitric oxide synthase inhibitors
- Pentoxifyline
- Soluble complement receptors (CR1)
- Anticoagulant such as:-
- Recombinant &, antitrypsin pittsburgh
- Antithrombin & protein C.

## REFERENCE

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