Management of Septic Shock

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Septic Shock:-

In sepsis associated with hypotension, besides in adequate fluid and perfusion, abnormalities may include, (but are not limited to) lactic acidosis, oliquria, or acute alteration in mental status. Sepsis is defined as systemic response to infection. In the absence of infection, it is called **Systemic Inflammatory Response Syndrome** and is characterized by at least two of the following:-

- Temperature greater than 38° or less than 36°.
- Heart rate greater than 90 beats per minute.
- Respiratory rate more than 20 per minute in Adults.
- Or $PaCO_2$ less than 32 mmHg.

Alteration in white blood cell count ($>12000mm^3$or $<4000mm^3$).[l]

The early phase of septic shock may produce symptoms and signs of volume depletion such as dry mucous membrane and cool clammy skin, tachycardia, bounding pulse with a widened pulse pressure, and cold extremities. Signs of possible infection include fever, localized erythema or tenderness, pulmonary consolidation, abdoyminal tenderness, and meningisms. Signs of end organ hypoperfusion include tachycardia oliquria, cyanosis, mottling of the skin, digital ischemia, altered mental status.

Laboratory Study:-

This includes arterial blood gases, lactic acid level, serum electrolytes, renal function, liver enzyme level, chest radiograph, cultures of blood, urine, sputum, and C.S.F. IF disseminated intravascular coagulation is suspected, fibrinogen, platelet count, PT, and PTT should be performed. [2]

Pathoyhsiolgy:-

Local inflammation and substances produced by the organisms, especially endotoxin, activate neutrophills, monocytes, and tissue macrophages.

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This results in a cascade of pro-inflammatory and anti-inflammatory cytokines and other mediators, such as Interlaken 1, Interlaken 8, Interlaken 10, tumor necrosis factor-alpha, prostaglandin E_1? endogenous corticosteroids, and catecholamines. The effects of this complex mediators cascade include cellular chemotaxis, endothelial injury and activation of the coagulation process. [3]

The initial cardiovascular response includes:-

Decreased systemic vascular resistance and depressed ventricular function. Low systemic vascular resistance occurs in response to substances elaborated from infecting agents, cytokines, mediators such as nitric oxide, and down regulation of peripheral catecholamine receptors. If the initial cardiovascular response is u not compensated, generalized tissue hypoperfusion results. [4]

Aggressive fluid resuscitation may improve cardiac output and systemic blood pressure resulting in a hemodynamic pattern of septic shock (ie, high cardiac index and low systemic vascular resistance). The response to volume loading in survivors of sepsis is ventricular dilatation. [5] while non survivors show little change in cardiac size on postmortem. However, despite improvement in central hemodynamics, the abnormalities in regional and microcirculatory blood flow often persist. The abnormalities may lead to cellular dysfunction, lactic acidosis, and ultimately multi-organ failure. Death from septic shock usually results from rapid and overwhelming progression of sepsis unresponsive to all therapeutic maneuvers, multi-organ failure, or secondary nosocomial infection 9from hospital organisms) or complications.

Complications:-

1. ARDS (Acute Respiratory Distress Syndrome): Is a major complication of sepsis and septic shock at a rate from 6-18%.
2. DIC (Disseminated Intravascular Coagulation): Is a major complication of sepsis and septic shock at a rate from 8-19% and 38% respectively.
3. ARF (Acute Renal Failure): At a rate of 51% in patients with septic shock.
4. Death is possible.

Management:-

Immediate resuscitation and stabilization

of the respiratory and cardiovascular systems are a priority in the managements of patients with septic shock. [6]

I. Pulmonary Dysfunction:

In septic patients many alteration in pulmonary function have been observed:

1. Significant disturbances of gas exchanges due to extensive right-to-left intrapulmonary shunting of blood flow.
2. Decreased lung compliance
3. Increased air way resistance related to small air way and alveolar collapse
4. increased pulmonary ventilation
5. Impairment of muscle efficiency.

Therefore, ventilatory support is an important first step:

1. O_2 should be administered immediately by a mask.
2. Arterial blood gases should be measured, arterial oxyhaemoglobin saturation should be maintained above 90% for e.g. by CPAP (Continuous Positive Air Pressure).
3. If this supportive measure is ineffective, ETT (Endo tracheal Tube) should be placed immediately with controlled ventilation if the PaO_2 is < 60 mmHg despite high flow of oxygen, respiratory rate more than 35 breath /min and vital capacity below 15ml/kg.
4. PEEP (Positive End Expiratory Pressure): low PEEP 5-10 cm H_20.

A balanced use of PEEP and supplemental oxygen can usually achieve an arterial saturation of 90%; about 85% of patients with septic shock require ventilatory support. [7]

II. Cardiovascular Dysfunction:

It is important to restore and maintain hemodynamic stability. Clinical parameters such as conscious level, heart rate, blood pressure, urine output and skin perfusion, with CVP (central venous pressure) and PCWP (pulmonary capillary wedge pressure) are important for restoring mean arterial pressure to 65-75 mmHg to improve organ perfusion. [8]

Fluids:-

The goal of fluid therapy is rapid volume expansion, which result in increased cardiac output and O_2 delivery, because of the vasodilatation and capillary leak that occur in septic shock. Our goal is to increase mean arterial pressure to 65-75 mmHg. Most adult patients require 1-2 litter of colloid or 4-8 litter of crystalloid to adequately restore circulating volume. The adult does of fluid crystalloid is 1-2 litter initially, followed by reassessment of hemodynamic response, while pediatric does is 20 ml/kg. IV (Intra Venous) initially administered rapidly, usually over 20-30 min. The major complication is interstitial oedema. Oedema of extremities is unsightly but insignificant complication. Brain & lung oedema potentially fatal, so the monitoring of cardiovascular and pulmonary functions are required. [9]

Fluids should be stopped when desired hemodynamic response is seen or pulmonary oedema developed. If the patient needs colloids, albumin, for certain types of shock or impending shock, is useful for plasma volume expansion and maintenance of cardiac output. A solution of isotonic sodium chloride and 5% albumin is available for volume resuscitation. Adult does is 250-500 ml.I.V. over 20-30 min with reassessment of hemodynamic response. Pediatric does is 4-5 ml/kg over 30 min.

If the hypotension is not responding to fluid therapy:

1. Alpha-adrenergic agonist are used. One drug that can boost systemic vascular resistance e.g epinephrine from 1-10 microgram/kg/min, if higher doses are needed, nor epinephrine (2-20 microgram/min) is added
2. Dobutamine 5-15 microgram to enhance contractility without excess tachycardia, dysrythmia or vasoconstriction.
3. Dopamine (2-5 microgram/kg/min) to preserve renal cortical blood flow, higher doses (4-12 microgram/kg/min) increase HR, contractility, venous tone and preload.
4. Sodium nitroprsside (0.1-5 microgram/min) for arterial dilatation to reduce after load and allow greater ejection from a depressed left ventricle.
5. Nitroglycerine (25-250 microgram/min) for venodilatation with minimal arterial dilatation.

Increased production of lactic acid is the result of global or regional ischemia. Lactic acidosis should be managed by treating the underlying disorder. The administration of bicarbonate is not beneficial to cardiovascular performance and should be reserved until Ph is below 7.2. [10]

III. Renal Dysfunction:

Hypotension and oliguria in septic patients are initially treated with rapid intravenous fluid administration. Repeated infusion of 0.5 litter boluses of fluid, each over 5-15 min is given until the B.P and urine output increase to acceptable level, or until signs of pulmonary congestion are seen as elevated jugular venous pressure with aggressive hemodynamic monitoring. [11]

Dialysis is required in fewer than 5% of patients with renal dysfunction.

IV. Antibiotics:

1. Pneumonia:-Second or third generation cephalosporin plus macrolide.
2. Urinary tract:-Ampicillin plus gentamicin or third generation cephalosporin.

3. Skin or soft tissue:-Nafacillin sodium (NaFcil, Nallpen) add metronidazole or clindamycin if anaerobic infection suspected.
4. Meningitis:-Third generation cephalosporin.
5. Intra abdominal:-Third generation cephalosporin plus metronidazol or clindamycin.
6. Primary bacteremia:-Ticarcillin and clavulanate potassium (Timentin) or piperacillinand tazobactam.

V. Nutritional Support of the Septic Patient:-fl21

With adequate nutritional support, reduction in morbidity and mortality has been observed. An estimate of energy requirements can be made using the Harris-Benedict equation of basal energy expenditure (BEE) where H= Height in cm, W=Weight in kg and A= Age in year.

BEE (Male) = 660 + (13.7 x W) + (5 x H) - (6.8 x A) kcal day -1 BEE (Female) = 655 + (9.6 x W) + (1.8 x H) - (4.7 x A) kcal day Total Energy = BEE x (Activity Factor) x (Stress Factor) Activity Factor: 1.2 Stress Factor: 1.2 mild 1.5 moderate 1.8 severe

Future Perspective:-

1. Anti-Endotoxin Therapy:- Early trials of Anti-endotoxin therapy with the human being and murine, monoclonal antibodies against endotoxin have demonstrated a decrease in the development of multiple organ dysfunction syndrome.
2. Filtration: The theoretical basis for this therapeutic strategy is the removal of the inflammatory mediators from the circulation by filtration, haemofiltration, or plasma filtration.
3. Selective Decontamination of the Digestive Tract: Therapy typically consists of oral administration of aminoglycoside, colistin and omphotericin B. Selective decontamination targets the potentially pathogeneitical gram-negative bacteria in the proximal gastrointestinal tract to avoid colonization of the respiratory system, which caused by organism from the GIT.
4. NSAID:- It inhibit cyclo-oxygenase which reduce the production of metabolites such as thromboxane A_2 (vasoconstrictor), prostcyclin (vasodilator) and prostaglandin E_2.
5. Drotrecogin Alpha-Therapy:- Drotrecogin alpha is recombinant form of human activated protein C, it has an anticoagulant action. Activated protein C inactivate factors Va and Villa, therapy preventing the generating of thrombin which decrease inflammation by inhabiting platelet activation, neutrrophil recruitment and mast-cell degranulation. Activated protein C has direct anti-inflammatory properties including blocking of the production of cytokines by monocytes and blocking cell adhesion.
6. Intensive Insulin Therapy in the ICU:- The aim of intensive insulin therapy is to maintain blood glucose level at 80-110 milligram/dl by administering insulin. Intensive insulin therapy was associated with an improvement of prognosis of septic patients compared with patients under conventional therapy in which glucose level range between 180- 200 milligram/dl.
7. Endothelial Cell Replacement:- It is well know that the endothelial cell play an active role in the pathophysiology of septic shock; these cells are frequently damaged or die as a result of the septic response, endothelial cell replacement may have in the future a role in the management of critically ill septic patients.
8. Immunomodulation in sepsis:- The I.V administration of immunoglobulin (IG) will neutralize and apsonize antibodies. This immunoglobulin may increase serum bactericidal activity, stimulateleucocytes and neutralize endotoxin and exotoxin.

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