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# Drug Related Problems that Occurred in Patient Sepsis Macrovascular Disease Complications General Hospital Treatment Room Central of the Army (Army Hospital) Gatot Subroto

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*Abstract-* Sepsis is a systemic inflammatory response syndrome: clinical inflammatory response to disturbances that cause infection or not infection1. Patient entered in the Emergency Room (ER) 8 October 2014, the diagnosis of sepsis patient ec furnier gangrene (scrotum), Haematemesis ec gastropathy uremikum, CKD stage V on HD with anemia, metabolic acidosis, CHF fc II, type II diabetes mellitus, hypertension, hepatitis B therapy received treatment for at GatotSubroto Army Hospital namely, Lasix, D40%, Insulin (Novorapid, Humalog), Meropenem, Levofloxacin, Farmadol, Omeprazole, Transamin, Vitamin K, Sodium Bicarbonate, Calcium Carbonate, Folic Acid, Vitamin B12, Valsartan, Amlodipine, Transfusion Package Red Cells (PRC), Triofusin e 1000, Tramal, Ca Gluconate, Metronidazole, Cefoperazone Sulbactam, Albumin transfusion, transfusion Fresh Frozen Plasma (FFP), the result of monitoring drug therapy patient obtained their multiple DRPs (*Drug Related Problems*), correlation between therapy with disease, Selection of appropriate medication, dosage regimen, interactions and contraindications.

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# Drug Related Problems that Occurred in Patient Sepsis Macrovascular Disease Complications General Hospital Treatment Room Central of the Army (Army Hospital) Gatot Subroto

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#### I. INTRODUCTION

epsis presence of pathogenic microorganisms or their toxins in the blood and other tissues, Systemic inflammatory response syndrome: clinical inflammatory response to disturbances that cause infection or not infection<sup>1</sup>. Responses appear in the form of  $\geq$  2 the following conditions: temperature > 38°C or < 36°C, frequency heart rate > 90 beats/min, respiratory frequency > 20 breaths/min, the white blood cells > 12000 cells/mL or < 4000 cells/mL or > 10% in the form of immature<sup>1</sup>. Severe sepsis: sepsis associated with organ dysfunction, septic shock: sepsis with hypotension simultaneously the presence of perfusion abnormalities<sup>1</sup>. Causinga frequent site of infection sepsis (21-68% Respiratory tract, urinary Channels 14-18%, 14-22% Intra Abdominal cavity): Sepsis by gramnegative bacteria (approximately 38% of the incidence Escherichia coli and Pseudomonas of sepsis) aeruginosa is bacteria the most frequently isolated in

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sepsis, Gram-positive (40%): *Staphylococcus aureus, Streptococcus pneumoniae, Staphylococcus coagulase negative and, Enterococcus.* The cause of fungal sepsis (17%): *Candida albicans* frequently causes sepsis in hospital patient<sup>1</sup>.

# II. CLINICAL EVALUATION

While in hospital the patient was given medication therapy are: Lasix 18 ampoules / 24 hours up to 1,5cc / hour because Lasix is very effective to cope with edema administration IVFD to the effect that faster with gradual dose. D40% 2 flacon / 3 hours up to 16 cc / hour as a replacement fluid and energizing, glucose solution is administered in treatment with Calcium, Sodium Bicarbonate, and Insulin for the emergency management of hyperkalemia. Triofusin e 1000 500 cc / 24 hours for obtaining calories and electrolytes needed through total and partial parenteral nutrition in patient with diabetes needs to be done to monitor blood sugar levels<sup>2</sup>.

Insulin 0,5 units / hour in NaCl 0,9% for patient undergoing surgery and require insulin infusion intravenously for 12 hours or more, the speed of infusion of insulin if blood sugar < 4 mmol / liter is given 0,5 units / hour for onward adjusted to the patient's clinical condition, after the patient began to eat and drink, give insulin subcutaneously use multiples of 4 units of insulin applies if < 200 mg / dL = 0 units, 201 - 250 mg / dL = 4 units, 251 - 300 mg / dL = 8 units, 301 - 350 mg / dL = 12 units, > 351 mg / dL = 16 units beyond<sup>2</sup>.

Meropenem 1 gram 3 times daily in this case as empirical therapy, while awaiting culture results come out, Meropenem be an option because of its broad spectrum for infection of gram-positive and gramnegative, aerobic and anaerobic, tousesoshould be based on culture results, while for patient impaired liver function and impaired renal function the dose and treatment regiment adapted to the patient's clinical condition, Cefoperazone Sulbactam 2 times a day 1 gram for gram-positive need for strong administration drip for 1 hour, 1 time a day Levofloxacin 500 mg is indicated for patient who have urinary tract infections are caused by infection with gram-positive and gramnegative, and dose adjustment regiment not promising therapy for patient with impaired renal function and liver function disorders, Metronidazole 500 mg 3 times also used for gynecological surgery sepsis with major activity against anaerobic bacteria colonic<sup>2.3</sup>.

Omeprazole 40 mg 2 times a day as therapy uremikum gastropathy and gastric ulcers and reduction during general anesthesia (acid aspiration prophylaxis) is given 40 mg in the afternoon and one day prior to surgery and then 40 mg 2-6 hours before surgery, Inpepsa suspension effective in treating ulcers stomach, protecting the mucosa from acid-pepsin in gastric ulcer timing of 2 gram 2 times a day (morning and before bed at night) or 1 gram 4 times a day 1 hour before meals and before bed at night, given for 4-6 weeks<sup>2</sup>.

Tramal 100 mg 3 times daily for pain, Farmadol given 3 times 1 gram to address moderate pain till mild postoperative pain and fever, Ca Gluconate quickly can lead to vasodilation of blood vessels, decrease in blood pressure, bradycardia and cardiac arrhythmias, and cardiac cause arrest therefore IV even can administration either bolus or continuous need to monitor blood pressure and pulse of this reaction is due to a decrease in potassium drastically in rapid decrease in potassium will result in a decrease in contractile muscle cells, including heart muscle cells resulting in a decrease in pulse and vasodilatation<sup>2,3</sup>.

Transamin injection of 500 mg 3 times a day is given to inhibit fibrinolysis so it can be useful to prevent bleeding, is used in patient with mild renal function disorders at the recommended dose reduction, whereas for patient with severe renal function impairment and avoid use in patient with impaired function liver needs to be monitored, Vitamin K 3 times daily 10 mg is needed for the production of blood clotting factors, for patient impaired liver function may have deficiencies vitamin K <sup>2,3</sup>

Sodium Bicarbonate 1 gram 3 times daily to cope with metabolic acidosis, in severe cases can be administered by intravenous Sodium Bicarbonate, Calcium Carbonate 500 mg 3 times daily is used as a phosphate binder in the treatment of hyperphosphatemia in renal failure complications<sup>2,3</sup>.

Folic Acid 15 mg 1 time a day is required for nucleoprotein synthesis and maintenance of normal erythropoiesis, folic acid stimulates the production of red blood cells and white blood cells, Vitamin  $B_{12}$  50 mg 3 times daily is important for growth, cell reproduction hematopoiesis, and nucleoprotein synthesis and meilin, Vitamin  $B_{12}$  also plays a role in the formation of red blood cells through the activity of folic acid coenzyme<sup>2</sup>.

Valsartan 160 mg 1 time a day for the treatment of hypertension that can be combined with other antihypertensives, Valsartan may be given to patient with heart failure, patient with hemodialysis, the patient is low in sodium, this group does not inhibit the breakdown of bradykinin that does not cause a dry cough, Amlodipine1 time a day 10 mg as antihypertensive, how it works inhibits calcium ion influx through the slow channel membran active cell, thereby affecting cardiac myocardial cells, and vascular smooth muscle cells and reducethe ability of myocardial contraction, the formation and propagation of electrical impulses in the heart, and systemic or coronary vascular tone, Amlodipine did not reduce myocardial contractility and does not cause deterioration in heart failure with a longer tenure so that it can be given once a day<sup>2,3</sup>.

PRC 500 cc of blood transfusion aims to improve the oxygenation of tissues and organs with a target of 8 g / dL, transfusion Albumin to overcome the shortage of Albumin in the body, can lead to instability Albumin shortage of water in the blood plasma, so that the blood volume is unstable and undergo body hoarding fluid which is often characterized by swelling, Albumin also act as transport in the body, including some elements of drugs and assist in the formation of a new body tissue, addition of Albumin transfusion transfusion patient also in Fresh Frozen Plasma (FFP) contains all plasma proteins that are fresh frozen plasma the goal is to reach 30% of normal clotting factor concentrations<sup>2</sup>.

#### III. Dosage and how to use

Lasix initial dose of 250 mg to 4 mg / min for 1 hour, the dose may be increased to 1 grams can be repeated every 24 hours. D40% given 1-3 liters / day, Triofusin e 1000 500 cc for 24 hours, use multiples of 4 units of insulin effect, if the blood glucose < 200 mg / dL = 0 unit, 201 - 250 mg / dL = 4 units, 251 - 300 mg / dL = 8 units, 301 – 350 mg / dL = 12 units, > 351 mg / dL = 16 units onwards. Meropenem 250 mg every 24 hours after the HD 500 mg every 8 hours, Cefoperazone Sulbactam 500 mg every 12 hours up to 1 gram a day, the initial dose after Hemodialysis Levofloxacin 500 mg to 250 mg every subsequent 48 hours for 7 - 14 days, Metronidazole 500 mg every 8 hours, Omeprazole 40 mg every 24 hours, Ranitidine 50 mg every 6-8 hours, Tramal 50 - 100 mg every 4 - 6 hours, Farmadol 1 g every 4 - 6 hours maximum 4 grams / day, Cagluconate 10 ml (2, 25 mmol) - 40 ml (40 mmol) of 10% / day, Transamin injection of 500 mg - 1 g every 8 hours, 10 mg Vitamin K Injection for 24 hours<sup>2,3</sup>.

Valsartan 40 mg every 12 hours dose adjustment 80 - 160 mg every 12 hours, Amlodipine 5 mg - 10 mg every 24 hours, Inpepsa suspension 2 - 4 g every 12 hours for 4 - 6 weeks up to 8 grams, 500 mg Sodium Bicarbonate rapid dehydration every 3-4 hours, later every 12 hours, Calcium Carbonate 500 mg every 8 hours, Paracetamol 500 mg - 1 grams every 4 - 6 hours maximum 4 grams, Folic Acid 5 mg every 24 hours depending on the disease Basically, Vitamin B12 50 -150 mcg or more given between meals every 8 hours<sup>2,3</sup>. Blood transfusion Package Red Cells (PRC), Albumin transfusion, Transfusion of Fresh Frozen Plasma (FFP)

# IV. LABORATORY RESULTS

Examination	Abnormal values	Normal value
	Routine Hematology	
Hemoglobin	7,8 *	13-18 g / dl
Hematocrit	23 *	40-52%
Erythrocyte	2,9 *	4,3 to 6,0 million / mL
Leukosite	14080 *	4800-10800µL
MCV	78 *	80-96fL
	Coagulation	
PT	13,4 *	10,2 to 12,2 seconds
APTT	48,4 *	29 to 40,2 seconds
Clinical Chemistry blood gas analysis		
pН	7,477 *	7,37 to 7,45
pCO <sub>2</sub>	23,2 *	33-44mmHg
pO <sub>2</sub>	42,7 *	71-104mmhg
Bicarbonate (HCO <sub>3</sub> )	17,3 *	22-29mmol / L
Base excess (BE)	-4,6	(-2) -3mmol / L
O <sub>2</sub> saturation	82,7 *	94-98%
Albumin	24 *	3,8 to 5,1 g / dL
Urea	172 *	20-50mg / dl
Creatinine	11,6 *	0,5-1,5mg / dl
Calcium (Ca)	7,2 *	8,6-10,3mg / dl
GDS	179 *	<140mg / dl
Sodium (Na)	134 *	135-147mmol / L

Calculations Estimate Creatinine Clearance (CrCl) based on the Cockcroft-Gault<sup>4</sup>.

CrCl =	Weight (kg) x (140-age)	
	72 x (Cs) cr (mg %)	
CrCl =	80 (kg) x (140-49) 72 x (11, 6 mg %)	
CrCl =	8, 71 mL/min	

# V. Drug Related Problems (DRPs)

#### 1. Correlation between therapy with disease

There was a clinical condition was not treated, namely hepatitis B based on ISO book Pharmacotherapy should be given hepatitis B vaccine therapy (HBIG).

*Pharmacist Intervention:* The dose of hepatitis B vaccine (HBIG) is usually 0,06 ml / kg IM administered in a single dose for 14 days<sup>1</sup>.

#### 2. Selection of appropriate medication

Selection of the drug wasnot safe for the patient's condition and dosing indispensable for these patient (CKD stage V) because some drugs can not be in clean when hemodialysis.

*Pharmacist Intervention:* Patient with stage V renal failure need dose adjustments are based on those calculations the dose should be decreased Creatinine Clearance Estimate of laboratory values<sup>5</sup>.

#### 3. Dose regimen

The dose, frequency and route of administration did not consider the effectiveness, safety, comfort, and not in accordance with the patient's condition? Meropenem 1 gram 3 times daily, Cefoperazone Sulbactam 2 times daily 1 gram, 1 time a day Levofloxacin 500 mg, Valsartan 160 mg 1 time a day

*Pharmacist Intervention:* Use of drugs tailored to the patient's clinical condition; Meropenem for ClCr < 10 mL / min to 250 mg for 24 hours, after hemodialysis given 500 mgevery 8 hours, Levofloxacin Cr 10-19 mL / min after hemodialysis therapy dose of 500 mg to 250 mg subsequently every 4 hours for 7 - 14 days, Cefoperazone Sulbactam ClCr <15 mL / min therapeutic dose of 0,5 grams for 12 hours up to 1 gram / day, Valsartan as an antihypertensive drug, administered dose of 160 mg lowered to 40 mg1 time / day in patient with Chronic Kidney Disease (CKD) on Hemodialysis<sup>5</sup>.

#### 4. Interactions and contraindications

There were interactions between drugs with drug, Potassium Chloride + Valsartan need for dose adjustment may increase potassium in the blood, Tramadol + Meropenem + Levofloxacin can affect the central nervous system resulting in convulsions, Insulin + Sucralfate should be avoided or dose adjustments of Insulin because of Sucralfate suspension containing carbohydrates so can interfere with blood glucose levels, Calcium Carbonate + Sucralfate + Amlodipine, a Calcium Carbonate can inhibit the action Sucralfate and Amlodipine, Lasix + Cefoperazone concurrent use can worsen kidney function requires monitoring of renal function<sup>6</sup>.

Pharmacist Intervention: Potassium Chloride + Valsartan discontinued due to the use of potassium normal laboratory values, Tramadol + Meropenem + Levofloxasin because this drug is needed in the treatment of patient were advised to use Meropenem precedence because  $T\frac{1}{2}$  of Meropenem shorter that 1 hour of tramadol with  $T\frac{1}{2}$  6 hours, while for Levofloxasin given every 48 hours for patient with CKD condition that can be given after use of Tramadol, Insulin + Sucralfate improved insulin dosage based on blood glucose levels. Calcium Carbonate + Sucralfate + Amlodipine, Amlodipine use of precedence by chewing and swallowed to accelerate the absorption of Calcium Carbonate inthe next administration and Sucralfate given within 1 hour after administration of Calcium Carbonate, Lasix + Cefoperazone the use of Lasix precedence 30-60 minutes of use Cefoperazone<sup>1,2,3,6,7</sup>.

# VI. CONCLUSION

Based on the assessment of the use of drugs were used, it can be concluded that, in patients with a diagnosis of sepsis macrovascular disease complications, found the presence of some DRPs (Drug Related Problems), correlation between therapy with disease, Selection of appropriate medication, dosage regimen, interactions and contraindications.

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