SRI LANKAN JOURNAL OF ANAESTHESIOLOGY

Volume 19 Number 1, January 2011

Editorial I

MARKERS OF SEPSIS, ARE THEY NECESSARY?

All of us who manage patients in the intensive care units have come across septic patients and have spent a good amount of our time in the intensive care unit with such patients. The reason being to make sure of the diagnosis and thereafter to prevent the patient from going into multiorgan failure as the mortality in such an event is very high, almost 50%. With every organ that fails the mortality increases by 20%. In fact it is one of the most common causes of mortality in the intensive care unit.[1] Early diagnosis, early goal directed therapy [2,3]and activated protein C has shown to reduce mortality to around 35-40%.

What is sepsis?

Sepsis is a disease entity. It is not a disease. It can be classified as a syndrome in the same lines as acute respiratory distress syndrome. The earliest disease form we see and should be alert to is the systemic inflammatory response syndrome (SIRS). The signs and symptoms are temperature > 38^{o}C or < 36^{o}C, white cell count of > 12,000cells / mm^3 or <4000cells / mm^3, heart rate of >90beats/min, A respiratory rate >20breaths / min or a Pa_{CO2} of 4.3kPa or less.

SIRS is diagnosed when two or more of the above symptoms and signs are present. It is usually self limiting but at times may lead to severe sepsis or septic shock.

There is a very definitive immunological component to sepsis. When there is suppression of the immune system as in trauma, surgery, burns and diabetes such patients are predisposed to severe sepsis and septic shock. When the inflammatory process continues unhindered due to a continuous surge of pro inflammatory cells such patients develop severe sepsis from SIRS.

In the late stage where anti inflammatory mediators predominate there is immune suppression or a state of anergy when the organs start to fail and finally the patient succumbs due to multi organ failure. When a patient reaches this stage it is very difficult to pull him back to normality. Therefore management of sepsis must be looked at very closely if we are to reduce the high mortality associated with it.

In fact sepsis has been closely linked to breast carcinoma in its evolution. The fact that treatment itself can cause deterioration in the patient is worrying. This is true in certain patients given antibodies against Tumour necrotizing factor (TNF) while some improved dramatically others deteriorated. The same can be said of the underlying causative organism whether it be gram positive, negative or fungal.

Therefore it might be prudent if we look at markers of sepsis just like markers of tumour in order to identify patients who are progressing from SIRS to severe sepsis.

Markers of sepsis

We all know with infection the inflammatory response come into play and the total white cell count increases. This along with blood culture are the age old investigations we carry out as soon as a septic patient is admitted to the intensive care unit.

In recent times we have also looked at C reactive protein, IL6 levels and procalcitonin levels as predictors of outcome in the early stage of sepsis. Sequential organ failure assessment score (SOFA)[4] can also be looked at when we need to determine or predict the outcome of the patient.

How effective are these markers?

White cell count as we all know increases due to the metabolic response to trauma following surgery. Unless the counts are very high we tend not to take it into account due to the reason mentioned earlier.

Blood culture takes seventy two hours for a result to be obtained so we are looking at an unnecessarily long duration in a critically ill patient who cannot wait that long for initiation of treatment. On the other hand the sample could be contaminated with a false positive or wrong organism.

C reactive protein (CRP) an acute phase protein increases in value within 6 hours but is non specific as it increases with tissue injury. This therefore cannot be used as a marker. It can be used to follow septic patients but is unable to predict the severity of the disease or outcome of the patient.

Procalcitonin (PCT) levels have shown much promise as there is a steady rise in the level of this hormone in critically ill septic patients with endotoxaemia. It can be used as an early marker of sepsis. PCT has been found to be more specific than CRP for sepsis induced inflammation. This is important as major surgical trauma may induce a non septic SIRS which is difficult to distinguish from sepsis.

IL6 which is a pro inflammatory mediator too has been looked at but since it remains elevated for 72 hours in major surgery without complications, we may have to look at the magnitude of elevation rather than an increase alone. Therefore quantification will be necessary as its rise has shown a direct relationship to tissue injury and septic morbidity.

SOFA score[4] has been shown to have a better predictive value than the above biochemical values. Better still would be to take into consideration a laboratory marker such as PCT together with a clinical evaluator such as SOFA which has been shown to correlate well for a better prediction of the severity of sepsis.

Therefore it is necessary that we make a good and effective marker an investigative tool for the diagnosis of these patients so that early effective treatment can be started. It is only by preventing multi organ failure that we can improve the outcome of these patients. Once a patient goes into multiorgan failure the mortality rate steadily increases.

Whenever a new diagnostic tool or treatment modality comes into focus we in the developing world have to consider the cost effectiveness of such treatment, more so with the free health service in the state sector. If we can reduce the mortality by early diagnosis with an effective marker or markers then it will definitely be cost effective when we consider the numbers of such patients.

References

1 Mokart D,Leone M, Sanini A, Brunn JP,Tison A, Delpero JR, Houvenaeghel G, Blache JL, Martin C. Predictive Preoperative factors for developing severe Sepsis after major surgery. *Br j Anaesth* 2005; **95(6)** 776-81

2. Mokart D,Merlin M, Sanini A, Brunn JP, Delpero JR, Houvenaeghel G, Moutardier V.Blache JL. Procalcitonin, Interleukin 6 and systaemic inflammatory response syndrome (SIRS): Early markers of postoperative sepsis after major Surgery.Br *j Anaesth* 2005; **94 (6)** 767 – 73
3. Rivers E, Nguyen B, Havstad S. Early goal directed therapy in the treatment of severe sepsis and septic shock. *N Engl J* Med 2001; **345:** 1368-77
4. Dhababa AA,Hagara B,Fall A,Rehak PH,List WF, Metzler H. *Br j Anaesth* 2006; **97 (4)** 503-8

Shirani Hapuarachchi*

Consultant Anaesthetist ,

Neuro Surgical Department,

The National Hospital of Sri Lanka

** Corresponding author. E – mail: hapu@sltnet.lk*