

## INTISARI

### Latar belakang:

Penggunaan mesin jantung-paru sewaktu proses operasi bedah jantung terbuka merupakan penyebab utama timbulnya SIRS, dan perkembangan SIRS lebih lanjut sulit diprediksi, bisa ringan, bisa menjadi sepsis, septik syok, bahkan gagal multi organ yang berakhir dengan kematian. Berbagai upaya pencegahan telah dilakukan antara lain: pemberian metilprednisolon intraoperasi (dicampurkan dengan *priming* mesin jantung-paru), atau pemakaian hemofilter yang dipasang pada sirkuit mesin jantung-paru, tetapi hasilnya belum optimal, terutama pada pasien dewasa. Oleh karena itu dilakukan upaya lain yaitu dengan kombinasi pemberian metilprednisolon dan pemakaian hemofilter.

### Tujuan Penelitian

Penelitian ini bertujuan untuk mengetahui efek pemberian kombinasi antara metilprednisolon praoperasi, metilprednisolon intraoperasi, dan hemofilter terhadap: kejadian SIRS, komplikasi pasca operasi, dan kejadian kematian pascaoperasi, pada pasien dewasa yang dilakukan operasi bedah jantung terbuka.

### Metode penelitian:

Penelitian ini adalah penelitian eksperimental dengan desain *Prospective Randomized Open-Blinded Evaluation*. Sembilan puluh lima pasien dewasa yang akan dilakukan pembedahan jantung dilakukan randomisasi blok sehingga didapat 48 pasien masuk kelompok A (mendapat metilprednisolon praoperasi, metilprednisolon intraoperasi, dan hemofilter) dan 47 pasien masuk kelompok B (kelompok standar, diberi metilprednisolon intraoperasi). Sampel darah untuk pemeriksaan TNF $\alpha$ , IL-6, dan C3 diambil saat sebelum induksi anesthesi, segera setelah sirkulasi luar tubuh dihentikan, 3 jam setelah selesai operasi, dan 24 jam setelah selesai operasi. Sedang suhu tubuh, denyut nadi, PaCO<sub>2</sub> atau frekuensi pernafasan, serta jumlah lekosit diukur pada 3 jam, 24 jam, 48 jam, dan 72 jam pasca operasi. Komplikasi dan kejadian kematian diamati selama kurun waktu 30 hari pascaoperasi.

### Hasil:

Bila dibandingkan dengan kelompok standar (kelompok B) maka kejadian SIRS pada kelompok A di 3 jam pascaoperasi di dapat lebih kecil (36,4% dibanding 63,6%) dan secara statistik berbeda bermakna  $p < 0,001$  dengan OR 8,40 (95% CI = 2,835-24,89). Pada sub grup analisis kejadian SIRS di kelompok A berkurang sebesar 44,0% dibanding pada kelompok B (RRR = 0,44 (0,245-0,585). Sedang di 24 jam pascaoperasi kejadian SIRS di kelompok A lebih kecil dibanding kejadian SIRS di kelompok B (43,1% dibanding 56,9%) dan secara statistik berbeda bermakna dengan  $p = 0,031$  OR 2,64 (95% CI = 1,08-6,44) dan pada subgroup analisis kejadian SIRS di kelompok A berkurang sebesar 29,1% dibanding di kelompok B (RRR=0,291(0,025-0,484). Untuk kejadian SIRS di 48 jam dan 72 jam pascaoperasi secara statistik tidak berbeda bermakna. Untuk pengaruhnya terhadap mediator proinflamasi (TNF- $\alpha$ , IL-6, dan C3), pada penelitian ini didapat bahwa besarnya kenaikan TNF- $\alpha$  di pengamatan saat mesin

jantung-paru dihentikan ada kecenderungan pada kelompok A lebih kecil dibanding pada kelompok B ( $2,33 \pm 8,64$  dibanding  $3,70 \pm 25,47$ ), tetapi secara statistik tidak berbeda bermakna. Selain itu didapat terjadi penurunan kadar C3 di 3 jam pascaoperasi pada kelompok A maupun kelompok B tetapi secara statistik perbedaan penurunan tersebut tidak bermakna. Bila dibanding kejadian komplikasi pada kelompok B, maka kejadian komplikasi pada kelompok A didapat lebih kecil (26,9% dibanding 73,1%), dan secara statistik perbedaan ini berbeda bermakna  $p=0,005$  dengan OR 3,97 (95% CI 1,476-10,71). Pada subgroup analisis kejadian komplikasi di kelompok A berkurang sebesar 63,9% dibanding kelompok B dengan RRR=0,639 (0,223-0,833). Pada penelitian ini didapat kejadian kematian di kelompok A lebih rendah dibanding di kelompok B (40% dibanding 60%) tetapi secara statistik tidak berbeda bermakna  $p=0,523$  ( $p>0,05$ ) dan pada subgroup analisis kematian di kelompok A berkurang sebesar 34,7% dibanding kelompok B RRR=0,347(-1.166-0,803).

#### Kesimpulan:

Kombinasi antara pemberian metilprednisolon praoperasi, metilprednisolon intraoperasi dan hemofilter, secara bermakna dapat menurunkan kejadian SIRS pascabedah jantung terbuka di 3 jam dan di 24 jam pascaoperasi, dan secara bermakna dapat menurunkan kejadian komplikasi pascaoperasi. Kombinasi ini cenderung menurunkan kejadian kematian pascaoperasi, tetapi secara statistik tidak bermakna. Ada kecenderungan kenaikan kadar TNF $\alpha$  di pengamatan segera setelah mesin-jantung paru dihentikan pada kelompok A lebih kecil dibanding pada kelompok B, tetapi secara statistik tidak berbeda bermakna.

#### Kata kunci:

Bedah jantung terbuka dewasa – hemofilter – metilprednisolon - SIRS – TNF $\alpha$ .

## ABSTRACT

### Background:

The use of the Heart–Lung Machine during open heart operation mostly will cause SIRS (systemic inflammatory response syndrome), which unpredictable progress, can progress into sepsis, septic shock, multiple organ failure and even lead to death. Various ways to prevent SIRS have been made among others by giving intraoperative methylprednisolone (mixed with priming heart -lung machine) or usage of hemofilter installed at the circuit of heart-lung machine. Some studies have shown that the prevention of SIRS is not yet optimal, especially in studies that are involving adult patients. Therefore, new approach using combination of preoperative methylprednisolone administration and hemofilter has been initiated.

### Objectives:

This study was performed to determine the effects of combination of preoperative methylprednisolone, intraoperative methylprednisolone, and hemofilter on the incidence of SIRS, postoperative complications, and the incidence of postoperative mortality in adult patients after open-heart surgery.

### Methods:

This study was an experimental study with design Prospective Randomized Open-Blinded Evaluation. Ninety-five adult patients undergoing cardiac surgery have been randomized into 48 patients within group A (received preoperative methylprednisolone, intraoperative methylprednisolone, and hemofilter), and 47 within group B (standart group and received intraoperative methylprednisolone). Blood samples were taken from all patients before anesthesia induction, immediately after the extra corporal circulations was stopped, 3 hours after completion of the operation, and 24 hours after completion of the operation for analysis of TNF $\alpha$ , IL-6 and C3. Medium body temperature, pulse, PaCO<sub>2</sub>, or respiratory rate, as well as leukocyte counts were measured at 3 hours, 24 hours, 48 hours, and 72 hours postoperatively. The incidence of complications and mortality were observed for 30 days postoperatively.

### Result:

When compared to the standard group (group B), the incidence of SIRS in group A in 3 hours postoperatively was significantly lower (36.4% compared to 63.6%,  $p < 0.001$ ) with OR 8.40 (95% CI = 2.835 to 24.89). In the subgroup analysis of the incidence of SIRS in group A was reduced by 44,0% than in group B (RRR = 0.44 (0,245-0,585). While in 24 hours postoperatively, the incidence of SIRS in group A was significantly than the incidence of SIRS in group B (43.1% compared to 56.9%,  $p = 0,031$ ) with OR 2.64 (95% CI = 1,08 to 6,44) and in the subgroup analysis of the incidence of SIRS in group A was reduced by 29,1% compared to in group B (RRR = 0.291 (0.025 to 0.484). For the occurrence of SIRS in 48 hours and 72 hours postoperatively, the difference was not statistically significant. The influence on levels of pro-inflammatory mediators (TNF- $\alpha$ , IL-6, and C3), our study showed that levels of TNF- $\alpha$  after the discontinuation of heart-lung machine in group A are lower than in group B ( $2.33 \pm 8.64$  compared to

3.70  $\pm$  25.47), but was not statistically significantly different. Additionally, levels of C3 in 3 hours postoperatively in group A was lower in group B but statistically not significant. When compared to group B, the incidence of complications in group A was significantly lower (26.9% compared to 73.1%,  $p = 0.005$ ) with an OR of 3.97 (95% CI 1,476 - 10.71). In the subgroup analysis of the incidence of complications in group A was reduced by 63,9% compared to group B with RRR = 0.639 (0.223 to 0.833). In this study, the incidence of mortality in group A was lower than in group B (40% compared to 60%) but was not statistically significant ( $p = 0.523$ ) and in the subgroup analysis of mortality in group A was reduced by 34,7% compared to group B RRR = 0.347(-1,166-0,803).

**Conclusions:**

Combination administration of methylprednisolone preoperative, intraoperative and hemofilter methylprednisolone could significantly decrease the incidence of postoperative SIRS open heart at time point 3 and 24 hours postoperatively, and could significantly decrease the incidence of postoperative complications. The combination of methylprednisolone and hemofilter tends to decrease the incidence of postoperative mortality, but it is not statistically significant. Levels of TNF $\alpha$  in the observation immediately after a cardiorespiratory machine discontinuation is lower in group A than in group B, but is not statistically different.

**Keywords:**

Adult open heart surgery – hemofilter – metilprednisolon – SIRS – TNF $\alpha$ .