Thoracic epidural anesthesia attenuates hemorrhagic-induced splanchnic hypo-perfusion in post-resuscitation experimental hemorrhagic shock

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Abstrak

Tujuan penelitian ini adalah untuk menilai pengaruh anestesia epidural torasik pada perfusi splanknik, translokasi bakteri, dan perubahan histopatologi organ-organ splanknik pada renjatan perdarahan eksperimental pada beruk (Macaca nemestrina). Enam belas Macaca nemestrina ditentukan secara acak masuk ke dalam salah satu dari dua kelompok, yaitu kelompok lidokain (n = 8), yang mendapat anestesia umum ditambah anestesi epidural torasik lidokain; dan kelompok salin, yang mendapat anestesia umum saja (n = 8) sebagai kontrol. Renjatan perdarahan dibuat dengan mengeluarkan darah hewan secara bertahap sampai tekanan darah arteri rerata (TAR) mencapai 40 mm Hg, dan dipertahankan selama 60 menit. Hewan kemudian diresusitasi dengan memberikan darahnya kembali disertai cairan ringer laktat (RL). Setelah resusitasi, diberikan lidokain 2% epidural pada kelompok lidokain dan salin pada kelompok kontrol. Resusitasi yang dilakukan setelah satu jam renjatan perdarahan, dengan variabel hemodinamik dan luaran urin kembali normal, menunjukkan bahwa pada kelompok salin tidak ada perbaikan perfusi splanknik. PgCO2, P(g-a)CO2, dan pHi menetap pada nilai kritis dan cenderung memburuk pada kelompok salin. Berlawanan dengan kelompok salin, pada kelompok lidokain perfusi splanknik cenderung membaik. Keadaan ini didukung dengan dijumpainya translokasi bakteri yang lebih sedikit dan perubahan histopatologi organ splanknik yang lebih baik. Penelitian ini menyimpulkan bahwa anestesia epidural torasik lidokain memperkecil hipoperfusi splanknik pasca-resusitasi renjatan perdarahan pada Macaca nemestrina. ***(Med J Indones 2008; 17: 73-81)***

Abstract

The purpose of present study was to assess the effects of thoracic epidural anesthesia on splanchnic perfusion, bacterial translocation and histopathologic changes in experimental hemorrhagic shock in short-tailed macaques (Macaca nemestrina). Sixteen Macaca nemestrinas were randomly assigned to one of two groups i.e. the lidocaine group (n = 8), receiving general anesthesia plus lidocaine thoracic epidural anesthesia; and the saline group (n = 8), receiving general anesthesia alone as control. Hemorrhagic shock was induced by withdrawing blood gradually to a mean arterial pressure (MAP) of 40 mm Hg, and maintained for 60 minutes. Animals were then resuscitated with their own blood and ringer lactate solution (RL). After resuscitation, epidural lidocaine 2% was given in the lidocaine group and saline in the control group. Resuscitation that was performed after one hour hemorrhagic shock, with hemodynamic variables and urine output returned to normal, revealed there was no improvement of splanchnic perfusion. PgCO2, P(g-a)CO2, and pHi remained in critical value and tended to deteriorate in the saline group. Contrast to saline group, splanchnic perfusion in lidocaine group tended to improve. This condition was supported by the finding of less bacterial translocation and better histopathologic changes in lidocaine thoracic epidural anesthesia group than in saline group. This study concludes that lidocaine thoracic epidural anesthesia attenuates splachnic hypoperfusion in post-resuscitation hemorrhagic shock in Macaca nemestrina. ***(Med J Indones 2008; 17: 73-81)***

Keywords: *thoracic epidural anesthesia, lidocaine, hemorrhagic shock, splanchnic hypoperfusion, bacterial translocation*

The main objective of resuscitation in a hemorrhagic shock is to replace the blood loss and to stop the source of hemorrhage. Although resuscitation is done successfully and the patient returns to normal state, the hemodynamic variables often return to the pre-shock state, it is not rare that at the end the patient would die in Intensive Care Unit (ICU) due to multiple organ failure (MOF). Several authors mentioned that there is a relationship between multiple organ failure and splanchnic hypo-perfusion.[1,2]

Splanchnic circulation plays a role as circulatory sink in acute hemorrhage to maintained brain and heart perfusion by way of sympathetic nervous system induced vasoconstriction. Prolonged reduction of splanchnic blood flow causes ischemia and hypoxia of splanchnic tissues. It also leads to increase the permeability of intestinal mucosa and facilitate bacterial translocation. The reperfusion of previously ischemic tissue also will activate the inflammation mediators' network.

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Experimental studies proved that hemorrhage with or without arterial hypotension will be followed by blood flow depression or arterial vasoconstriction which last for long period on mesenteric area despite sufficient resuscitation. Pain and tissue injury due to trauma also stimulate the sympathetic nervous system which worsen reduction of microcirculation in splanchnic area.

In anesthesiology, epidural anesthesia is one of methods that can be applied to reduce the sympathetic activity. Thoracic epidural anesthesia (TEA) can inhibit splanchnic sympathetic nervous system completely. The local anesthetic which is injected into the epidural space and absorbed by the blood vessels in that space is expected to have a systemic effect to prevent ischemia-reperfusion syndrome.

Shibata et al[3] reported that high TEA in dogs improved the survival from experimental hemorrhagic shock. Adolphs et al[4] in their experimental study in rats reported that TEA proved to improve intestinal microcirculation during hypotension due to acute hemorrhage. This also reduce leucocytes rolling – an early stage of inflammation reaction to low flow.

Based on the fact that inadequate splanchnic perfusion may cause multiple organ failure which increases the risk of death in critically ill patient and that the TEA effects are thought to improve splanchnic perfusion, this experimental study was done to evaluate the effects of TEA given after reperfusion on the splanchnic perfusion in hemorrhagic shock.

METHODS

This experimental study was conducted in IPB Veterinary Hospital, Bogor. The study protocol was approved by the Animal Care and Use Committee IPB, Bogor. Sixteen healthy adult *Macaca nemestrinas* were randomly assigned into two groups, i.e. lidocaine group (n=8) and saline group as control (n=8). After a 12 hour fasting for food (water *ad libitum*) prior to induction, both groups were anesthetized with ketamine during preparation, under which an epidural catheter was inserted at T7-8 and gastric tonometry catheter was inserted under fluoroscopy guidance. The position of the catheter was confirmed by fluoroscopy using 2 ml of iopamidol contrast medium. The animals were then mechanically ventilated under general anesthesia (endotracheal intubation facilitated with succiniylcholine, N_2O - O_2: 50% - 50%, halothane 0.5% and rocuronium) using *Amsterdam Infant Ventilator*, maintained normocapnia ($PaCO_2 \pm 40$ mm Hg). Central venous catheter was inserted through femoral vein for central venous pressure (CVP) monitoring and administration of maintenance fluid. Ringer Dextrose 5% (RD) was used as fluid and calories replacement during fasting, and Ringer Lactate (RL) as maintenance fluid. Arterial catheters were placed in both femoral arteries for hemodynamic monitoring and blood withdrawal. Hemorrhagic shock was induced by withdrawing blood gradually to a mean arterial pressure (MAP) of 40 mm Hg, and maintained for 60 minutes. Animals were then resuscitated with their own blood and crystalloid solution (RL). Post resuscitation, in the treated group epidural lidocaine 2% was given and the control group received saline. During this study $PgCO_2$, $P(g\text{-}a)CO_2$, pHi, hemodynamic parameters, acid-base balance and lactate were monitored. Specimens for blood culture were taken before shock and at the end of study. Biopsies of the intestinal, liver, and kidney were done. Hemodynamic parameters were monitored using PiCCO *semi-invasive transpulmonary thermodilution technique*. Blood gas analysis, acid base and blood lactate level were measured by *I-Stat Analyzer*. Splanchnic perfusion was measured by gastric tonometry Datex Ohmeda/ GE, which measured PgCO2, P(g-a)CO2 and pHi continuously. Histopathology's studies were done by Pathology and Lipid Lab, PSSP LPPM-IPB, Bogor, and blood cultures by Prodia Lab, Bogor.

The statistical analysis was done with Student T-test and General Linear Model Repeated Measures and One-Way Anova. Mann Whitney was used if the analysis can not be done with the previous methods. $P < 0.005$ was considered statistically significant and the values were expressed with standard deviation. The software used was SPSS 13.0 and for the Mann Whitney test was Minitab 11 for Windows.

RESULTS

No significant differences were noted between two groups with respect to body weight, body length, age, and bleeding volume (Table 1). Radiographic findings indicated that contrast medium was spreading from approximately T1 to T11 in saline group and from C6 to T11 in lidocaine group.

Hemodynamic Variables in Pre-Hemorrhagic Shock

No significant differences were evident in baseline pre-hemorrhagic shock hemodynamic variables between the two groups, except cardiac index (CI) (Table 1). Although CI pre-hemorrhagic shock in lidocaine group significantly less than control group, the splanchnic perfusion pre-hemorrhagic shock between the two groups were similar based on gastric tonometry. $PgCO_2$, $P(g\text{-}a)CO_2$, and pHi in pre-hemorrhagic shock did not differ significantly between the two groups and were within the normal range (Table 2).

Table 1. Characteristics of *Macaca nemestrina* and Hemodynamic Variables in Pre-Hemorrhagic Shock

	Group	n	Mean	Standard Deviation (SD)	p
Body Weight (kg)	Saline	8	12.74	2.77	> 0.05
	Lidocaine	8	12.14	2.99	
Body Length (cm)	Saline	8	95.69	5.68	> 0.05
	Lidocaine	8	93.37	6.76	
Age (yrs)	Saline	8	13.87	3.23	> 0.05
	Lidocaine	8	16.50	3.82	
Bleeding Volume (mL)	Saline	8	207.37	89.45	> 0.05
	Lidocaine	8	230.25	69.79	
MAP (mm Hg)	Saline	8	95.75	13.45	> 0.05
	Lidocaine	8	96.25	13.71	
HR (beats/min)	Saline	8	121.88	32.31	> 0.05
	Lidocaine	8	105.88	22.14	
CVP (mm Hg)	Saline	8	5.38	2.77	> 0.05
	Lidocaine	8	7.13	2.75	
CI (L/min/m^2)	Saline	8	3.32	0.52	< 0.05
	Lidocaine	8	2.72	0.41	

MAP: mean arterial pressure, HR:heart rate, CVP:central venous pressure, CI:cardiac index

Table 2. $PgCO_2$, $P(g\text{-}a)CO_2$, pHi, Blood Acid Base Balance and Lactate in Pre-Hemorrhagic Shock

	Group	n	Mean	Standard Deviation (SD)	p
$PgCO_2$ (kPa)	Saline	8	6.35	1.62	> 0.05
	Lidocaine	8	6.69	2.36	
$P(g\text{-}a)CO_2$ (kPa)	Saline	8	0.47	2.07	> 0.05
	Lidocaine	8	1.14	1.83	
pHi (unit)	Saline	8	7.38	0.13	> 0.05
	Lidocaine	8	7.34	0.10	
pHa (unit)	Saline	8	7.39	0.09	> 0.05
	Lidocaine	8	7.41	0.06	
$PaCO_2$ (mmHg)	Saline	8	44.21	10.60	> 0.05
	Lidocaine	8	41.74	5.06	
BE (mmol/L)	Saline	8	0.75	2.96	> 0.05
	Lidocaine	8	1.37	2.33	
Lactate (mmol/L)	Saline	8	1.44	0.91	> 0.05
	Lidocaine	8	1.94	1.21	

$PgCO_2$: partial pressure of gastric CO_2, $P(g\text{-}a)CO_2$: partial pressure difference of gastric and arterial CO_2, pHi: gastric intramucosa pH

Acid Base Balance and Blood Lactate in Pre-Hemorrhagic Shock

No significantly difference of pHa (arterial pH), PaCO2 (partial pressure of arterial CO2), and BE (base excess) between the two groups in pre-hemorrhagic shock and they were within the normal limit (Table 2).

Fluid Infusion

Beside their own blood, animals also received crystalloid infusion (Ringer Lactate solution) for resuscitation and, Ringer Dextrose 5% solution for fluid and calories requirement during fasting. Total amount of fluid infusion in both group were not significantly difference during experimental study (Table 3).

Hemodynamic variables, acid base balance and blood lactate after resuscitation and after epidural anesthesia

At 90th minute after resuscitation with blood and crystalloid, hemodynamic variables returned to the normal limit pre-shock condition, blood acid base and lactate were not significantly difference between the two groups before administration of TEA (Table 4).

Table 3. Fluid Infusion during Experimental Study

	Group	n	Mean	Standard Deviation (SD)	p
Total of Infusion (mL)	Saline	8	3062.50	1015.50	> 0.05
	Lidocaine	8	3562.50	821.04	
Ringer Lactate (mL)	Saline	8	2375.00	1060.66	> 0.05
	Lidocaine	8	3000.00	1224.74	
Ringer Dextrose 5% (mL)	Saline	8	687.50	458.06	> 0.05
	Lidocaine	8	562.50	623.21	

Table 4. Hemodynamic Variables, Blood Acid Base and Lactate after resuscitation

	Group	n	Mean	Standard Deviation (SD)	p
MAP (mmHg)	Saline	8	77.25	19.83	> 0.05
	Lidocaine	8	86.88	21.78	
HR (beats/min)	Saline	8	136.13	18.16	> 0.05
	Lidocaine	8	129.25	14.77	
CVP (mmHg)	Saline	8	6.75	5.17	> 0.05
	Lidocaine	8	9.00	3.25	
CI (L/min/m^2)	Saline	8	2.78	1.11	> 0.05
	Lidocaine	8	2.27	0.98	
pHa (unit)	Saline	8	7.27	0.16	> 0.05
	Lidocaine	8	7.27	0.08	
$PaCO_2$ (mmHg)	Saline	8	49.33	13.43	> 0.05
	Lidocaine	8	41.13	3.58	
BE (mmol/L)	Saline	8	-7.62	5.83	> 0.05
	Lidocaine	8	-7.75	3.58	
Lactate (mmol/L)	Saline	8	5.26	2.52	> 0.05
	Lidocaine	8	4.99	1.81	

Table 5. Hemodynamic Variables, Blood Acid Base and Lactate at 270th minute

	Group	n	Mean	Standard Deviation (SD)	p
MAP (mmHg)	Saline	7	54.43	28.577	> 0.05
	Lidocaine	8	73.75	32.221	
HR (beats/min)	Saline	7	133.86	40.043	> 0.05
	Lidocaine	8	112.63	30.859	
CVP (mmHg)	Saline	7	8.29	5.707	> 0.05
	Lidocaine	8	9.00	3.295	
CI (L/min/m^2)	Saline	6	2.1483	1.02539	> 0.05
	Lidocaine	7	1.9314	0.92353	
pHa (unit)	Saline	7	7.3086	0.05984	> 0.05
	Lidocaine	8	7.2860	0.14725	
$PaCO_2$ (mmHg)	Saline	7	40.2857	6.64691	> 0.05
	Lidocaine	8	41.9625	9.25680	
BE (mmol/L)	Saline	7	-4.7143	4.92322	> 0.05
	Lidocaine	8	-7.0000	5.73212	
Lactate (mmol/L)	Saline	7	4.2557	2.22966	> 0.05
	Lidocaine	8	4.8863	3.14749	

After resuscitation and epidural anesthesia administration (at the end of study – at 270th minute) hemodynamic variables, blood acid base and lactate in both groups were not significantly difference (Table 5).

PgCO2, P(g-a)CO2, and pHi changing during experimental study

PgCO2 changing

At 30th and 60th minute of hemorrhagic shock, PgCO2 in both groups increased according to shock duration (Figure 1a). After resuscitation, at 90th minute and subsequently, PgCO2 in saline group tended to increase until the end of experiment (270th minute). While PgCO2 in lidocaine group after resuscitation tended not to increase and even decreased. At 90th minute, PgCO2 in saline group was: 19.07 ± 8.02 kPa and PgCO2 of lidocaine group was: 11.03 ± 7.96 kPa. At 150th minute, the values were 19.54 ± 8.59 versus 9.94 ± 8.36 kPa; And at 270th minute, the values were 20.71 ± 9.75 kPa and PgCO2 lidocaine: 10.11 ± 8.34 kPa. PgCO2 between group were significantly difference since the minutes of 90th, 150th till 270th (one-way Anova p = 0.038; 0.023 and 0.041; respectively). This suggest that splanchnic perfusion lidocaine group better than saline group.

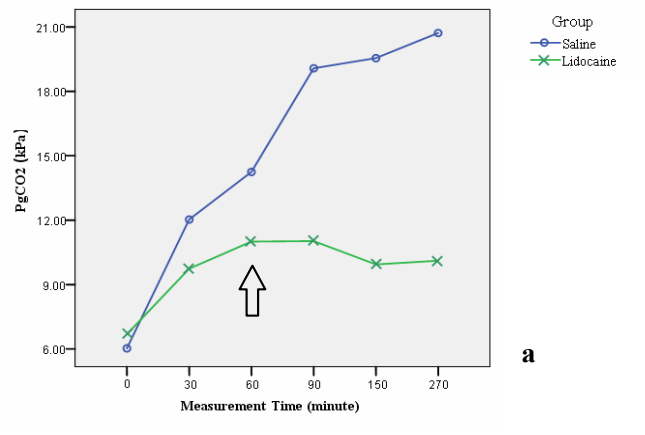
P(g-a)CO2 changing:

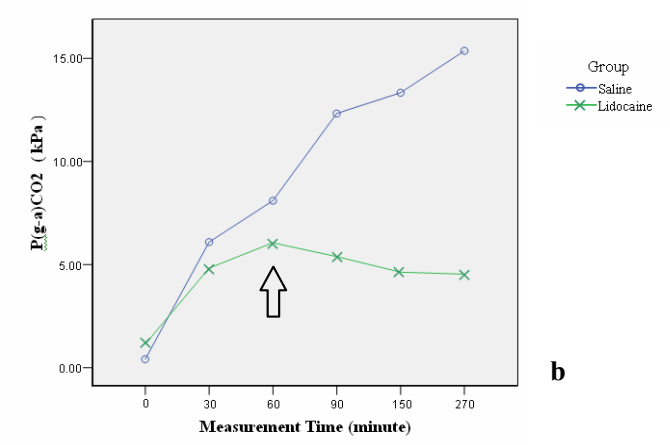
P(g-a)CO2 of both group start from pre-hemorrhagic shock, at 30th minute and 60th minute shock appeared to increase according to shock duration (Figure 1b). After resuscitation, minutes 90th and so forth P(g-a)CO2 in saline group continued to increase until the end of experiment (12.32 ± 8.98 mm Hg, 13.33 ± 9.70 mm Hg, and 15.36 ± 9.55 mm Hg, respectively). Contrast to saline group, the P(g-a)CO2 in lidocaine group tended to decrease since minute 90th (5.38 ± 8.13 mm Hg, 4.63 ± 7.44 mm Hg, and 4.53 ± 7.38 mm Hg, respectively). P(g-a)CO2 between groups were significantly difference since the minutes of 150th till 270th (one-way Anova p = 0.035 and 0.028, respectively)

The increasing P(g-a)CO2 in saline group suggest deterioration of splanchnic perfusion, while decreasing P(g-a)CO2 in lidocaine group indicated a changing toward improvement of splanchnic perfusion.

pH Gastric Intramucosa changing:

Figure 1c shows pH gastric intramucosa (pHi) changing during experimental study. pHi in both groups during hemorrhagic shock, at 30th minute in saline group was 7.10 ± 0.22 and in lidocaine group was 7.12 ± 0.21; at 60th minute in saline group was 7.00 0.19 and in lidocaine group was 7.07 ± 0.21. After resuscitation, from 90th, 150th minute to the end of experiment at 270th minute, pHi in saline group appeared always lower than lidocaine group.





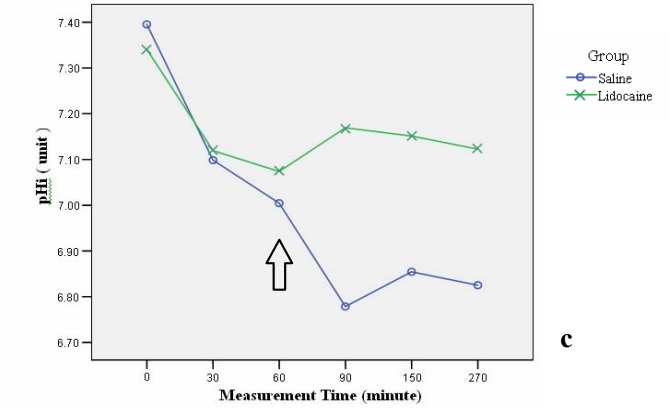


Figure 1a, b, c. $PgCO_2$, $P(g\text{-}a)CO_2$, and Gastric intramucosa pH (pHi) changing during experimental study 0^{th} to 60^{th} minute: hemorrhagic shock

Arrow : epidural anesthesia starts

Bacterial translocation

The results of blood culture taken at the end of study (270th minute), were difference from those taken before shock (0 minute), as follows

1. Saline group :
   - *Lactococcus garvieae,* found in one animal
   - *Streptococcus viridans,* found in two animals
   - *Serratia mercescens,* found in one animal
   - *Escherichia coli,* found in two animals
   - *Pseudomonas aeruginosa*, found in one animal

   There were 7 bacterial translocations in 8 animals (87.5%)
2. Lidocaine group :
   - *Serratia marcescens*, found in three animals
   - *Streptococcus viridans*, found in one animal

   There were 4 bacterial translocations in 8 animals (50%)

Bacterial translocations which originate from gastro-intestinal tract in saline group occurred more frequently than in lidocaine group (87.5% vs 50%).

Histopathology changing

Histopathology examination results were arranged according to the degree of cell changing and necrosis cell per a microscope view.

Degree 1: no change

Degree 2: mild changing, which cell damage less than 25%

Degree 3: moderate changing, with cell damage 25-50%

Degree 4: moderate to severe changing, which means cell damage 50- 75%

Degree 5: severe changing, which means cell damage about 75 - 100%

Histopathology results of duodenum in lidocaine group were better than saline group (p=0.0456). Other intraabdominal organs, even not significantly difference, appeared better in lidocaine group than saline group (except ileum) (Table 6).

DISCUSSION

Normal value of PgCO2 is < 6.5 kPa, P(g-a)CO2 is ~ 1 kPa, and pHi is > 7.35. PgCO2 is thought critical if > 8.65 kPa; and P(g-a)CO2 is critical if > 3.33 – 4.66 kPa. (1 kPa = 7.52 mm Hg). Gastrointestinal mucosa hypoperfusion is present if pHi less than 7,32; $PgCO_2$ and $P(g\text{-}a)CO_2$ higher than critical value.[5]

So, splanchnic hypoperfusion condition as predicted in this hemorrhagic model can be obtained, which detected by any changing of PgCO2, P(g-a)CO2, and pHi that after resuscitation, were in the range of critical splanchnic perfusion value.

Splanchnic hypoperfusion which occurred during hemorrhagic shock in this study was consistent with other previous studies with different model.[6-9] Resuscitation that was performed after one hour hemorrhagic shock with crystalloid and blood transfusion, and hemodynamic variables and urine output returned to normal, revealed there was no improvement of splanchnic perfusion detected by PgCO2, P(g-a)CO2, and pHi that remained in critical value and tended to deteriorate in the saline group. This matter agrees with Scannel et al study[9] reported that blood flow to splanchnic organs remained depressed after resuscitation even though blood flow to brain and kidney increased. Also, Edouard et al[6] reported that a sustained splanchnic vasoconstriction remained occurred even though the adequate management have been done with attention to blood pressure and cardiac output.

Table 6. Degree of Histopathology changing

Organ	Group	n	Median	p*	CI 95%
Liver	Saline	8	4	0.1973	-0.000 - 1.000
	Lidocaine	8	3		
Kidney	Saline	7	4	0.0946	-1.001 - 3.000
	Lidocaine	5	3		
Duodenum	Saline	8	3.5	0.0456	0.000 - 1.999
	Lidocaine	8	3		
Jejunum	Saline	8	4	0.4278	0.000 - 1.000
	Lidocaine	8	3.5		
Ileum	Saline	8	3	0.5557	-1.000 - 1.000
	Lidocaine	8	4		
Colon	Saline	8	3	0.3151	-0.999 - 2.000
	Lidocaine	8	3		

* Mann Whitney Test

After resuscitation at 90th minute and subsequently, splanchnic perfusion in saline group revealed progressively deteriorated, while in lidocaine group, it tended to improve. This study result was consistent to other previous studies. Adolphs et al.[4] which used rat as hemorrhagic model reported that thoracic epidural anesthesia preserved gut from decreased microvascular perfusion and from increased leukocytes-endothelium interaction which related to hemorrhage/retransfusion. In another study, Sielenkamper et al.[10] using intravital microscope to measure rat ileum mucosa blood flow during TEA (catheter tip at T7-9), reported that TEA increased mucosa blood flow and reduced irregular flow patterns such as stop-and-go flow in the capillary networks of the gut mucosa.

Contrast to the previous experimental study reports in animals or clinical studies, in which hemorrhagic shock was induced after epidural anesthesia. In this study thoracic epidural anesthesia was performed after hemorrhagic shock had occurred that was after resuscitation. Thoracic epidural anesthesia (TEA) was reported by several investigators could improve splanchnic perfusion[10-12]. Sielenkamper et al.[10] reported that TEA increased gut mucosa blood flow and reduced intermittent flow in villous microcirculation in an experimental rat perfusion pressure. Kapral et al.[11] reported that thoracic epidural anesthesia in patients who underwent major abdominal surgery was associated with better splanchnic perfusion. Jomura et al.[12] also reported that epidural anesthesia reduced mortality rate of emergency abdominal surgery patients compared to general anesthesia. Those studies suggest that TEA may prevent splanchnic hypoperfusion. While in this study, where TEA was administered at post-hemorrhagic shock resuscitation, the similar result was found, i.e. the splanchnic perfusion was improved.

Difference to above studies, Meissner et al.[13] using microsphere technique in dogs, reported that high thoracic epidural (T1-5) did not alter blood flow to splanchnic organ. The non alteration of blood flow to splanchnic area in this study can be explained by the fact that splanchnic sympathetic nerves (T5-T12) was not affected by this high epidural block.

Two other studies reported the effects of epidural anesthesia on gastric intramucosa pH during aortic reconstruction surgery.[14, 15] These both studies did not find any beneficial effect of epidural anesthesia on gastric intramucosa pH. However, the pH measurement was performed in stomach while epidural catheter tip placed at L3-4 and T9-10, respectively. Thus, in both studies it appeared that epidural block did not include upper part of splanchnic organ during the measurement of intervention effect.[14, 15] At difference to two above studies, in this study, the catheter was inserted at T7-8 intervertebral space and the contrast medium was observed spreading from C6 to T11. So that lidocaine from TEA can be confirmed to include splanchnic sympathetic innervations (T5-11) which covered stomach in which tonometry measurement was placed.

In addition to inhibit nerve transmission, lidocaine has a significant anti-inflammatory property,[16] and has a strong inhibitory effect on cytokine response to endotoxemia.[17] Ai et al.[18] reported that TEA (tip of catheter at T8-T10) slowed progression of intestinal ischemia during hypoxia and give protection to an increasing portal endotoxin concentration.

There is developing evidence showing that lidocaine has direct effect on G protein-coupled receptors, such as lysophosphatidic acid (LPA) receptor[19], which involve in platelet activation, inflammation and wound healing, as also thromboxane receptor[20], which involve in platelet aggregation and release of NE contain granules.

Blood culture results taken at the beginning and at the end of the study revealed that in saline group more positive bacterial culture was found which originated from gastrointestinal tract organisms, compared to lidocaine epidural group. These findings indicated that bacterial translocation opportunity is higher in saline group than lidocaine group. This condition is in agreement with histopathology results which showed that gut condition (except ileum) of saline group was worse than lidocaine group.

These study results, revealed that TEA can preserve splanchnic perfusion better than saline after re-suscitation in hemorrhagic shock. This is supported by histopathology and blood culture results. Histopathology results proved gut (except ileum), liver and kidney in lidocaine epidural group appeared better than saline group.

It is concluded that thoracic epidural anesthesia with lidocaine gives better protection on splanchnic perfusion after experimental hemorrhagic shock in *Macaca nemestrina* as witnessed by less bacterial

translocation and better histopathologic appearance compared to saline.

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