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INDONESIAN JOURNAL OF ANESTHESIOLOGY AND REANIMATION
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Original Article

PROFILE OF AIRWAY PATENCY, RESPIRATORY RATE, $PaCO_2$, AND PaO_2 IN SEVERE TRAUMATIC BRAIN INJURY PATIENTS (GCS <9) IN EMERGENCY ROOM DR. SOETOMO GENERAL ACADEMIC HOSPITAL SURABAYA

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ABSTRACT

Introduction: Traumatic Brain Injury (TBI) is the most common neurotrauma with high morbidity and mortality. Many guidelines recommend the use of mechanical ventilation for severe TBI patients, but there are limited resources of procuring ventilator machine in hospitals especially in developing countries. Yet it is not comparable with the number of TBI patients. **Objective:** This study is purposed to provide the profile of ventilation and oxygenation (airway patency, RR, $PaCO_2$, and PaO_2) in severe TBI patients (GCS<9) admitted in the Emergency Room (ER) of Dr. Soetomo General Academic Hospital Surabaya. **Method and Material:** This is a retrospective study using medical records of patients with TBI who were admitted in the ER of Dr. Soetomo General Academic Hospital from January to December 2017. The patient's general characteristics, blood gas analysis ($PaCO_2$, PaO_2), airway patency recorded and analyzed. **Results and Discussion:** Thirty-seven severe TBI patients were included in the analysis. 30 men (81.1%) and 7 women (18.9%) with an average of 37±16 years old (range: 5-65) were studied. Most of the patients (94.6%) had MAP between 60 and 160 mmHg, $PaCO_2$<35 mmHg (72.9%), PaO_2>60 mmHg (100%), RR>20 breaths per minute (70.2%), and patent airways (64.9%) with simple support of oxygen. 8.1% of all of those patients had $PaCO_2$>45 mmHg. **Conclusion:** Most of the severe TBI admitted in the ER of Dr. Soetomo General Academic Hospital had hypocapnia or respiratory rate higher than the normal range. Though one-third of the patient has partial obstruction of the airway, no significant hypoxemia is found.

Keywords: $PaCO_2$; PaO_2; RR; Airway Patency; Severe TBI; GCS; MAP

ABSTRAK

Pendahuluan: Cedera otak adalah kasus neurotrauma yang paling umum dengan morbiditas dan mortalitas yang tinggi. Banyak pedoman merekomendasikan penggunaan ventilasi mekanik pada pasien cedera otak berat. Namun di banyak rumah sakit di negara berkembang, pengadaan ventilator masih terbatas dibandingkan dengan jumlah pasien cedera otak berat. **Tujuan**: Penelitian ini bertujuan untuk memberikan profil ventilasi dan oksigenasi (patensi jalan nafas, frekuensi nafas, $PaCO_2$ dan PaO_2) pada pasien cedera otak berat (GCS <9) di ruang resusitasi Instalasi Gawat Darurat (IGD) Rumah Sakit Dr. Soetomo Surabaya. **Metode dan Bahan:** Penelitian ini merupakan studi retrospektif dengan menggunakan rekam medis pasien cedera otak berat yang dirawat di ruang resusitasi IGD Rumah Sakit Dr. Soetomo dari bulan Januari hingga Desember 2018. Data umum pasien, analisis gas darah ($PaCO_2$, PaO_2), pantensi saluran nafas dicatat dan dianalisis. **Hasil dan Pembahasan:** Tiga puluh tujuh pasien cedera otak berat dianalisis. 30 pria (81,1%) dan 7 wanita (18,9%) dengan rata-rata 37±16 tahun (rentang: 5-65) diteliti. Sebagian besar pasien memiliki MAP antara 60 dan 160 mmHg (94,6%), $PaCO_2$<35 mmHg (72,9%), PaO_2> 60 mmHg (100%), frekuensi nafas>20 napas per menit (70,2%), dan jalan nafas atas bebas (64,9%) dengan bantuan oksigen tambahan. Namun, 8.1% pasien mengalami $PaCO_2$>45 mmHg. **Kesimpulan**: Sebagian besar pasien cedera kepala berat yang dirawat di ruang resusitasi IGD Rumah Sakit Dr. Soetomo mengalami hipokapnia atau tingkat pernapasan lebih tinggi dari kisaran normal. Meskipun sepertiga dari pasien mengalami obstruksi parsial pada jalan nafas, tetapi tidak ditemukan hipoksemia yang signifikan.

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Kata kunci: $PaCO_2$; PaO_2; Frekuensi Nafas; Patensi Jalan Nafas; GCS; Cedera Otak Berat; MAP

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INTRODUCTION

Traumatic Brain Injury (TBI) is the most common neurological disease with high morbidity and mortality. One of the main causes is traffic accidents, which occupy the top 10 global causes of death in 2016. (1) TBI patients in developing countries are worse than in developed countries. (2) This also explains the mortality rate due to traumatic brain injury in Indonesia is higher compared to international standards. Severe TBI is the category of brain injury that has a high mortality rate. (3)

Death in patients with severe TBI can occur due to a decrease in the quality of the patient's condition including impaired ventilation and oxygenation, such as hyperventilation or hypoventilation. Hyperventilation is a set attempt to autoregulate the brain in reducing intracranial pressure due to primary brain injury. This will result in a decrease in $PaCO_2$. (4)

On the other hand, a decrease in consciousness that occurs in severe brain injury causes upper airway obstruction so that hypoventilation occurs. The hypoventilation causes hypercarbia which is characterized by increased $PaCO_2$ and hypoxia which is characterized by decreased PaO_2. (5)

Therefore, guidelines for the management of severe TBI recommend mechanical ventilators use in patients with severe TBI. (6)(7)

However, in some countries, especially developing countries like Indonesia, procuring ventilators is still a problem. This problem occurs because of the relatively high price and cost of ventilator use, the need for a good education in the installation of ventilators, and the lack of research on mechanical ventilator protocols. (8) For example, as the main referral hospital in eastern Indonesia, Dr. Soetomo General Academic Hospital, the number of ventilators is not sufficient to meet the needs of all patients who need a ventilator.

Therefore, we want to find out whether there is a tolerance in the implementation of guidelines for the management of severe TBI patients regarding the indication of mechanical ventilator installation.

METHOD AND MATERIAL

This research is an observational retrospective study using a descriptive research design. The study population is all aged>5 years patients with severe TBI (Glasgow Coma Scale/GCS<9) admitted 2017 in the Emergency Room (ER) of Dr. Soetomo General Academic Hospital from January to December 2017 and had blood gas analysis data ($PaCO_2$, PaO_2), Mean Arterial Pressure (MAP), primary survey data (respiratory rate and airway patency) before definitive airway apparatus was installed. The research used the total sampling technique.

All data was collected just after admitting to the ER of Dr. Soetomo General Academic Hospital and before definitive breathing apparatus installation as seen in the medical records as approved by the ethics committee Dr. Soetomo General Academic Hospital Surabaya.

RESULT AND DISCUSSION

The total number of available patients' medical records is 86. Among these, 37 medical records meet to study criteria. The

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mean (standard deviation/SD) range is 37±17 years old with the range between 5 to 65 years old. The average GCS with an absolute number is 6±2. Grouping data is presented in Table 1.

Table 1. Distribution of Severe TBI Patients Based on Mean Arterial Pressure (MAP)

MAP	N	Percentage (%)
<60	2	5.4
≥60 and <160	35	94.6
≥160	0	0
TOTAL	**37**	**100**

This study found that most patients have MAP between 60 to 100 mmHg (94.6%). The increase of blood pressure is a result of the brain's compensation in dealing with Increased Intracranial Pressure (ICP) that occur due to brain injury. (8) Increased blood pressure is in line with the brain's efforts to keep Cerebral Pressure Perfusion (CPP) constant. (4)(9) CPP is the difference between MAP and ICP. An increase in ICP, which occurs in brain injury, can cause a decrease in CPP. Therefore the brain, through brain autoregulation, will try to improve MAP to keep CPP constant. Brain autoregulation can occur when MAP is between 60 to 160 mmHg. (4)

In this study, we found that most of the TBI patients admitted in the ER of Dr. Soetomo General Academic Hospital based on MAP were still in acceptable brain auto-regulation range.

Distribution of Severe TBI Patients Based on $PaCO_2$

The average $PaCO_2$ of the subjects was 32.6±8.4 mmHg with a range of 17.9 to 59 mmHg. Grouping data is presented in Table 2.

When ICP increases, as in the case of brain injury, compensated hyperventilation will occur to decrease $PaCO_2$. (4) This is an attempt by the brain to reduce ICP by vasoconstriction that induced the reduction of blood volume. (4)

Table 2. Distribution of Severe TBI Patients Based on $PaCO_2$

$PaCO_2$ (mmHg)	N	Percentage (%)
<30	17	45.9
≥30 and <35	10	27.0
≥35 and <45	7	18.9
≥45	3	8.1
TOTAL	**37**	**100**

But some patients had hypercarbia. According to Cranshaw and Nolan (5), hypoventilation can occur in severe TBI patients as the result of a decrease of awareness. Decreased awareness can cause the reduction of pharyngeal tones and results in airway obstruction. It is linear with the data that shows most of severe TBI patients who admitted in the ER of Dr. Soetomo General Academic Hospital with $PaCO_2$ increases also experienced airway obstruction. (10)

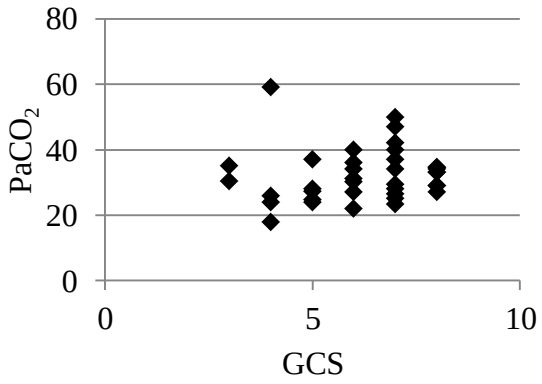

Figure 1. Distribution of Severe TBI Patients Based on $PaCO_2$ vs GCS

From Figure 1, it was found that there is a clear distribution of data between $PaCO_2$ and GCS. Severe TBI patients who come with low GCS tend to have low $PaCO_2$ and vice versa. This is quite different from a similar study conducted by Pfernninger and Linder (11) in Germany who also obtained a correlation between $PaCO_2$ and GCS of TBI patients

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measured at the scene and had not been intubated and ventilated. However, Pfernninger and Linder found that TBI patients who come with low GCS tend to have high $PaCO_2$ and vice versa. But there are differences in data collection time between their study and our study. Their blood sample was taken within the first few minutes after the accident. On the other hand, Dr. Soetomo General Academic Hospital is a referral hospital. This makes many patients who admit to the ER of Dr. Soetomo General Academic Hospital had a chance to visit another hospital before a Dr. Soetomo General Academic Hospital and only a few patients had come directly after the incident.

Distribution of Severe TBI Patients Based on PaO_2

The average PaO_2 of the sample was 183.5±91.5 mmHg with a data range of 61.8 to 423.6 mmHg. Grouping data is presented in Table 3.

Table 3. Distribution of Severe TBI Patients Based on PaO_2 with simple device of oxygen support

PaO_2 (mmHg)	N	Percentage (%)
<60	0	0
≥60 and <80	5	13.5
≥80 and ≤200	18	48.6
>200	14	37.8
TOTAL	**37**	**100**

Hypoxemia is a secondary result that often occurs in patients with TBI. (5) Therefore, Guidelines for the Management of Severe TBI recommend (7) oxygenation monitoring to avoid PaO_2<60 mmHg. Table 3 shows that all of the patients with severe brain injury who admitted to the ER of Dr. Soetomo General Academic Hospital have no problems with oxygenation according to the Guidelines for the Management of Severe TBI 3rd Edition.

Dr. Soetomo General Academic Hospital has its PaO_2 standard in the treatment of severe TBI patients who admit in Dr. Soetomo General Academic Hospital (12), namely PaO_2 80-200 mmHg. Based on Dr. Soetomo General Academic Hospital standards, all of the patients with GCS <9 automatically will get the oxygen support with a simple device. Our study shows that 84.6% patient who admitted in the ER of Dr. Soetomo General Academic Hospital did not experience hypoxia with PaO_2≤80. There was 13.5% suffered slightly hypoxia.

Distribution of Severe TBI Patients Based on Respiratory Rate

The average Respiratory Rate (RR) of the sample was 25±7.4 breaths per minute with a data range of 15 to 45 breaths per minute. Grouping data is presented in Table 4.

Table 4. Distribution of Severe TBI Patients Based on Respiratory Rate

Respiratory Rate (breaths per minute)	N	Percentage (%)
<12	0	0
≥12 and ≤ 20	11	29.7
>20 and ≤ 35	20	54
>35	6	16.2
TOTAL	**37**	**100**

According to Tülin and Nihan (13) in the discussion regarding intensive care management in TBI, there are indications based on respiration status when deciding ventilation in patients, one of which is respiratory rate>35 or <5 breaths per minute. Table 4 shows that most of the patients with severe TBI in the ER of Dr. Soetomo General Academic Hospital in 2017 did not meet one indication of ventilator use based on breath frequency.

However, based on the range of RR revealed by Yuan, Drost, and McIvor, most of severe TBI patients had RR>20 breaths per

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minute. (14) This means most of the patients had a severe brain injury in the ER of Dr. Soetomo General Academic Hospital experienced an increase in the RR from the normal range. Increased RR from this normal range can be an indication for mechanical ventilator instillation in patients with severe TBI in the ER of Dr. Soetomo General Academic Hospital. If ICP increases (as in the case of brain injury), hyperventilation occurs, so that $PaCO_2$ will decrease. This reduction in $PaCO_2$ is done as an effort to vasoconstrict the blood vessels of the brain so that Cerebral Blood Fluid (CBF) remains constant. (4)

Distribution of Severe TBI Patients Based on Airway Patency

Patients' airway is classified according to their additional breath sounds and there were 4 categories of additional breath sounds, namely free upper airway (no additional breath sounds), partial obstruction (snoring), fluid obstruction (gargling), and mixed obstruction (snoring and gargling). Grouping data is presented in Table 5.

Table 5. Distribution of Severe TBI Patients Based on Additional Breath Sounds

Additional Breath Sounds	N	Percentage (%)
Nothing	24	64.9
Snoring	5	13.5
Gargling	4	10.8
Snoring dan *Gargling*	4	10.8
TOTAL	**37**	**100**

Decreased awareness of TBI can also cause upper airway obstruction due to pharyngeal tone, including the base of the tongue. The decreased pharyngeal tone will cause upper airway obstruction which causes hypoventilation. (5) However, based on the data that have been collected, shown in Table 5, it is found that most of the patients had no problems with the upper airway, or in this case, had free upper airway. This shows that most of the patients with severe TBI in the ER of Dr. Soetomo General Academic Hospital has no internal problems with the upper airway.

CONCLUSION

Most of the patients with severe brain injury (GCS <9) who admitted in the ER of Dr. Soetomo General Academic Hospital tend to experience hypocarbia ($PaCO_2$ <35 mmHg) with increasing RR, but there is no oxygenation problem that is significant with relatively good upper airway patency.

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Conflict of Interest

There is no conflict of interest to be declared.

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Original Article

KNOWLEDGE OF GENERAL PRACTITIONAIRE DOCTORS AND MIDWIVES WHO HAS AND HAS NOT ATTENDED NEONATAL RESUSCITATION COURSE HAS NO SIGNIFICANT DIFFERENCE

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ABSTRACT

Introduction: Infant death is most prominent in the neonatal period. The success of neonatal resuscitation practice has many contributing factors. One of which is the health workers' knowledge of the Neonatal Resuscitation Program (NRP) algorithm. Therefore, it is necessary to conduct studies to evaluate the health workers' knowledge of the Neonatal Resuscitation Program who are educated in neonatal resuscitation course and has taken part in Neonatal Life Support practice in primary health care (PHC) **Objective:** This study aims to analyze the knowledge of general practitioners and midwives who has or has not attended in neonatal resuscitation course in Surabaya PHC **Methods and Materials:** this research is descriptive, cross-sectional research. All Basic Emergency Obstetric and Newborn Care (BEmONC) PHC in Surabaya which are Jagir PHC, Banyu Urip PHC, Medokan Ayu PHC, Tanah kali Kedinding PHC, Tanjungsari PHC, Balongsari PHC, Sememi PHC, Simomulyo PHC is included in this research from 2018 to 2019. A nine-item questionnaire referenced from The Textbook of Neonatal Resuscitation 7th Edition is given to ten respondents in each BEmONC PHC. **Results and Discussion:** from the total sample of 78 respondents, 32 (41,0%) receive a high score, 20 (25,7%) receive a middle score, and 26 (33,3%) receive a low score. The data shows that there is no significant score difference between respondents who has or has not participate in the NRP course (p=0,419). **Conclusion:** There is no correlation between difference knowledge midwives and general practitioners who had and had not attended neonatal resuscitation training at basic emergency obstetric and newborn care in public health center Surabaya.

Keywords: Knowledge; Neonatal Resuscitation Program; Neonatal Resuscitation Course; General Practitioner; Midwives

ABSTRAK

Pendahuluan: Kematian bayi berjumlah paling tinggi pada periode neonatal. Keberhasilan resusitasi neonatus dipengaruhi oleh berbagai faktor dalam suatu institusi kesehatan. Salah satu faktor tersebut adalah pengetahuan tenaga kesehatan tentang algoritma Neonatal Resuscitation Program (NRP). Maka, evaluasi tenaga kesehatan, terutama dokter umum dan bidan yang telah mengikuti pelatihan resusitasi neonatus dan melakukan praktik resusitasi neonatus di puskesmas sangat diperlukan. **Tujuan:** penelitian ini bertujuan untuk menganalisis pengetahuan dokter umum dan bidan yang sudah dan belum mengikuti pelatihan resusitasi neonatus di puskesmas Surabaya. **Metode dan Bahan:** penelitian ini adalah penelitian deskriptif dan cross-sectional. Seluruh puskesmas Pelayanan Obstetri Neonatal Emergensi Dasar (PONED) yaitu Puskesmas jagir, Puskesmas Banyu Urip, Puskesmas Medokan Ayu, Puskesmas Tanah kali Kedinding, Puskesmas Tanjungsari, Puskesmas Blongsari, Puskesmas Sememi, Puskesmas Simomulyo adalah puskesmas yang dipakai dalam penelitian ini dari 2018 sampai 2019. Sejumlah sembilan pertanyaan kuesioner yang direferensikan dari Textbook of Neonatal Resuscitation, edisi ketujuh diberikan kepada sepuluh responden di setiap puskesmas. **Hasil dan Pembahasan:** dari total sampel sejumlah 78, Hasil pengetahuan resusitasi neonatus bidan dan dokter di puskesmas Surabaya yang baik berjumlah 32 responden (41,0%), yang cukup sebanyak 20 responden (25,7%), dan yang kurang

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berjumlah 26 responden (33,3%). Penelitian ini tidak menemukan perbedaan signifikan antara responden yang sudah dan yang belum mengikuti pelatihan resusitasi neonatus (p=0,419). **Kesimpulan:** Perbedaan pengetahuan antara bidan dan dokter umum yang sudah dan belum mengikuti pelatihan resusitasi neonatus di puskesmas PONED Surabaya tidak signifikan.

Kata kunci: Pengetahuan; Neonatal Resuscitation Program; Pelatihan Resusitasi Neonatus; Dokter Umum; Bidan

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INTRODUCTION

The neonatal period is the highest death rate out of all periods of life. It is stated by WHO that the death rate of the neonatal period is 46% among the children mortality under the age of 5. (1) Therefore, WHO conducts a project "Millennium Development Goal (MDG) 4" to decrease the child mortality rate by two thirds from 1990 to 2015. (2)

Neonatal mortality in Indonesia is also monitored and evaluated. Although the neonatal mortality rate in Indonesia is relatively high in 2016 (13.7/1000), the mortality rate has decreased throughout the years. (3) This is also the problem in East Java Province. The neonatal mortality rate in East java is 14/1000 in 2015. (4) Previous studies describe that the Java-Bali region is more prepared than other regions in overall trained health worker, drugs, facilitation, and transportation. (5)

Compared to East Java, Surabaya has a relatively lower infant death rate in 2016. The infant death rate in Surabaya is 19.55/1000, whereas the infant death rate in East java is 23,60/1000. (6) Despite the lower death rate, Infant death rate in Surabaya is still high. Therefore, more studies are necessary to evaluate causes of neonatal death.

One of the factors that may inhibit the progress is the lack of knowledge by trained health cares in doing neonatal resuscitation. Indonesia's primary health cares, mainly the Basic Emergency Obstetric and Newborn Care (BEmOC) are the first line of health services in handling neonatal resuscitation. In Surabaya, there are 63 PHC and 21 of which helps mothers with labor that requires hospitalization. However, there are only 8 PHCs that has the title of Basic Emergency Obstetric And Newborn Care. (7) Thus these 8 PHCs are responsible for resuscitating neonates from all 63 PHCs when they aren't referred to a hospital.

In this present study, we aim to investigate the knowledge difference of doctors and midwives who have and have not taken a neonatal resuscitation courses. This study may draw more attention to these healthcare's knowledge of neonatal resuscitation and provide the data to conduct more neonatal resuscitation course.

METHOD AND MATERIAL

This is a descriptive quantitative cross-sectional research located at 8 Emergency Neonatal and Obstetrics Services in public health Surabaya in Public Health Center Surabaya These PHCs are Jagir PHC, Banyu Urip PHC, Medokan Ayu PHC, Tanah kali Kedinding PHC, Tanjungsari PHC, Balongsari PHC, Sememi PHC, Simomulyo PHC. The time used for conducting this research may differ for every primary health care, however, generally it is conducted from December 2018 to July 2019. Through stratified random sampling, 10 respondents from each PHC which was filtered through

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several inclusion and exclusion criteria were asked to answer a questionnaire which was referenced from The Textbook of Neonatal Resuscitation, 7th edition. We divide the occupations by a ratio of 7 midwives to 3 GPs, as the ratio is similar to the population.

The inclusion and exclusion criteria we used to filter out unsuitable respondents:

Inclusion criteria:

1. Respondents must be midwives or general practitioners practicing BEmOC in the Primary Health Care.
2. Respondents have to agree and sign the information for consent and informed consent forms.

Exclusion criteria:

1. Paid leave respondents.
2. Respondents in the process of taking further study.

The 7th edition Textbook of Neonatal Resuscitation is the latest neonatal resuscitation textbook consisting of up-to-date recommendations. It is made by the American Academy of Pediatrics and the American Heart Association.

IBM SPSS Statistics, version 23 was used for statistical analysis. Pearson Product Moment for the validity test and Cronbach's Alpha for the reliability test is used to ensure the questionnaire is valid and reliable. Mann-Whitney U test, a comparative non-parametric test is used to compare the respondent's knowledge. Differences between respondents who have participated in the NLS course and respondents who have not participated were considered to be significant when the P-value was <0.05.

RESULT AND DISCUSSION

Seventy-Eight subjects have partaken in this questioner about neonatal resuscitation as seen in table 1. Similar research is done in Muhammadyah Gresik Hospital also has a similar percentage of the respondent with adequate knowledge (45.8%). (8)

Midwives are known to be a partner for women to give them support and education throughout their pregnancy period and their puerperal. Midwives are also responsible for helping women during labor, educating, and detecting complications of mother and child's health. (9) Therefore, there are more midwives than doctors practicing in BEmONC PHCs. This is proven with the data from the Ministry of Health Republic of Indonesia. (10)

Table 1. Characteristics of the Respondents

Characteristics	Frequency (N=78)	Percentage (%)
Profession		
Midwife	57	73.1
General Practitioner	21	26.9
NLS Course Participation		
Participate	10	12.8
Did not participate	68	87.2
Knowledge		
Good	32	41
Moderate	20	25.7
Bad	26	33.3

The result in table 2 shows that there is no significant difference between these two groups. The grade percentage of respondents who have taken NLS Course in Karanganyar District PHC is similar to the grade percentage in BEmONC Primary Health Care in Surabaya. (11)

Table 2. The Knowledge Based on NLS Course Participation

NLS Course Participation	Knowledge							
	Good		Moderate		Bad		Total	
	n	%	n	%	n	%	n	%
Have	2	20.0	5	50.0	3	30.0	10	100.0
Have not	30	44.1	15	22.1	23	33.8	68	100.0
P-Value = 0.419								

There is no significant difference between respondents who participated in the NLS

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course and respondents who did not participate in the NLS course. Generally, the factors that may contribute to the knowledge of a course is course effectiveness and knowledge retention.

Studies show that there is significance between pre-test and post-test of respondents participating in the NLS course. (12)(13) Therefore, the insignificant difference in knowledge may not be caused by NLS course effectiveness, but caused by NLS knowledge retention. Mosley and Shaw also discussed that the knowledge of respondents who practice neonatal resuscitation 5 times in a month have a significant difference to respondents who practice neonatal resuscitation once a month. Knowledge retention is also important for basic life support courses as the knowledge also decreased after 1 month because the fewer the practice. (14)

CONCLUSION

In conclusion, the knowledge difference between midwives and general practitioners who have participated and have not participated in the NLS course in BEmONC primary health care in Surabaya is not significant. This indifferent knowledge may be caused by inadequate retention of NLS knowledge of midwives and GPs who have participated in the NLS course.

Further research is needed to evaluate the current retention program and determine the appropriate action. Other research is needed to find the most effective retention program to maintain the NLS knowledge.

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Conflict of Interest

This research does not have any conflict of interest.

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Original Article

EFFECTIVITY COMPARISON OF KETAMINE AND MORPHINE AS POST-OPERATIVE ANALGESIC IN SPINAL SURGERY

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ABSTRACT

Introduction: Patients who undergo spinal procedure, experience the post-operative pain as the major problem. From the Visual Analog Scale (VAS), patients scale their pain around 8. An inadequate pain management could fasten the healing process and reduce patient life quality. Opioid group as the gold standard still inflicts several problems, such as respiratory depression. Moreover, the combination NSAID and opioid which used to suppress the side effect, still burden the healthcare cost. In a research of analgesic, through the discovery of N-Methyl D Aspartate receptor, researchers found an explanation of the ketamine effect in relieve chronic and intense pain which safer and cheaper. **Method and Material:** This research using single blind randomized control trial. Comparing 0.25mg/kg ketamine IV followed by ketamine 0,1mg/kg/h for the intervention group and 0.02mg/kg/h of morphine for the control group to manage the first 24 hours pain sensation. If patient VAS was more than 4, patient would get additional 0.5mg/kg ketamine (intervention group) and 25µg fentanyl (control group). **Result and Discussion:** From 17 patients each groups, the VAS values were better in control group rather than on intervention group. Low dose ketamine can't be compared with morphine to manage post spinal procedure pain. There were no hemodynamic changes, respiratory rate depression, loss of consciousness and hallucination, nystagmus, vomiting and hyper salivation. Even though 11.8% of the subject were nausea. The morphine group tends to experience hemodynamic changes and loss of consciousness in the first 12 hours but still within normal range. In the control group, 47.1 % patients were having nausea in the first hour, but only 17.6% of them who actually vomited. **Conclusion:** The analgesic effect of morphine is higher than ketamine, but the amount effect of ketamine is lower than morphine so that ketamine is more effective and safer given in the room.

Keywords: Post Spinal Procedure Pain; VAS; Low Dose Ketamine; Morphine

ABSTRAK

Pendahuluan: Pasien yang menjalani operasi tulang belakang, sering kali mengeluhkan nyeri pasca-operasi sebagai masalah utama. Berdasarkan Visual Analog Scale, pasien mengaku nyeri yang dirasakannya berada pasa skala 8. Penanganan nyeri yang tidak adekuat yang dapat menganggu penyembuhan nyeri dan menurunkan kualitas hidup pasien. Gold standard dari pereda nyeri yakni opiod masih menimbulkan beberpa masalah, seperti distress napas. Lebih lanjut lagi, kombinasi dari NSAID dan opioid untuk menurunkan efek samping pada dampak kenaikan biaya perawatan pasien. Dalam sebuah penelitian analgesic, melalui penemuan reseptor N-Methyl D Aspartate, menjelaskan bahwa ketamine dapat meredakan nyeri kronis dan berat dengan biaya yang lebih rendah dan efek samping yang minimall. **Metode dan Bahan:** Penelitian ini merupakan peneilitian eksperimen yang menggunakan single blind randomized trial control yang bertujuan untuk membandigkan manfaat ketamin IV 0,25mg/kg yang di dilanjutkan dengan ketamin 0,1mg/kg/jam untuk kelompok perlakuan dan 0,02mg/kg/jam morfin pada grup kontrol untuk mengatasi nyeri 24 jam pertama. Jika pasien mengeluh VAS>4, pasien mendapatkan tambahan 0.5mg/kg ketamine untuk grup coba dan 25µg fentanyl untuk grup kontrol. **Hasil dan Pembahasan:** Jumlah sampel yang didapatkan untuk masing - masing kelompok ada 17 orang, dimana VAS pada kelompok perlakuan lebih tinggi dibandingkan pada kelompok kontrol. VAS kelompok perlakuan lebih tinggi dari kelompok kontrol Pada kelompok ketamin tidak didapatkan perubahan pada hemodinamik, seperti frekuensi napas, penurunan kesadaran, halusinasi, nystagmus, muntah dan hipersalivasi. Salah satu keluhan yanh sering timbul adalah mual (11.8%). Hal yang berbeda dijumpai pada kelompok morfin dimana ditemukan kecenderungan penurunan hemodinamik, disertai penurunan kesadaran dan frekuensi napas. Kejadian mual pada hampir 24 jam pertama

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tertinggi pada jam ke-1 47.1% dan muntah 17.6%. **Kesimpulan:** Efek Analgetik Morfin lebih tinggi dibandingkan Ketamin, sedangkan jumlah efek samping ketamine lebih rendah dari morfin sehingga ketamine lebih efektif dan aman diberikan diruangan.

Kata kunci: Nyeri Pasca Operasi Tulang Belakang;VAS; Ketamin Dosis Rendah; Morfin.

INTRODUCTION

Pain is one of the most frequently complained by patient who have performed spinal surgery. This is supported by data that show more than 50% of patients complain of pin after surgery as their major problem. (1), the inadequate pain management will disrupt the healing process due to the activation of endocrine stress response resulting in increase in sympathetic tone and catabolic hormone. The inhibited healing process results in an increase of patient's hospitalization duration, affect mental status, and reduce the quality of life of the patient. (2)

Post spinal operative pain includes moderate to severe pain indicated by a VAS scale of more than 7. Post discectomy, patients often complain the severe pain (with VAS scale of 8). (3) This pain due to incisional pain from the skin to the bones and also the pain arise from nerve lesions. (4) Chronic pain is also felt by 80% who undergone elective lumbar puncture and received opioid drugs. The damage of nerve fibers due to spinal surgery also cause neuropathic pain that can cause interference to the somatosensory system. (5)

In 2012, 131 cases of elective spinal surgery had been carried out at Dr. Soetomo General Academic Hospital Surabaya. The most common cause of spinal surgery is fracture both trauma and non-trauma (spondylitis TB, malignancy, and idiopathic). The combination of ketorolac and tramadol is often used to relieve pain on a VAS scale of 4 – 6. On the other hand, a combination of 1 mg/hour of morphine and ketorolac can reduce pain to VAS 3. (6) This proves that analgesic administration has not been able to completely eliminate the post-spinal surgery pain. Provision of rapid and adequate analgesics is needed to accelerate the healing process and reduce the number of diabetic ulcers caused by long time immobilization.

Nowadays, opioids are the gold standard therapeutic given to deal with acute and chronic pain. One of the opioid drugs that is often given is morphine. Morphine is a prototype of an endogenous opioid hormone that can bind with endogenous opioid receptor and cause the effects of respiratory depression, nausea, vomiting, indigestion, urinary retention, allergies, and risk of tolerance. The existence of serious side effects caused by opioid group cause the use of opioid requires strict observation. Analgesic effects can also be obtained from NSAID group. Side effects that caused by NSAID are disorders of gastrointestinal system, decreased kidney function, and affect the platelet aggregation process. (5)

N-Methyl D Aspartate (NMDA) receptors also play role in causing pain. Pain causes the excitement of glutamic acid to form NMDA-glutamic complex bonds. This complex contributes to the increasing of the intensity and amplitude of pain felt. These NMDA receptors are spread from the peripheral nerves to the central nervous system. (7)

Ketamine, the non-competitive inhibitor of glutamate will inhibit the formation of NMDA-glutamate complex bonds by binding

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to NMDA receptors through the binding of phencyclidine side (PSP). This complex will inhibit the excitation of pain and reduce the secretion of glutamate. (8) Ketamine giving can be done through subcutaneous injection, intravenous injection, intramuscular injection, and intrathecal injection without the effect of respiratory depression. As an analgesic, ketamine can be given intravenously or subcutaneously at a dose of 0.2 – 0.5 mg/kg followed by intravenous administration of 0.05 – 0.2 mg/kg/hour as a maintenance dose. (9) Therefore, the use of ketamine can reduce the need of morphine, resulting in preventable side effect and tolerance of morphine.

METHOD AND MATERIAL

This study used a single blind randomized trial control. Held in the Surgical Center Building and Aster Ward (UPI A) Dr. Soetomo General Academic Hospital in September – October 2012. Patients who met the inclusion criteria were divided into 2 groups: the test group and the control group. The inclusion criteria are the patients have PS (Physical Status) 1 and 2, aged 15 to 55 years old, have normal BMI, elective surgery with non-trauma case. The population came from patients who were indicated for spinal surgery in September – October 2012. The test group was treated using IV ketamine at a dose of 0.25mg/kg followed by administration of 0.1mg/kg/hour, while the control group received morphine 0.02mg/kg/hour. The minimum population size is 16 patients for each group. The sample size was determined using unpaired analytical and numeric sampling formulas.

Pain scale assessed with VAS and has been conducted every 3 hours after the drug administered (3^{rd}, 6^{th}, 9^{th}, 12^{th}, 15^{th}, 18^{th}, and 24^{th} hour). In addition, the hemodynamic monitoring including respiration rate, blood pressure, heart rate, and consciousness were also documented. After administering the analgesics, the side effect was also assessed at 1^{st} and 15^{th} minute, 1^{st}, 3^{rd}, 6^{th}, 9^{th}, 12^{th}, 15^{th}, 18^{th}, and 24^{th} hour. During the observation period, if the pain was obtained the VAS scale of 3, the patient will receive and additional analgesics using intravenous fentanyl at a dose of 25mg for the control group and ketamine 0.5mg/kg for the test group.

Patients' data were recorded including the age, sex, weight, type of surgery, and the duration of surgery. The normality of the data was tested using Kolmogorov-Smirnov sample. To compare the level of sedation and VAS in two groups, a statistical analysis was performed with the independent sample T-test if samples were normally distributed or the Mann-Whitney U test if the sample distribution was not normal.

RESULT AND DISCUSSION

From the study, there were 34 patients fulfilled the sample criteria at RSUD Dr. Soetomo and were randomized and divided into 2 groups; test and control group.

From 34 patients, the average age of patients given ketamine was 42.6 years old and 40.2 years old for patients given morphine. The average patient body weight was 58kg for the test group and 51.2kg for the control group. The normality of age and weight data was tested statistically using Kolmogorov-Smirnov test and founded the insignificant data in each group ($p>0.05$). Chi square test was performed to analyze the homogeneity in sex and the type of surgery and showed there was not significant in both groups ($p>0.05$). The duration of surgery in the ketamine group was 177.4 minutes and morphine group 224.1 minutes. The Kolmogorov-Smirnov test was

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found to be significant in both groups with p<0.05.

Sedation Level

The sedation levels were evaluated using the Ramsay Sedation Scale (RSS) and analyzed using the Mann-Whitney U test.

The assessment of sedation scale in patients given ketamine shows a faster response to the stimulus. In the third observation period, there was a decrease of 1 point on the RSS scale. In addition, on 24th hour after surgery, found that the consciousness and cooperative improvement in the group of patients who received ketamine. On the other hand, in the morphine group, the patient was cooperative on 5th hour post drugs administration and the consciousness continually improved on 6th to 18th hour. The patient seemed more sensitive and anxious, but calmed down after 21st hour. Based on the results of statistical analysis, found a significant difference in the first hour and 9th to 18th hour after surgery with p<0.05. However, there was no significant difference at 3rd to 6th hour and 21st to 24th hour of observational time.

Table 1. The differences in Ramsay Sedation Scale (RSS) in the two groups

Observational time	Ketamine (n=17)	Morphine (n=17)	P value
post operation	3(2-4)	2(1-4)	0.001**
1st	3(2-4)	2(1-4)	<0.0001**
3rd	2(2-3)	2(1-4)	0.601*
6th	2(1-3)	2(1-3)	0.211**
9th	2(2-3)	3(1-4)	0.031**
12th	2(2-3)	3(1-3)	0.073*
15th	2(1-3)	3(1-3)	0.009**
18th	2(2-3)	3(1-4)	0.027**
21st	2(2-3)	2(1-3)	0.107*
24th	2(1-3)	2(1-3)	0.491*

Note: Mann-Whitney U test
*= not significant (p>0.05)
**=significant (p<0.05)

The assessment of sedation scale in patients given ketamine shows a faster response to the stimulus. In the third observation period, there was a decrease of 1 point on the RSS scale. In addition, on 24th hour after surgery, found that the consciousness and cooperative improvement in the group of patients who received ketamine. On the other hand, in the morphine group, the patient was cooperative on 5th hour post drugs administration and the consciousness continually improved on 6th to 18th hour. The patient seemed more sensitive and anxious, but calmed down after 21st hour. Based on the results of statistical analysis, found a significant difference in the first hour and 9th to 18th hour after surgery with p<0.05. However, there was no significant difference at 3rd to 6th hour and 21st to 24th hour of observational time.

Visual Analog Scale

The comparison of Visual Analog Scale between the two groups was analyzed using the Mann-Whitney U test. This method was chosen because of the characteristic of the data.

Table 2. The Visual Analog Scale (VAS) observation in the Ketamine and Morphine groups.

Observational time	Ketamine (n=17)	Morphine (n=17)	P value
post operation	3(2-5)	2(0-3)	0.010**
1st	3(1-5)	2(0-3)	0.044**
3rd	2(1-4)	1(0-3)	0.030**
6th	2(1-5)	1(0-3)	0.012**
9th	2(1-5)	1(0-3)	<0.0001**
12th	2(1-5)	0(0-1)	<0.0001**
15th	2(0-3)	1(0-1)	<0.0001**
18th	2(0-4)	0(0-1)	<0.0001**
21st	2(0-3)	1(0-2)	0.003**
24th	1(0-3)	1(0-1)	0.001**

Note: Mann-Whitney U test
*= not significant (p>0.05)
**=significant (p<0.05)

From the test group, the mean VAS at the first hour was on a scale of 3. In patients with a VAS >4 received additional analgesics. On the other hand, in the control group with morphine, a lower VAS was obtained from the

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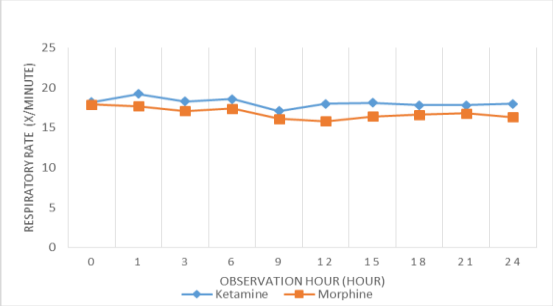
first hour (VAS<2) and continued to improve in 3rd hour after the spinal surgery. VAS analysis between the ketamine and morphine groups showed significant differences ($p<0.05$) at all hours of observation

a. The Effect of Giving Ketamine and Morphine on Respiration

The side effects between the ketamine and the morphine group were analyzed using the Independence T test. Observation of the respiratory rate is needed to monitor the side effects of the drug. After 24 hours of observation, data were obtained that between the ketamine and morphine groups were found



to be significantly different at the 12th, 15th, and 24th hour observations. The respiratory rate on morphine administration tended to slow down from the 12th hour but was still in the normal range. Meanwhile, the respiratory rate of ketamine group remained in the normal range.

Figure 1. Respiratory rate during 24 hours of observation after ketamine and morphine administration.

b. The Effect of Ketamine and Morphine Administration on Hemodynamics

Ketamine and morphine have been known to have effects on hemodynamics. Blood pressure (systole and diastole), heart rate, and mean arterial pressure for 24 hours were recorded.

The mean systolic pressure in the ketamine group before surgery was 130mmHg and decreased to 120mmHg. In the morphine group the decrease in systolic pressure occurred significantly at 9th hour from 120mmHg to 100mmHg. Based on the results of statistical analysis on both drugs, there were no significant systolic changes. The results of systolic analysis did not show significant differences between the two groups at 9th, 21st, and 24th hour. However, there were statistically significant differences at 12th, 15th, and 18th hour of observation.

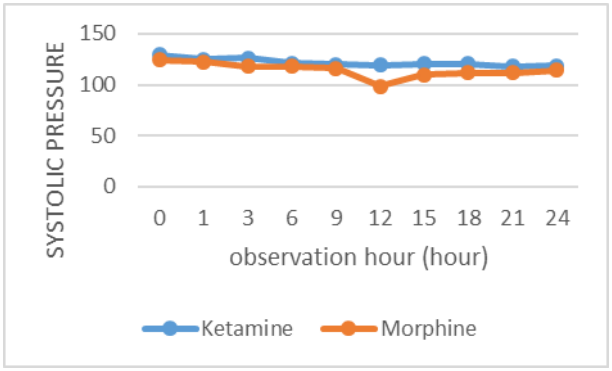


Figure 2. The changes in systolic blood pressure during 24 hours observations on ketamine and morphine administration.

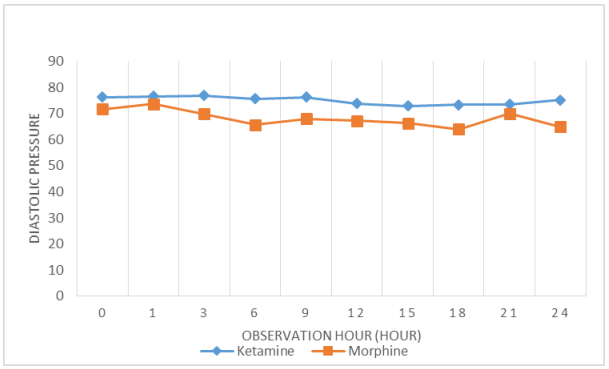


Figure 3. The diastolic changes during 24 hours of observation on the ketamine and morphine administration.

The 24-hour diastolic changes observation showed significant differences at the 3rd, 6th, 9th, 18th, and 24th hour between the ketamine and morphine groups ($p<0.05$). Similar diastolic pressures were obtained at all hours of observation. The diastolic of morphine group was the highest at 1st hour and lowest at 18th hour of observation. All diastolic values were within normal range (60-90mmHg).

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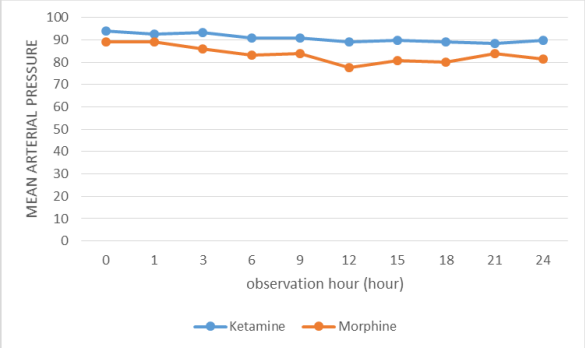

Figure 4. Mean Arterial Pressure during 24 hours of observation on ketamine and morphine administration.

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All observations in the ketamine group showed a mean arterial pressure of more than 80mmHg. Meanwhile, the administration of morphine caused a decrease in MAP below 80mmHg at the 12th hour of observation. Mean arterial pressure in the ketamine group tended to be higher than in the morphine group.

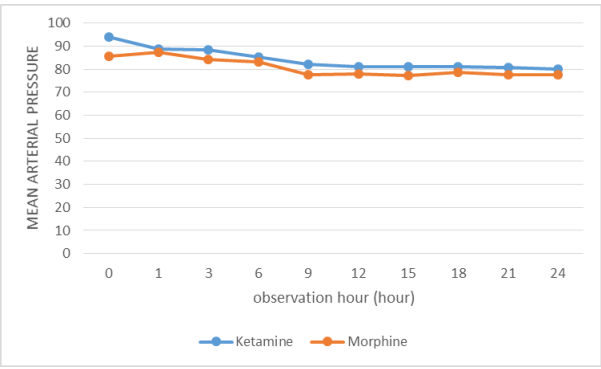

Figure 5. The average heart rate changes in the ketamine and morphine administration.

Heart rate at 24 hours of observation showed no significant difference between administration of ketamine and morphine. The highest heart rate in the ketamine group was 88x/minute, which gradually slowed down to 80x/minute at 24th hour postoperative. The highest heart rate in the morphine group at initial observation was 85x/minute which gradually slowed down to 79x/minute. The ketamine group tended to have higher heart rate than the morphine group.

c. Nausea

The incidence of nausea in both groups was analyzed using the chi square test. A significant difference was obtained at 0 hour ($p<0.05$). In other observations, no significant difference was obtained. Patients who received ketamine felt nauseous at the 1st and 3rd hour as much as 11.8% of the total patients. Morphine induce nausea in 8 patients (47.1%) at 0 and 1st observational hour. Complaints of nausea gradually decreased after the 3rd to 24th hour of observation. However, patients who received morphine did not complain for nausea started at 15th to 24th hour.

Table 3. The occurrence of nausea within 24 hours of observation

Observational time	Ketamine (n=17)	Morphine (n=17)	P value
post operation	0	8 (47.1%)	0.003**
1st	2 (11.8%)	8 (47.1%)	0.057*
3rd	2(11.8%)	3(17.6%)	1.000*
6th	0	4(23.5%)	0.103*
9th	0	3(17.6%)	0.227*
12th	0	1(5.9%)	1.000*
15th	0	0	0
18th	0	1(5.9%)	1.000*
21st	0	1(5.9%)	1.000*
24th	0	0	0

Note: chi square test
*= significant ($p>0.05$)
**= not significant ($p<0.05$)

d. Vomiting

Vomiting was only found in the morphine group at 0 and 1st observation hour, in 3 patients. After 9 o'clock, no more complaints of vomiting were found.

Table 4. The occurrence of vomiting within 24 hours of observation

Observationaal time	Ketamine (n=17)	Morphine (n=17)	P value
post operation	0	3(17.6%)	0.227*
1st	0	3(17.6%)	0.227*
3rd	0	0	0
6th	0	2(11.8%)	0.485*
9th	0	1(5.9%)	1.000*
12th	0	0	0
15th	0	0	0

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18th	0	0	0
21st	0	0	0
24th	0	0	0

Note: chi square test
*= significant (p>0.05)
**= not significant (p<0.05)

e. Hyper-salivation

The ketamine administration can cause hyper-salivation. Even though, during the observational time, the incidence of hyper-salivation was not found.

f. Nystagmus and hallucination

The psycho-mimetic effect of ketamine is hallucinations and visual distortion (nystagmus). In this study, these effects were not obtained at all hours of observation.

Morphine is an effective and powerful analgesic for dealing with visceral and somatic pain. (3) On the other hand, giving bolus morphine 0.15mg/kg can cause sedation effects. (10) Administering a maintenance dose of 0.02mg/kg/hour can reduce pain to VAS 0 within 24 hours after a spinal procedure. (11) In continued administration, the effects of analgesia and sedation can be extended due to the formation of morphine glucoronate which is known as an active metabolite product. Prolonged effect of analgesia and sedation can last up to 8 hours of surgery. (2)

Ketamine works by inhibiting glutamate at the NMDA receptor through the phencyclidine side. This causes ketamine to play an indirect role in inhibiting the transmission of pain impulses, especially in central sensitization. As an analgesic, ketamine works with low doses, ranging around 0.2-0.5mg/kg. This low dose ketamine can be used to relieve acute and chronic pain. The effect of ketamine will be felt 30 minutes after administration. (12) Continuous administration will prolong the effects of analgesia. This situation can occur because metabolite products from ketamine also have an analgesic effect as much as 1/3 – 1/10 times the effect of the initial molecule. Ketamine has a stronger analgesic effect on post-spinal pain procedures. Pain caused by spinal surgery procedures is included in severe pain because it causes musculoskeletal damage and nerve pain that has the potential to cause neuropathic pain. (4)

A study on the administration of ketamine in femur surgery says that at the initial dose of ketamine 0.25mg/kg followed by 0.1mg/kg can reduce pain to VAS 1-3, by causing side effects in the form of nausea. (12) If this dose increase, ketamine can cause hallucinations, nausea, and vomiting. (13)

In this study, 0.25mg/kg ketamine was followed by 0.1mg/kg/hour given. The VAS mean obtained was 3 and gradually decreased to 1 after 24 hours of observation. When patients who had received ketamine, but still complained of pain more than VAS 3, they received analgesic resuscitation with ketamine 0.5mg/kg/hour. At the initiation dose and ketamine maintenance above, there is accumulation of ketamine and its metabolites in the blood so that it can relieve pain at 21th hour of observation. However, evidence of the need for analgesic resuscitation shows that the existing dose of ketamine is still insufficient to cope with postoperative pain.

Observations on the side effects of both drugs have been made during this study. Even though both drugs are given in low doses, the accumulation of the drug and its metabolic products can be dangerous. (2)(9) Morphine directly works in the respiratory center in the brain stem and slow down the respiratory rate. (9) Respiratory depression can be a direct result of the accumulation of morphine and its metabolites. (14) On the other hand, ketamine does not affect ventilation. The respiratory

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rate only decreases if ketamine is given together with other anesthetics. (15) However, things that need to be considered in the use of ketamine is an increase in salivation and secretory tracheal production which can increase the risk of aspiration. (9) Hyper-salivation in this study was not possible, this is likely due to anti-sialagogue administration during pre-surgery. Administration of morphine and ketamine during this study did not cause respiratory problems.

The impact of morphine administration on the cardiovascular system is depression in the myocardium and sympathetic nerve function. Both of these cause a decrease in blood pressure and cardiac output. In addition morphine also has a stimulatory effect on the vagal nerve, stimulate vagal excessively, causing bradycardia. (9)(14) Meanwhile, administration of ketamine causes stimulation of the sympathetic nerve and inhibits the absorption of norepinephrine at synapses. (9)(16)

In the administration of ketamine at a dose of 0.25-0.5mg/kg IV, it can provide hypnosis effects and electroencephalographic changes. (12) In the administration of low-dose ketamine (20-40mg) for MRI procedures in patients weighing 70kg, ketamine can inhibit motor function, impulse pain, and provide psychometric effects. (17)

The percentage of nausea and vomiting during all types of surgery is 25-30%. Nausea and vomiting occur due to stimulation at the center of vomiting. Stimulation can originate from the cerebellum (pain, anxiety, senses, and vestibular disorders), cranial afferent nerve that stimulate solitary tracts (N X, N V, N VII, N IX, N XII), and stimulation of the chemoreceptor trigger zone (CTZ) at the base ventricles. (4) In addition, patient factors, type of surgery, surgical techniques, and anesthesia also increase the risk of postoperative nausea and vomiting (PONV). (18) The presence of opioid receptors on CTZ causes the administration of morphine with a low dose even though it can still cause nausea and vomiting.

Ketamine affects the dissociation center and causes 10-30% of adults to experience misperceptions, which are temporary, shown by hallucinations, delirium, and nightmares. This situation can occur in the administration of ketamine at a dose of more than 2mg/kg intravenously. (9)(16) Midazolam given just before surgery can reduce the psycho-mimetic effect of ketamine. (16)

CONCLUSION

Based on the results of the study found that the analgesic effect of morphine is higher than ketamine, but the amount effect of ketamine is lower than morphine so that ketamine is more effective and safer given in the room.

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Literature Review

FLUID RESUSCITATION IN TRAUMA

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ABSTRACT

Introduction: Trauma is a problem faced every day in the emergency room of the hospital where the researcher works. The degree of trauma from the mildest to life threatening can be found in sufferers. The cause of death in trauma sufferers is hypovolemic shock due to bleeding. The amount of blood loss volume from the patient can be estimated by looking at the clinical signs of the patient. **Literature Review:** In the condition of tissue hypo-perfusion, it will cause a chain process which will eventually lead to cell death. Hypo-perfusion causes anaerobic metabolism, lactic acidosis (coagulopathy, enzyme dysfunction), Na-K pump malfunction (cellular swelling and cell death), there is hypothermia (increase of oxygen demand, coagulopathy). Hypo-perfusion will cause a vicious circle, in which processes that aggravate one another will occur. With the administration of fluids (crystalloid, colloid, transfusion) will improve the hypo-perfusion that occurs in the body. **Conclusion:** The management of hypovolemic shock due to bleeding requires an understanding of the physiology and pathophysiology that occurs due to bleeding. To get maximum results and improve outcome from sufferers, it needs solid team work. Treatment can be different depending on the conditions, equipment and facilities of the hospital / emergency room as well as the policies of each place.

Keywords: Fluid Resuscitation, Trauma, Emergency Room, Hypo-perfusion

ABSTRAK

Pendahuluan: Trauma merupakan masalah yang dihadapi sehari – hari pada ruang gawat darurat rumah sakit tempat kita bekerja. Derajat trauma mulai yang paling ringan sampai mengancam jiwa bisa kita temukan pada penderita. Penyebab kematian pada penderita trauma adalah syok hipovolemia karena perdarahan. Jumlah volume kehilangan darah dari penderita bisa diperkirakan dengan cara melihat tanda klinis dari penderita. **Review Literatur:** Pada kondisi hipoperfusi jaringan akan menyebabkan terjadinya proses berantai yang pada akhirnya akan menimbulkan kematian sel. Hipoperfusi menyebabkan metabolisme anaerob, asidosis laktat (coagulopathy, gangguan fungsi enzim), kegagalan fungsi pompa Na-K (cellular swelling dan kematian sel), terjadi hipotermia (peningkatan oxygen demand, coagulopathy). Hipoperfusi akan menyebabkan lingkaran setan, dimana akan terjadi proses yang saling memperberat satu sama lain. Dengan pemberian cairan (kristaloid, koloid, tranfusi) akan memperbaiki hipoperfusi yang terjadi pada tubuh. **Kesimpulan:** Penatalaksanaan syok hipovolemia akibat perdarahan diperlukan pemahaman tentang fisiologi dan patofisiologi yang terjadi akibat perdarahan. Untuk mendapatkan hasil yang maksimal dan memperbaiki *outcome* dari penderita dibutuhkan *team work* yang solid. Penanganan bisa berbeda tergantung kondisi, peralatan dan sarana rumah sakit / Unit Gawat Darurat, serta kebijakan dari masing – masing tempat.

Kata Kunci: Resusitasi cairan, Trauma, Ruang Gawat Darurat, Hipoperfusi

INTRODUCTION

Trauma is a problem faced every day in the emergency room of the hospital where the researcher works. The degree of trauma from the mildest to life threatening can be found in sufferers. The causes of death in patients at the beginning were damage to the heart / large blood vessels and severe damage to the central nervous system which made it difficult to get help. The next cause is hypovolemic shock due to bleeding, death due to bleeding can still be prevented and get help quickly and precisely. The slowest causes of death are infection and failure of organ, these can be prevented by adequate management at the onset of trauma and adequate intensive care facilities. (1)(2)(3) (Figure 1 & Figure 2)

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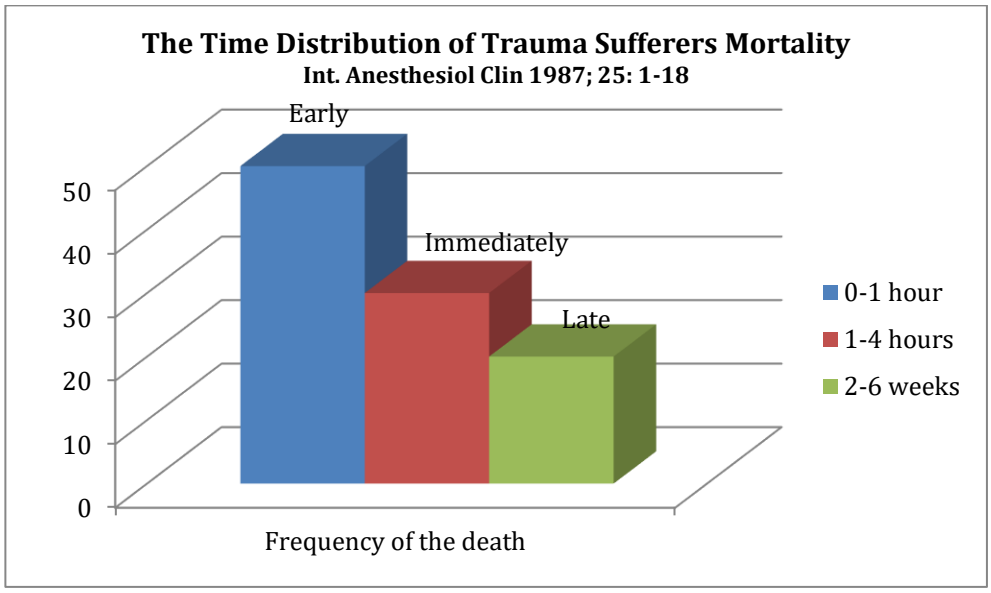

Figure 1. The Time Distribution of Trauma Sufferers Mortality

Table. Causes of death by timing category

Immediate and early deaths	Late deaths	Postdischarge
Brain injury	Infection	Cardiovascular disease
Hemorrhage	Multiple-organ failure	Second major trauma
	Brain injury	Neurologic disease
	Hemorrhage	Malignancy

Figure 2. Table of the Cause Death by Timing Category

LITERATURE REVIEW

The cause of death in trauma sufferers is hypovolemic shock due to bleeding. The amount of blood loss volume from the patient can be estimated by looking at the clinical signs of the patient. The trauma score classified hypovolemic shock into 4 classes of bleeding with different clinical signs. (4) (Table 1) Hypovolemic shock decreases oxygen supply to tissues resulting in an imbalance between demand and oxygen supply, leading to an oxygen deficit. The more severe the shock that occurs, the greater the oxygen deficit and at some point will cause the irreversible damage of cells / tissues. (5) (Figure 3) Thus, the condition of hypovolemic shock / tissue perfusion disorders must be addressed immediately to prevent further damage. In patients with hypovolemic shock due to trauma there is an oxygen delivery decrease, due to the decline of stroke volume / cardiac output (drop preload) and decreased Hb. Initially, this condition could be compensated for by increasing the other components from oxygen delivery (raise heart rate, vasoconstriction, intravascular fluid shift), but if the process of hypo-volemia continues, there will be a condition of greater damage. The target of given fluid resuscitation is to prevent tissue hypo-perfusion, avoiding "trias of death" (coagulopathy, hypothermia, acidosis) and avoid organ failure. (6)(7)

In the condition of tissue hypo-perfusion, it will cause a chain process which will eventually lead to cell death. Hypo-perfusion causes anaerobic metabolism, lactic acidosis (coagulopathy, enzyme dysfunction), Na-K pump malfunction (cellular swelling and cell death), there is hypothermia (increase of oxygen demand, coagulopathy). Hypo-

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perfusion will cause a vicious circle, in which processes that aggravate one another will occur. With the administration of fluids (crystalloid, colloid, transfusion) will improve the hypo-perfusion that occurs in the body.(7)

Classification of hypovolaemic shock and changes in physiological variables

	Class I	Class II	Class III	Class IV
Blood loss				
%	<15	15-30	30-40	>40
ml	750	800-1500	1500-2000	2000
Blood pressure				Very low
Systolic	Normal	Normal	Decreased	Barely
Diastolic	Normal	Decreased	Decreased	recordable
Pulse (beats/min)	Normal	100-120	120 (thready)	120 (very thready)
Capillary refill	Normal	Slow (>2 seconds)	Slow (>2 seconds)	Undetectable
Respiratory rate	Normal	Tachypnoea	Tachypnoea (>20/min)	Tachypnoea (20/min)
Extremities	Normal	Pale	Pale	Clammy, cold
Mental state	Alert	Restless or aggressive	Anxious, drowsy, aggressive	Drowsy, confused or unconscious

Figure 3. Table of Classification of Hypo-volaemic Shock and Changes in Physiological Variables

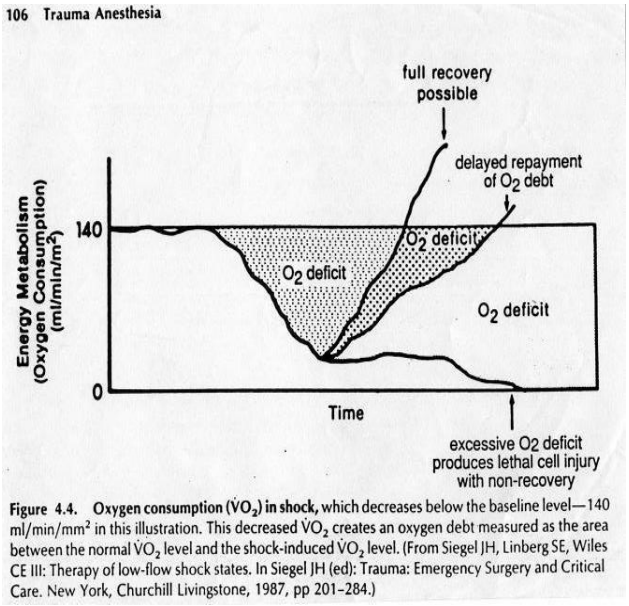

Figure 4.4. Oxygen consumption ($\dot{V}O_2$) in shock, which decreases below the baseline level—140 ml/min/mm² in this illustration. This decreased $\dot{V}O_2$ creates an oxygen debt measured as the area between the normal $\dot{V}O_2$ level and the shock-induced $\dot{V}O_2$ level. (From Siegel JH, Linberg SE, Wiles CE III: Therapy of low-flow shock states. In Siegel JH (ed): Trauma: Emergency Surgery and Critical Care. New York, Churchill Livingstone, 1987, pp 201–284.)

Figure 4. Oxygen Consumption (VO_2) in Shock

The choice of resuscitation fluid ideally meets the following criteria: filling intravascular volume quickly, accurately predicting the amount, having the same composition as extracellular fluid, perfectly metabolized / excreted, does not cause negative metabolic or systemic side effects, is cheap, and gives "outcome" which is good for sufferers. For now, the type of fluid that can meet all of the above criteria is still not available, so medical personnel must be able to choose which fluid is the most suitable for the patient's condition, the availability of tools and fluids and the policies of the hospital. The composition of resuscitation fluids commonly used in daily practice can be seen in Table 1. (8)(9)

Resuscitation fluids have their respective advantages and disadvantages (Figure 5). At the start of resuscitation it is most important to restore the volume of bleeding lost to maintain oxygen supply. Currently, the hemodilution technique with blood replacement fluids is still considered a fairly effective way to fill the volume lost due to bleeding. Where we work crystalloids are still the first choice with consideration: cheap, fast availability, safe and beneficial in the hemodilution technique. If the bleeding continues, or it is predicted that it cannot be stopped quickly (surgery / referral facility) then damage control resuscitation is an option to prevent further damage.

Apart from restoring the lost blood volume, it is important to stop bleeding as soon as possible. If you perform fluid resuscitation but on the other hand the bleeding continues, resuscitation becomes useless. The more the patient loses blood and the more fluids that are not physiological for bleeding, the worse outcome of the patient, aggravated if the patient experiences prolonged hypo-perfusion.

To stop or at least reduce bleeding can be done by damage control resuscitation in a way: damage control surgery (surgery/angiography), permissive hypotension, and hemostatic resuscitation.

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a. Stopping bleeding immediately (pressure dressing, fracture immobilization, applying C-clamp/ pelvic sling) or surgery and angiography.

Table 1. Table of Characteristic of Resuscitation Fluids

Solute	Plasma	Colloids				Crystalloids			
		4% albumin	6% HES 130/0.4	Dextran	Gelatin	Normal saline	Ringer's lactate	Hartmann's solution	Plasma-Lyte
Na^+	135 to 145	148	154	154	154	154	130	131	140
K^+	4.0 to 5.0	0	0	0	0	0	4.5	5	5
Ca^{2+}	2.2 to 2.6	0	0	0	0	0	2.7	4	0
Mg^{2+}	1.0 to 2.0	0	0	0	0	0	0	0	1.5
Cl^-	95 to 110	128	154	154	120	154	109	111	98
Acetate	0	0	0	0	0	0	0	0	27
Lactate	0.8 to 1.8	0	0	0	0	0	28	29	0
Gluconate	0	0	0	0	0	0	0	0	23
Bicarbonate	23 to 26	0	0	0	0	0	0	0	0
Osmolarity	291	250	286 to 308	308	274	308	280	279	294
Colloid	35 to 45	20	60	100	40	0	0	0	0

Osmolarity (mOsm/L); colloid (g/L); all other solutes (mmol/L).

Isotonic Crystalloids		
0.9% saline	Inexpensive Compatible with blood	Dilutes blood composition Hyperchloremic metabolic acidosis
Lactated Ringer's	Inexpensive Physiologic electrolyte mix	Dilutes blood composition Contains calcium, may clot blood
Plasmalyte-A	Inexpensive Physiologic electrolyte mix	Dilutes blood composition
Colloids		
Albumin	Rapid volume expansion	Expensive No proved benefit Dilutes blood composition
Starch solutions	Rapid volume expansion	Coagulopathy with first-generation products No proved benefit Dilutes blood composition
Hypertonic saline	Rapid volume expansion Improved outcomes in TBI patients	Rapid increase in blood pressure m exacerbate bleeding Dilutes blood composition
Red blood cells	Rapid volume expansion Increased oxygen delivery	Expensive, limited resource Requires cross-matching TRALI Viral transmission
Plasma	Rapid volume expansion Clotting factor replacement	Expensive, limited resource Cross-matching required TRALI Viral transmission
Fresh whole blood	Rapid volume expansion Carries oxygen Includes clotting factors and platelets Ideal fluid for early resuscitation	Unavailable in civilian practice – Logistics (low demand) – Time required for viral testing

Figure 5. Respective Advantages and Disadvantages Resuscitation Fluids

b. *Permissive hypotension* :
- Not giving too much fluid and making blood pressure "normal"
- Done if the possibility of bleeding continues
- Target blood flow to meet the vital organs of the heart and brain
- Clinical: palpable radial artery pulsation (systolic> 80 mmHg)
  Drawdown
- Not suitable for head trauma
- Secondary organ hypo-perfusion
- Causes organ failure and sepsis

c. *Hemostatic Resuscitation* by providing

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tranexamic acid and transfusion of blood clotting components: *Fresh Frozen Plasma*: *Packed Red Cell* = 1: 1, *Fresh Whole Blood*, Platelets, Cryoprecipitate, *Recombinant Factor VII*.

In patients with hypovolemic shock, a vicious circle can occur trias of death. Shock causes anaerobic metabolism and causes decreased contractions myocard as well as hypothermia. Hypothermia causes coagulopathy, which causes more bleeding and causes the shock to get worse. Cause coagulopathy from bleeding shock caused by tissue damage, fibrinolysis, shock, hypothermia, hemodilution, acidosis, inflammation, and hypocalcemia (Figure 6). (6)(7)

Causes of acute coagulopathy of trauma-shock

Causes	Effects
Tissue trauma	Exposing the subendothelial matrix with platelet activation Liberation of Factor VII and thrombin
Fibrinolysis	Tissue thromboplastin increases in the resence of thrombin
Shock	Mechanism unknown; related to depletion of Protein C
Hypothermia	Inhibits coagulation serinases. Decreases platelet function
Haemodilution	Dilution of clotting factors. Incorporation of colloids into clot.
Acidosis	Reduction of Xa-Va prothrombinase complex activity Platelet form spheres which are devoid of aggregating tendency
Inflamation	Activated by neutrophils with platelet dysfunction Monocyte adherence to platelets
Hypocalcaemia	Due to citrate in blood and blood components

Figure 6. Table of the Causes of Acute Coagulopathy of Trauma Shock

Blood transfusions are considered given in order to prevent *oxygen delivery* decline and prevent *coagulopathy*. The administration of transfusions in patients with bleeding shock can use PRC/WB/FWB and plasma components (FFP, platelets, cryoprecipitate and *recombinant factor VII*). Management of trauma and shock due to bleeding is primarily to stop bleeding, improve hemodynamics, and not worsen coagulation function. (Figure7). (7)(10)(11)

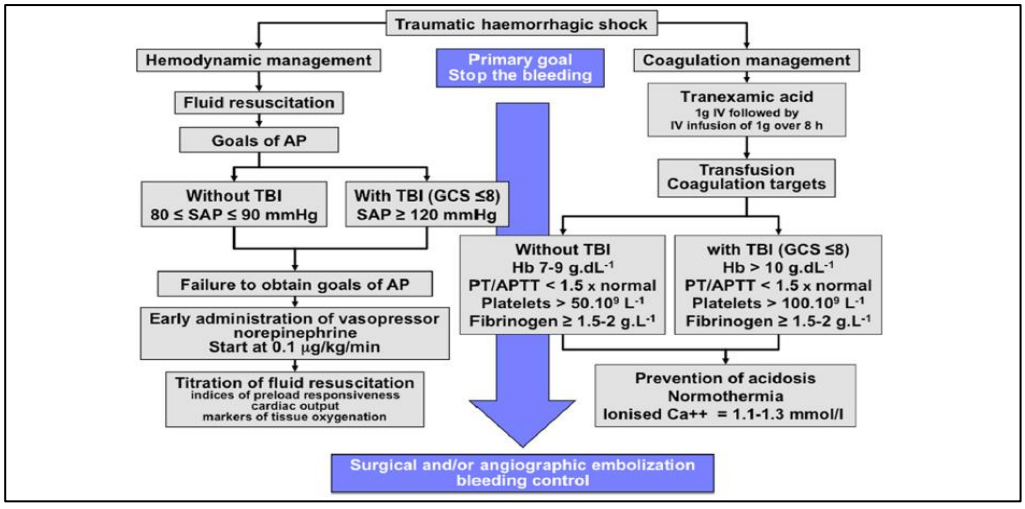

Figure 7. Flowchart of Initial Management of Traumatic Hemorraghic Shock

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There are three results of therapy in shock due to bleeding, namely:

a. *good response* (circulation improves, normovolemia and bleeding stops)
b. *transient response* (circulation improves then falls again, still hypovolemia and bleeding continues)
c. *no response* (circulation does not improve with fluid resuscitation, hypovolemia still remains and bleeding continues) (4)

At *transient response* or *no response* consider for *damage control resuscitation* (*damage control surgery*, *permissive hypotension*, *hemostatic resuscitation*) to reduce blood loss and provide excess blood replacement fluids.

CONCLUSION

The management of hypovolemic shock due to bleeding requires an understanding of the physiology and pathophysiology that occurs due to bleeding. To get maximum results and improve *outcome* from sufferers, it needs solid *team work*. Treatment can be different depending on the conditions, equipment / facilities for the hospital / emergency room as well as the policies of each place.

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Literature Review

TRANSPORTATION AND THE USE OF OXYGEN

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ABSTRACT

Introduction: All living things need a certain amount of oxygen which is obtained from free air, which is continuous throughout life, but cannot be stored in the body as a reserve. Oxygen is distributed throughout the body to the mitochondria of cells which are used in metabolic processes along with glucose to produce ATP (energy source for cell activity) and remove carbon dioxide (CO_2). **Literature Review:** The exchange of oxygen as a metabolic material for the body and carbon dioxide as the end product of the body's metabolism is done through a process called respiration. Blood pumped by the heart carries oxygen from the lungs to all body tissues and brings back the blood containing carbon dioxide from the tissues back to the lungs for gas exchange. Oxygen transport in the blood takes two forms, namely bound to hemoglobin/Hb (the largest) and dissolved. Meanwhile, the transportation of carbon dioxide in the blood takes 3 forms, namely: carbonic ion (the largest), dissolved, and binds to Hemoglobin. **Conclusion:** The consumption of oxygen in the body requires processes and is associated with several organ systems. If one of the systems is not functioning properly, it can cause oxygen deficiency, thus the cells do not consume enough oxygen, which can cause anaerobic metabolism and if it becomes severe it will cause the death of cells, organs, and the individual.

Keywords: Oxygen Transportation; Respiration; O_2; CO_2; Hemoglobin

ABSTRAK

Pendahuluan: Semua mahluk hidup membutuhkan oksigen dalam jumlah tertentu yang didapatkan dari udara bebas, berlangsung terus menerus selama kehidupan, namun tidak dapat disimpan dalam tubuh sebagai cadangan. Oksigen didistribusikan ke seluruh tubuh hingga mitokondria sel yang digunakan dalam proses metabolisme bersama dengan glukosa untuk menghasilkan ATP (sumber energi aktifitas sel) dan membuang karbondioksida (CO_2). **Review Literatur:** Pertukaran gas oksigen sebagai bahan metabolisme tubuh dan carbondioksida sebagai hasil akhir metabolisme tubuh melalui proses yang disebut respirasi. Darah yang dipompa jantung membawa oksigen dari paru ke seluruh jaringan tubuh dan membawa kembali darah yang mengandung karbondioksida dari jaringan kembali ke paru untuk mengadakan pertukaran gas. Transportasi oksigen di dalam darah melalui 2 bentuk yaitu terikat hemoglobin / Hb (paling besar) dan terlarut. Sedangkan transportasi karbondioksida dalam darah melalui 3 bentuk yaitu : ion carbonic (paling besar), terlarut, dan berikatan dengan Hb. **Kesimpulan:** Konsumsi oksigen didalam tubuh memerlukan proses dan berkaitan dengan beberapa sistem organ tubuh. Jika salah satu sistem tidak berfungsi dengan baik bisa menyebabkan defisiensi oksigen sehingga sel tidak cukup mengkonsumsi oksigen, bisa menyebabkan metabolisme anaerob dan jika memberat akan menyebabkan kematian sel , organ dan individu itu sendiri.

Kata Kunci: Transportasi Oksigen; Respirasi; O_2; CO_2; Hemoglobin

INTRODUCTION

All living things need a certain amount of oxygen which is obtained from free air, which is continuous throughout life, but cannot be stored in the body as a reserve. Oxygen is distributed throughout the body to the mitochondria of cells which are used in metabolic processes along with glucose to produce ATP (energy source for cell activity) and remove carbon dioxide (CO_2). The tissues of the body require a constant supply of oxygen to be delivered to cells known as Delivery Oxygen (DO_2). Oxygen delivery in a minute is

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influenced by the amount of oxygen component in the arterial blood (Content Arterial O_2/CaO_2) and the volume of blood pumped in a minute (Cardiac Output/CO) (Figure 1). Any abnormality of one of these components results in disruption of oxygen supply to tissues/cells. Severe oxygen deficiency conditions result in anaerobic metabolism and can lead to cell death. (1,2)

Blood pumped by the heart carries oxygen from the lungs to all body tissues and brings back the blood containing carbon dioxide from the tissues back to the lungs for gas exchange. Cardiac output pumped by the heart depends on the volume of blood pumped once contracted (stroke volume) and the frequency of the heart's pump in a minute (heart rate) (Figure 1). Any interference with one of the components, for example heart rate or stroke volume, without adequate compensation for the other components, will cause a reduction of cardiac output and oxygen supply to tissues.

The amount of oxygen in arterial blood (CaO_2) is determined by the amount of hemoglobin (functions to bind oxygen), the fraction/percentage of oxygen bound to hemoglobin (SaO_2), and arterial blood-dissolved oxygen in small amounts affected by oxygen partial pressure (PaO_2) (Figure 1). Any disturbance in one of the components, such as low hemoglobin or a decrease in arterial blood saturation (desaturation), will result in reduced oxygen supply to the tissues. (1,2)

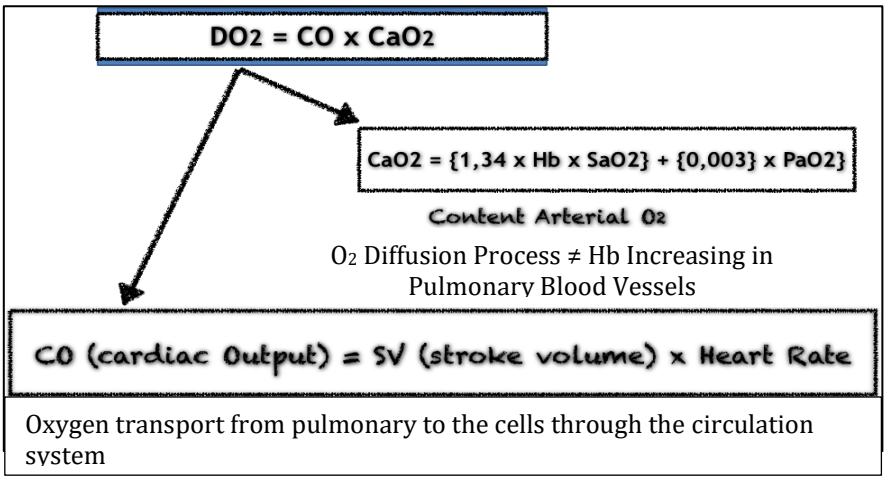

Figure 1. Oxygen Delivery

LITERATURE REVIEW

The exchange of oxygen as a metabolic material for the body and carbon dioxide as the end product of the body's metabolism is done through a process called respiration. Respiration is divided into two, namely external respiration (the exchange of O_2 and CO_2 with outside air) and cellular respiration (intracellular metabolism consumes oxygen and produces CO_2) (Figure 2). Free air contains 20-21% oxygen, the rest is nitrogen (78%), and other gases in very small amounts (CO, CO_2, etc). The air pressure at 1 atmosphere is 760 mmHg and the partial pressure of oxygen (PaO_2) in free air is about 160 mmHg. The largest component of free air that is inhaled during inhalation is 21% oxygen and 78% nitrogen. Whereas the gas content during exhalation is 17% oxygen, 78% nitrogen, and 4% CO_2. Oxygen used for metabolism is about 4-5% of the inhaled air. (3)

Oxygen Cascade

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Oxygen is inhaled from free air and is sent to the mitochondria in the cells through the body's ventilation and circulation systems. The partial pressure of oxygen in free air will gradually decrease up to the mitochondria. oxygen again drops in the aveoli because there is a carbon dioxide component in the alveoli of about 100 mmHg. Then the oxygen will undergo diffusion, increasing the partial pressure of oxygen from the veins, which was originally 40-45 mmHg, in the arteries the partial pressure of oxygen will be 90-95 mmHg (taking into account the physiological shunt of the body containing CO_2). Oxygen will be sent with blood to the arterioles, to the interstitial

During inhalation with free air, the oxygen pressure of about 160 mmHg will drop because it is humidified by the air in the respiratory tract to 150 mmHg. After passing through the airway, the partial pressure of

cells, the oxygen pressure becomes 40-45mmHg. In cell plasma, oxygen pressure becomes 20-25 mmHg and the partial pressure of oxygen in the mitochondria becomes 1-10 mmHg. In venous blood system, the partial pressure of oxygen is around 40-50 mmHg which will return to the lungs and begin the diffusion process and return to the initial cycle (Figure 3). (3)

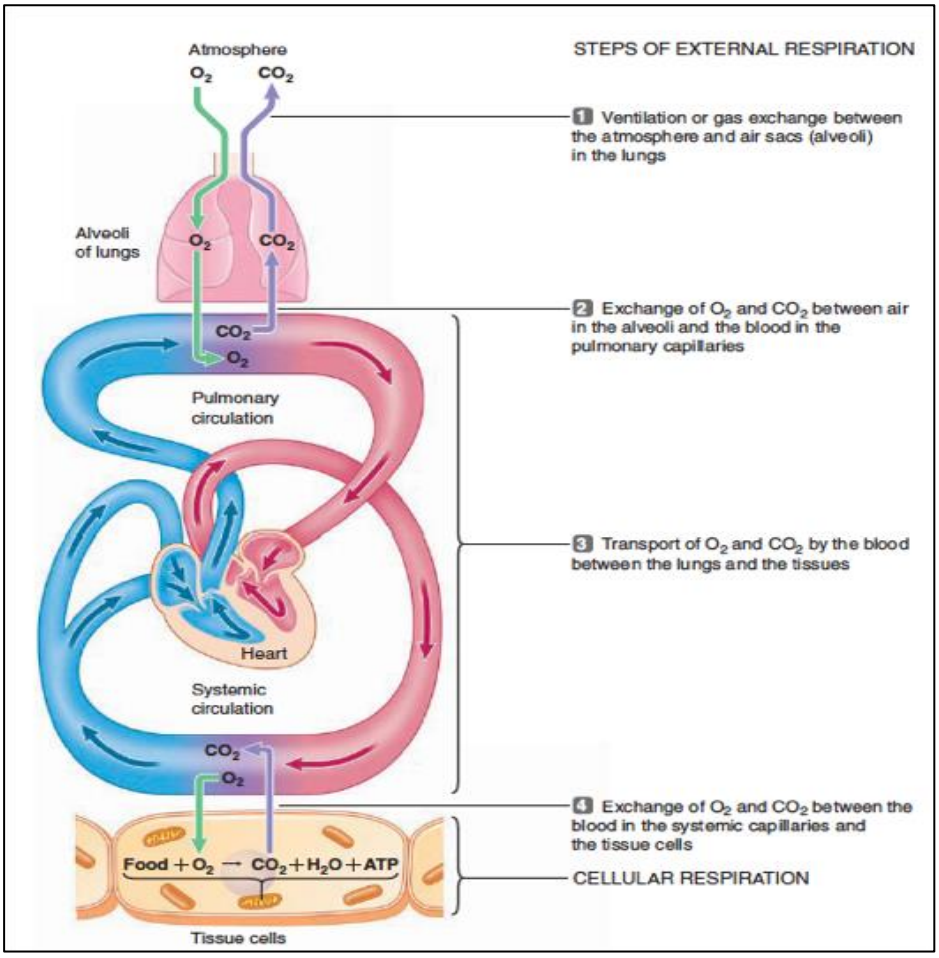

Figure 2. Steps of External Respiration

CO_2 as a result of metabolism has a partial pressure of CO_2 from the veins about 40-45 mmHg is sent to the lungs where it will diffuse and is excreted through the exhaled air around 35-40 mmHg.(3)

Oxygen transport in the blood takes two forms, namely bound to hemoglobin/Hb (the

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largest) and dissolved. Meanwhile, the transportation of carbon dioxide in the blood takes 3 forms, namely: carbonic ion (the largest), dissolved, and binds to Hb (Figure 4). Most of the diffused oxygen will be bound by Hb and each Hb molecule binds 4 O_2 molecules. The amount/fraction in percent of oxygen bound to Hb is represented in oxygen saturation, if all hemoglobin binds to 4 molecules causes the saturation to be 100%. (3,4)

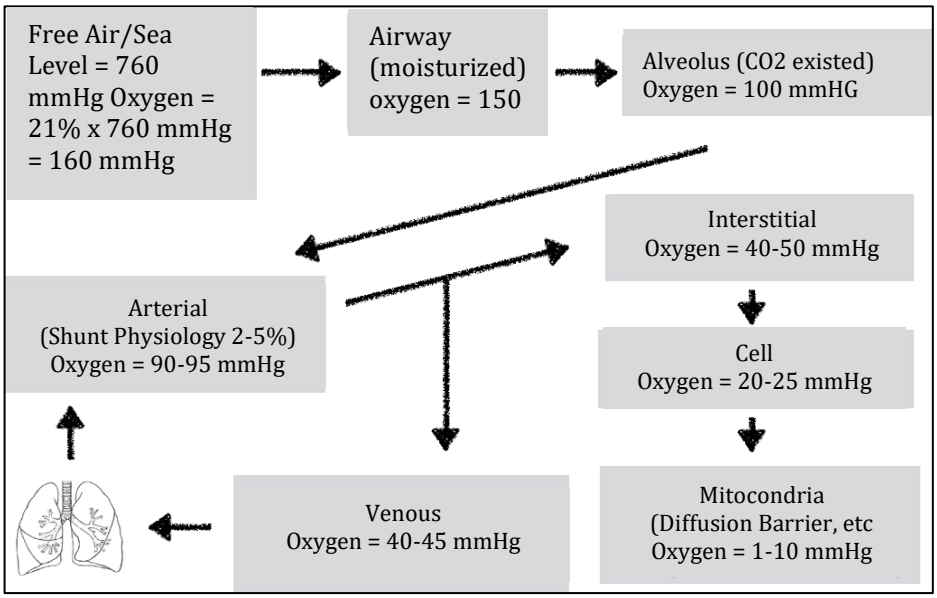

Figure 3. Oxygen Cascade

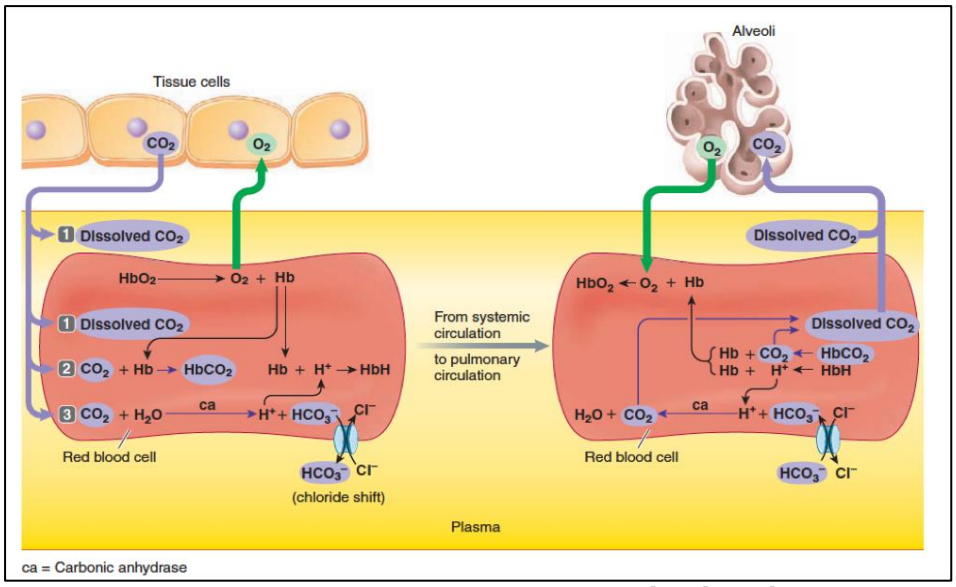

Figure 4. Transport Oxygen & Carbondioxyde

In body tissues, the oxygen released to the tissues causes the oxygen bound to hemoglobin to decrease thus the blood saturation in the veins will decrease. The tendency of hemoglobin to bind or release oxygen is influenced by several factors. This is reflected in oxygen dissociation curve. The oxygen curve shifts to the right under conditions of acidosis, hypercarbia, febris, and an increase in blood levels of 2,3 DPG. This

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causes oxygen to be released more easily from hemoglobin. The oxygen curve shifts to the left under conditions of alkalosis, hypocarbia, hypothermia and a decrease in 2,3 DPG. This makes it difficult for oxygen to escape from hemoglobin (Figure 5). (1,3,4)

In the lungs, O_2 is easier to bind to Hb because of uptake H^+ by HCO_3^- to reform CO_2 (expelled on exhalation) causes alkalosis, thus shifting the oxygen dissociation curve to the left. This process causes an increase in oxygen uptake and a decrease in CO_2 affinity, thus CO_2 is easier to remove. This is known as Haldan effect. In contrast, in tissues, cell produce CO_2 which reacts with H_2O is then broken into H^+ and HCO_3^- thus making the condition slightly acidotic, causing the oxygen dissociation curve to shift to the right (oxygen is more easily released by hemoglobin). Moreover, CO_2 which binds to hemoglobin reduces the affinity of hemoglobin for oxygen, thus O_2 is easier to release into the network. This is known as Bohr effect.(4)

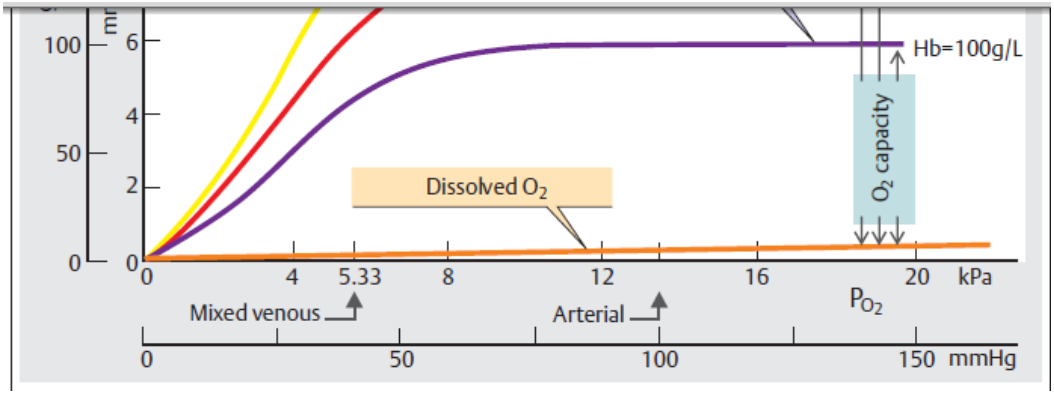

Figure 5. Oxygen Discociation Curve

When it reaches the cellular level, oxygen is taken up by the mitochondria for use in aerobic metabolic processes. Oxygen, along with glucose, produces 36 ATP, carbon dioxide (CO_2), and water (H_2O). If the body's metabolism does not use oxygen, anaerobic metabolism will occur which only produces 2 ATP and lactic acid. (1,5) Normally, the body needs O_2 250 ml/minute and produces CO_2 200 ml/minute. Produced CO_2 divided by consumed O_2 is called respiratory quotion. Respiratory quotion differs in the use of different energy sources (carbohydrates/fat/protein), overall respiratory quotion range is 0.8. (4)

One of the evaluations of tissue use of oxygen is by counting oxygen extraction ratio/O_2 ER. O_2ER is obtained by calculating the ratio uptake of O_2 (VO_2) with oxygen delivery (DO_2) with the equation $O_2ER = VO_2/DO_2$. In this equation, the same values for Hb, CO and 1.34 are obtained, then the equation $O_2ER = (SaO_2\text{-}SvO_2)/SaO_2$ will be obtained. At SaO_2 100% (full saturated) then O_2 ER = SaO_2 - SvO_2. Venous saturation is taken from the pulmonary artery or central venous catheter. The result of this equation shows the level of oxygen consumption by the cell. Normally the value of O_2ER is 20-30%. If O_2ER is over 30%, it indicates a decrease of oxygen delivery (e.g. anemia or low cardiac output), thus oxygen debt can occur. Oxygen debt causes anaerobic metabolism. If the increase is more than 50%, it indicates inadequate tissue oxygenation and is in a dangerous stage. If O_2ER is less than 20%, it indicates that oxygen cannot be used by cells.

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This can occur in cell dysfunction e.g. in sepsis and septic shock.(1)

Causes of oxygen deficiency/hypoxia can occur from the lung level (airway disturbance and ventilation), decreased transport capacity (anemia), heart pump failure, vasoconstriction or vasodilation, abnormal tissue diffusion (edema), and use of abnormal O_2 e.g. mitochondrial poisoning, sepsis). All of the above can cause impaired tissue oxygenation and lead to anaerobic metabolism (Figure 6). (6)

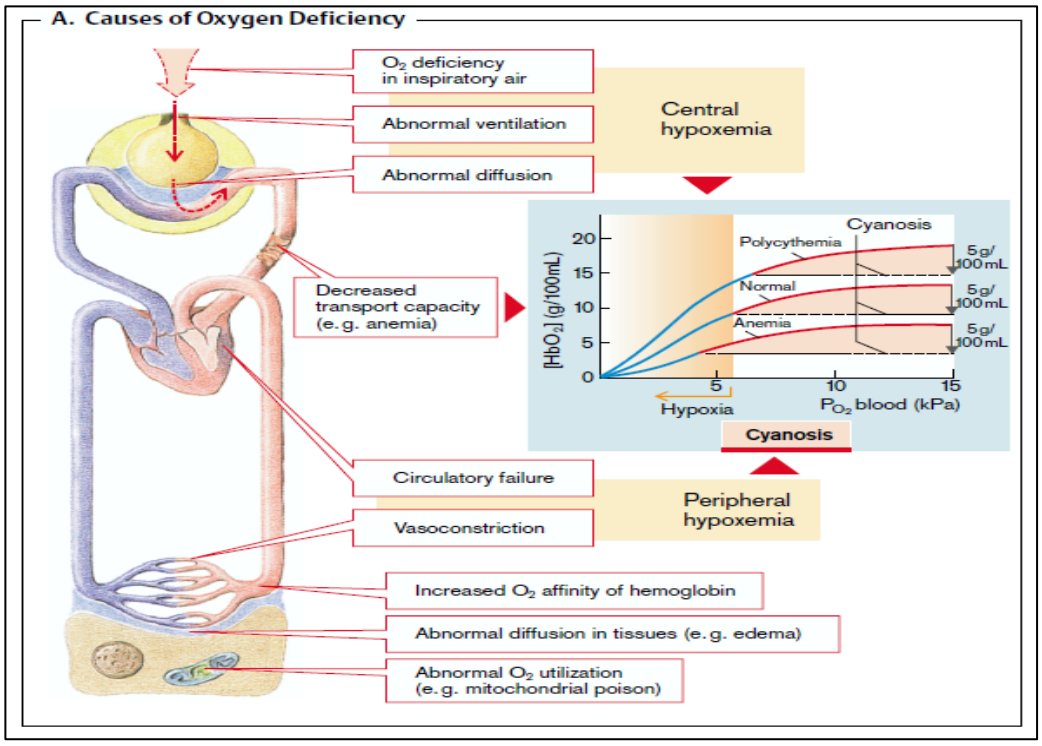

Figure 6. The Cause of Oxygen Deficiency

CONCLUSION

The consumption of oxygen in the body requires processes and is associated with several organ systems. If one of the systems is not functioning properly, it can cause oxygen deficiency, thus the cells do not consume enough oxygen, which can cause anaerobic metabolism and if it becomes severe it will cause the death of cells, organs, and the individual.

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