TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENT	J III
ENGLISH ABSTRACT	V
THAI ABSTRACT	VII
LIST OF TABLES	X
LIST OF ILLUSTRATIONS	XIII
LIST OF ABBREVIATION	XVIII
INTRODUCTION	1
CHAPTER I. LITERATURE REVIEW	3
CHAPTER II. MATERIALS AND METHODS	37
CHAPTER III. RESULTS	51
CHAPTER IV. DISCUSSION	79
REFERENCES	94
APPENDIX	106
CURRICULUM VITAE	129

LIST OF TABLES

Table	es	Page
1	Antioxidant defense systems with enzymes	17
	and their roles in prevention cell damage by	
	cytotoxic O ₂ species	
2	Antioxidant defense systems with substance	18
	and their roles in prevention cell damage by	
	cytotoxic O ₂ species	
3.	Postural drainage position	30
4.	Characteristic of pediatric patients in group A and B	54
5.	The concentration of MDA in the serum and tracheal	55
	aspirates (TA) of the 1 st day and the 6 th day in group	
	A and B	
6.	The concentration of GSH in the serum and tracheal	55
	aspirates (TA) of the 1 st day and the 6 th day in groups	
	A and B	
7.	The concentration of alpha-tocopherol in the serum	56
	and tracheal aspirates (TA) of the 1st day and the 6th day	
	in group A and B	
8.	The concentration of HA in the serum samples and	56
	tracheal aspirates (TA) of the 1st day and the 6th day	
	in group A and B	
9.	The lung injury score and oxygenation (PaO ₂ /FiO ₂)	62
	on the first day and sixth day in group A and group B	

es .	age
The concentrations of MDA, GSH, Vit E, and HA in	64
tracheal aspirates (TA) of six day during physical therapy	
The correlation values of GSH, MDA, Vit E, and HA	72
in blood and tracheal aspirates, lung injury score,	
PaO ₂ /FiO ₂ ratio of the 1 st day in group A treatment	
The correlation values of GSH, MDA, Vit E, and HA	73
in blood and tracheal aspirates, lung injury score,	
PaO ₂ /FiO ₂ ratio of the 1 st day in group B treatment	
The correlation values of GSH, MDA, Vit E, HA in blood	74
and tracheal aspirates, lung injury score, PaO2/FiO2 ratio	
of the 1 st day in group A and B treatment	
The concentrations of GSH, MDA, Vit E, HA, lung injury	90
Score, and PaO ₂ /FiO ₂ ratio between improved and	
non-improved group from all patients	
Information of pediatric patients in group A and B in	123
Age, clinical problem, primary diagnosis and sputum cultu	ıre.
	The concentrations of MDA, GSH, Vit E, and HA in tracheal aspirates (TA) of six day during physical therapy The correlation values of GSH, MDA, Vit E, and HA in blood and tracheal aspirates, lung injury score, PaO ₂ /FiO ₂ ratio of the 1 st day in group A treatment The correlation values of GSH, MDA, Vit E, and HA in blood and tracheal aspirates, lung injury score, PaO ₂ /FiO ₂ ratio of the 1 st day in group B treatment The correlation values of GSH, MDA, Vit E, HA in blood and tracheal aspirates, lung injury score, PaO ₂ /FiO ₂ ratio of the 1 st day in group A and B treatment The concentrations of GSH, MDA, Vit E, HA, lung injury Score, and PaO ₂ /FiO ₂ ratio between improved and non-improved group from all patients

LIST OF ILLUSTRATIONS

Figure	es I	Page
1. (A)	Anatomy of pulmonary structure	4
(B)	The bronchial tree	4
(C)	Alveolar section	4
2.	Component of the extracel lular matrix	5
3.	The alveolar structure in cross section.	7
4.	The mechanism of oxygen-dependent bacterial killing	10
	in a phagocytes.	
5.	Proposed mechanism for formation of lipid peroxidation	13
	from arachidonic acid	
6.	Hyaluronic acid (HA) structures	14
7.	The early events in the evolution of lung inflammation.	15
8.	Structure of Glutathione	19
9.	The mechanism of GSH in detoxification of free radicals.	21
10.	Chemical structure of alpha-tocopherol (Vit E)	22
11.	Inhibition the oxidation of lipid by alpha-tocopherol.	23
12.	Scheme of free radical-induced lipid peroxidation tissue	24
	damage and antioxidants defense.	
13.	The levels of antioxidants in plasma and lung epithelial	33
	lining fluid.	
14.	The hypothesis illustration of chest physical therapy (CPT	36
	for preventing secretion accumulation or atelectasis that	
	attach microbial.	

LIST OF ILLUSTRATIONS

Figure	es	Page
15.	The concentrations of MDA in serum and in tracheal	57
	aspirates of group A and B in the 1st day and the 6th day	
16.	The concentrations of GSH in blood and in tracheal	58
	aspirates of group A and B in the 1 st day and the 6 th day	
17.	The concentrations of Vit E in plasma and in tracheal	59
	aspirates of group A and B in the 1 st day and the 6 th day	
18.	The concentrations of HA in serum and in tracheal	60
	aspirates of group A and B in the 1 st day and the 6 th day	
19.	The lung injury score (LIS) and the PaO ₂ /FiO ₂ ratio of	63
	group A and B in the 1 st day and the 6 th day.	
20.	The changes of malondialdehyde (MDA) levels	66
	in tracheal aspirates (TA) of group A and B within	
	six days of physical therapy	
21.	The changes of glutathione (GSH) levels in tracheal	67
	aspirates (TA) of all subjects in six days of physical there	ару
22.	The changes of alpha-tocopherol (Vit E) levels	68
-	in tracheal aspirates (TA) of all subjects in six days of	
	physical therapy	
23.	The changes of hyaluronic acid (HA) levels in tracheal	69
	aspirates (TA) of all subjects in six days of physical thera	ру
24.	The changes of lung injury score (LIS) of group A and	70
	B in six days of Physical therapy	

Figure	es P	age
25.	The changes of PaO ₂ /FiO ₂ ratio of group A and B	71
	in six days of physical therapy	
26.	Scatter plots showing relationship between	76
	Malondialdehyde (MDA) in tracheal aspirates and	
	oxygenation index (PaO ₂ /FiO ₂ ratio) of the 1 st day	
	in all subjects	
27.	Scatter plots showing relationship between	77
	Alpha-tocopherol in tracheal aspirates and oxygenation	
	index (PaO2/FiO2 ratio) of the 1st day in all subjects	
28.	Scatter plots showing relationship between	78
	hayaluronic acid (HA) in tracheal aspirates and	
	oxygenation index (PaO2/FiO2 ratio) of the 1st day in	
	all subjects	
29.	Scatter plots showing relationship between	91
	MDA and HA in tracheal aspirates in improved-group	
30.	Scatter plots showing relationship between	91
	MDA and HA in tracheal aspirates in non-improved group)
31.	Scatter plots showing relationship between	92
	MDA in tracheal aspirates and PaO ₂ /FiO ₂ in improved-	
	group	
32.	Scatter plots showing relationship between	92
	MDA in tracheal aspirates and PaO ₂ /FiO ₂ in non-improved	ŀ
	group	
33.	Standard curve of malondial dehyde (MDA)	109

Figur	res 🕓	Page
34	The quality control chart showing intra-and inter assay	110
	precision of the MDA concentration with TBARs assay	
35.	Standard curve of various glutathione (GSH) concentration	, 111
36.	The quality control chart showing intra-and inter assay	112
	precision of glutathione concentration with DTNB method	
37.	The quality control chart showing intra-and inter assay	113
	precision of hyaluronic acid (HA) with ELISA based-assay	•
38.	A typical curve of competitive inhibition ELISA assay	114
39.	Standard curve of \(\Omega\)-tocopherol (Vit E) concentrations	115
40.	The quality control chart showing intra-and inter assay	116
	precision of α-tocopherol (Vit E) with HPLC.	
41.	The HPLC-chromatogram of standard α-tocopherol.	117
42.	The HPLC-chromatogram of sample \alpha-tocopherol	118
) Pictur	res .	Page
1.	The condition of pediatric patient under vital monitoring	119
	with EKG, and baby bird ventilator (A), ventilator support	ed
	with endotracheal tube (ET) (B)	
2.	The chest X-ray film showed the right upper lobe	120
	Atelectasis.	

Pictur	res	Page
3.	The pediatric patient who received group A treatment	121
4.	The pediatric patient who received group B treatment	121
5.	The films of chest x-ray in the 1st day and in the 6th day	122
	of physical therapy	

XVII

LIST OF ABBREVIATIONS AND SYMBOLS

ALI Acute lung injury

APTA American physical therapy association

ARDS Acute respiratory distress syndrome

BPD Bronchopulmonary dysphasia

CAT Catalase

CLD Chronic lung diseases

CPT Chest Physical Therapy

CV Coefficient of variation

dl deciliter

DTNB Dithionitobenzoic acid

E• Alpha-tocopherol radical

ELF Epithelial lung fluid

ELISA Enzyme linked-immunsorbance assay

GP Glutathione peroxidase

GSH Reduced Glutathione

GSSG Oxidized Glutathione

HA Hyaluronic acid

H₂O₂ Hydrogen peroxide

HOO• Perhydroxyl radicals

HPLC High performance liquid chromatography

IRDS Idiopathic respiratory distress syndrome

L liter

LIS Lung injury score

LOO• Lipid peroxyl radical

XVIII

LH Lipid molecules

MDA Malondialdehyde

MDI Metered dose inhaler

mg miligram

mmH₂O millmetre water

NADPH Nicotinamide adenine dinucleotide phosphate

ng nanogram

nM nanomolar

¹O₂ single oxygen

OH• hydroxyl radical

O₂ Superoxide radical

PaO₂/FiO₂ arterial oxygen tension to fractional concentration of

inspirated oxygen

PEEP Positive end-expiratory pressure

PUFAs Polyunsaturated fatty acid

RCV Routine condition variation

RDS Respiratory distress syndrome

ROO• Peroxyl radical

SE. Standard Error

SOD superoxide dismutase

TBA Thiobarbituric acid

TBARs Thiobarbituric acid reaction substrate

UA Uric acid

μM micromolar

Vit E Alpha-tocopherol

W/V Weight per volume

INTRODUCTION

The morbidity and mortality rates of neonatal patients in the hospital have been shown very high. Pneumonia is still being a common disease in the report at the acute care unit, Maharaj Nakon Chiang Mai hospital. Data from January, 1997 to November, 1999, have shown that 207 neonate patients who were admitted in acute care unit, died with lung infection.

Lung infection is either upper respiratory tract or lower respiratory tract infection from virus or bacteria induce the poor lung function and structural changes. In the biochemical theory and some evidents show that free radicals cause of lung tissue damage. Free radicals such as superoxide radical (O2-), hydroxyl radical (OH[•]), hydrogen peroxide (H₂O₂), peroxyl radical, and hypochlous acid, are produced from macrophage, neutrophil activity and catabolic cellular metabolism. Higher amount of free radicals can both directly and indirectly destroy the protein and lipid structures with the oxidation and peroxidation processes respectively. The results of reaction can be detected with various substrate products, such as lipid peroxide; malondialdehyde (MDA), degraded extracellular matrix; hyaluronic acid (HA) in the blood. The protection of the free radicals can be performed by antioxidants which are divided into two classes, enzyme group and non-enzyme group. In both, antioxidant groups, reduction of free radical-induced toxicity by the coupling of free radical with specific antioxidant. Alpha-tocopherol (vit E) and glutathione (GSH) are very interesting antioxidant in that protect parenchyma cell. The common complication of lung infection and pneumonia that commonly occurs in patients are their secretion accumulation and atelectasis. The main source of recurrent lung infection with bacteria is the accumulating secretion. It can be treated

by many methods such as suction with sterile technique, and antibiotic. Important solutions which have been performed for a long time is chest physical therapy with specific techniques, such as postural drainage, percussion, vibration, suction and aerosal therapy.

Free radicals activity can be detected with the end product of lipid peroxidation; MDA, or proteoglycan degraded product; HA. Whereas antioxidants such as GSH and Vit E are detected for the balanced control of free radicals. A few data show the relationship between the lung injury with other substances, especially MDA concentration in the blood. The evaluated methods for these substances are still on the blood, being performed in animal experiments and in the incubated patients. For tracheal aspirate (TA) is an interested sample for evaluation free radicals and antioxidants, because it is easily collected. Only a few studies use TA samples for detecting asthma patients.

Therefore, this study plans to determine the effects of two chest physical therapy programs which use to release the secretion accumulation and atelectasis of patients with lung injury. The biochemical compounds, such as MDA, HA, GSH, and Vit E under the interventions for six days consecutively and aimed to reduce the secretion accumulation and atelectasis. All substances are determined in blood and TA samples, and show the correlation among them.