

NEBULIZED COMBINED LIGNOCAINE AND
SALBUTAMOL IN TREATMENT OF ACUTE ASTHMA
(A PILOT STUDY)

by

DR. YUNG CHEE TIEN

Dissertation Submitted In
Partial Fulfillment Of The
Requirement For The
Degree Of Master Of Medicine
(EMERGENCY MEDICINE)

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LIST OF ABBREVIATIONS

DBP	Diastolic Blood Pressure
FEV1	Forced Expiratory Volume at One Second
PEFR	Peak Expiratory Flow Rate
PR	Pulse Rate
RR	Respiratory Rate
SBP	Systolic Blood Pressure

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ABSTRAK

Rawatan Nebulizer Gabungan Lignocaine Dan Salbutamol Untuk Penyakit Serangan Akut Asma

PENGENALAN

Rawatan penyakit asma di Jabatan Kecemasan pada hari ini adalah satu cabaran kepada semua doctor pakar kecemasan and juga paramedik-paramedik. Banyak jenis rawatan untuk penyakit asma telah diperkenalkan kebelakangan ini, dan akhir-akhir ini, ubat bius pun telah didapati mempunyai ciri-ciri yang boleh memberi keberkesanan dalam rawatan penyakit asma. Sebelum ini, didapati ubat bius mempunyai kebolehan untuk mengurangkan kesempitan saluran paru-paru. Ubat bius ini adalah Lignocaine.

Ubat lignocaine sering digunakan untuk sebagai bius dan juga untuk rawatan jantung. Ia mempunyai masa untuk bertindak yang singkat . Selain daripada keberkesanaan untuk mengurangkan kesempitan saluran paru-paru, ia juga didapati mempunyai ciri-ciri untuk mengurangkan radang.

OBJEKTIF KAJIAN

Objektif kajian ini adalah untuk menyelidik keberkesanaan gabungan nebulizer lignocaine dengan salbutamol bila dibandingkan dengan rawatan nebulizer salbutamol dalam serangan akut asma. Kajian ini ingin juga melihat kesan-kesan sampingan daripada rawatan gabungan salbutamol and lignocaine.

KAEDAH

Satu kajian prospektif telah dijalankan ke atas 50 pesakit yang datang ke Jabatan Kecemasan dan memerlukan rawatan untuk serangan akut asma. Pesakit yang memenuhi kriteria akan dipilih untuk diberi rawatan gabungan nebulizer salbutamol dengan lignocaine ataupun rawatan nebulizer salbutamol. Sukatan "peak expiratory flow rate", tekanan darah, kadar nadi dan pernafasan, dan saturasi oksigen menggunakan peralatan SPO2.

KEPUTUSAN

Keputusan daripada 50 pesakit yang memerlukan rawatan nebulizer untuk serangan akut asma menunjukkan gabungan nebulizer salbutamol dengan lignocaine mempunyai keberkesanaan yang sama dengan rawatan nebulizer salbutamol. Nilai peratusan kenaikan PEFR yang didapati dalam masa 15 minit adalah 20.92 ± 28.23 (Salbutamol) and 18.01 ± 22.09 (Gabungan), dan nilai p 0.687. Nilai peratusan kenaikan PEFR yang didapati dalam masa 30 minit adalah 33.91 ± 34.79 (Salbutamol) and 36.02 ± 41.15 (Gabungan) dengan nilai p 0.846. Daripada 25 pesakit yang mendapati rawatan gabungan salbutamol and lignocaine, 9 pesakit mengalami rasa kebas di dalam mulut dan 16 pesakit mengalami kedua-dua kebas di mulut dan rasa pahit.

KESIMPULAN

Rawatan gabungan nebulizer salbutamol dan lignocaine didapati tidak mempunyai kelebihan mengurangkan kesempitan saluran paru-paru untuk pesakit serangan akut asma jika dibandingkan dengan rawatan nebulizer salbutamol. Tidak ada kesan-kesan sampingan yang baru disebabkan oleh ubat lignocaine telah berlaku.

ABSTRACT

Nebulized Combined Lignocaine And Salbutamol In Treatment Of Acute Asthma (A Pilot Study)

INTRODUCTION

Management of asthma in Emergency Department remains a challenge to all Emergency Physician and Allied Health Personnel. Various modality of treatment has surfaced since the last decade and lately, anaesthetic medications have found a place in treatment of mild to moderate asthma patients. Anaesthetic medications have long been found to have direct effect on airway smooth muscle and it causes relaxation of the bronchial smooth muscles. The anaesthetic medication in question is Lignocaine.

Lignocaine is an local anaesthetic and anti-arrythmic medication that is easily available. It has a rapid onset of action and short duration of action. Lately it has been found to have property to attenuate reflex bronchoconstriction and also anti-inflammatory.

STUDY OBJECTIVE

The objective of this study is to compare the result of relief of bronchoconstrictions in patients with acute asthma when they are given either combined nebulized lignocaine & salbutamol or salbutamol only. This study also would like to document the side effects of combined nebulized lignocaine and salbutamol.

METHOD

A prospective study was conducted on 50 patients who had come to the emergency department and required treatment for acute exacerbation of mild to moderate asthma. Patients who fulfilled the criterias for inclusion were randomized to receive either plain salbutamol or combined salbutamol with lignocaine nebulized treatment. Measurements of peak expiratory flow rate and other clinical datas such as blood pressure, pulse rate, respiratory rate and oxygen saturation level will be taken in intervals.

RESULTS

The results from 50 patients requiring treatment for acute exacerbation of asthma showed that there were no significant difference between those randomized to receive plain salbutamol treatment and those receiving combined salbutamol and lignocaine nebulizers. At 15 minutes of treatment, the mean percentage of increased PEFR value of 20.92 ± 28.23 (Single) and 18.01 ± 22.09 (Combined) . The p value seen was 0.687 at 15 minutes interval of treatment. Even at 30 minutes of treatment shows the mean percentage value of increased PEFR at 33.91 ± 34.79 (Single) and 36.02 ± 41.15 (Combined) with p value of 0.846 . Out of 25 patients who were given combined salbutamol and lignocaine treatment, 16 patients experienced numbness of the oral cavity and 9 patients experienced both bitterness taste and numbness of the oral cavity.

CONCLUSION

Combined salbutamol and lignocaine did not have a better relief of bronchoconstriction as compared to salbutamol nebulization in mild to moderate asthma. The expected side effects of lignocaine were encountered and there were no new ones.

1. INTRODUCTION

Management of asthma patients in worldwide emergency department centers remains a challenge to all physicians and allied health personnel. Various modalities of treatment for this group of patients are available and have proven their efficacy till today, but they are not being used without their own side effects. In addition to this, patients with acute exacerbation of asthma presents themselves to emergency department in various degree of severity, either walking in or brought in unconscious by family members. With this, the treatment of asthma patients remains a challenge to any medical personnel.

All emergency departments in Malaysia have specialized section in their establishment for the sole treatment of asthma. These group of patients are given the “green lane” priority where asthmatic patients will be given treatment first for their exacerbation attacks while the doctor in charge of the emergency department attends to other cases of higher priority. Usually these asthma bays are manned by allied health personnel like staff nurses and medical assistants. Severe asthma cases are not managed in asthma bay and are triaged straight to red zone and attended immediately by the doctor in-charge.

2. LITERATURE REVIEW

Asthma is a chronic disease of the airway which can cause significant morbidity to the patient from all age groups if proper therapy is not instituted. In genetically predisposed individuals, asthma is a chronic inflammation of the lung airways caused by environmental factors. The major symptoms face by these group of patients are episodic obstructions in the airway and also presence of reversible bronchial hyperresponsiveness. Recent rise in asthma prevalence are due to dramatic changes in industrialized cultures (Umetsu *et al.*, 2002). This causes dysregulation in the T Helper Cell 2 – biased immune response and the overproduction of interleukins. This dysregulation is readily induced in the modern environment leading to lung inflammation, airway eosinophilia, increased mucous production in the airway and airway hyperactivity.

Various pharmaceutical companies are striving daily to come out with an anti-asthmatic drug that is effective, provides instant relief, convenient dosing regime and most importantly, at an affordable price and minimal side effects.

In the Emergency Department, doctors and nurses have been using various types of anti-asthmatics. It ranges from the inhaled β 2-agonists (salmeterol and formoterol), methyl-xantines and anti-cholinergics. Inhaled glucocorticoids like budesonide, fluticasone propionate and beclomethasone are the most effective treatment available for the control of various degrees of asthma severity (Barnes, 2004).

2.1 LIGNOCAINE (LIDOCAINE)

Lately, local anaesthetic agents have been getting attention around the world in the treatment of asthma. The particular anaesthetic agent in question is Lignocaine (Lidocaine). This local anaesthetic agent is an amino-amide and has fast onset of action and short duration of action. Being an amino-amide, it's metabolized in the liver. The mechanism of action is blockage of voltage-gated sodium channels in excitable tissue, primarily the nerves (Katzung, 2007) It has been used regularly as local anaesthesia of the airway in the flexible bronchoscopy procedure in medical centres around the world as recommended by the British Thoracic Society (2001). The total dose of lignocaine (lidocaine) should be limited to 8.2 mg/kg in adults (approximately 29 ml of a 2% solution for a 70 kg patient) with extra care in the elderly or those with liver or cardiac impairment.

In 1999, lignocaine in both intra-venous and inhalational form was used to attenuate reflex bronchoconstriction in response to histamine challenge and found that both intravenous and inhalational lignocaine provides good results (Groeben *et al.*, 1999). The additional key point in this study is that they found the plasma level of lignocaine in patients that were given the inhalational way was significantly lower than the intravenous route. Therefore, nebulized lignocaine holds a promise to be another bronchodilator agent in treating patient with bronchoconstriction episodes. Earlier on, bronchoconstriction can also be reduced by lignocaine in exercise induced asthma (Enright *et al.*, 1980).

Lignocaine has a particular side effect when used alone in the airway as itself can provoke bronchoconstriction, seen in Basenji-Greyhound dogs with hyperactive airways when they are given lignocaine inhalation and observed high resolution computed tomography (Bulut *et al.*, 1996). This property of inhaled lignocaine was easily countered when in 2000, combinations of salbutamol, salbutamol and lignocaine combined and a placebo for on a histamine challenge via inhalational route. It was noted that salbutamol and lignocaine provides good attenuation to the reflex bronchoconstriction (Groeben *et al.*, 2000). Some of the patients that were given inhaled lignocaine experienced bronchoconstriction, but those on both inhaled salbutamol and lignocaine showed that the initial bronchoconstriction can be prevented. In this article it was recommended that the combination of salbutamol and lignocaine be used if instrumentation of the airway is required to mitigate the bronchoconstriction,

In 1996, it was incidentally found out from patient who had just undergone bronchoscopy, that their bronchoalveolar lavage fluid contains significant high amount of lignocaine and that lignocaine potently shortens eosinophil survival (Ohnishi *et al.*, 1996). It was noted that (i) lignocaine inhibited eosinophil survival by causing apoptosis rather than necrosis ; and (ii) the mechanism of cell death was clearly time dependent, requiring at 24 hours of exposure to lignocaine (Okada, 1998). Moreover, it is well established that lignocaine at high concentrations can also block potassium channels (Olschewski *et al.*, 1996).

This effect is quite similar to those of the glucocorticoids that is being used in the treatment of asthma. With this new found property of lignocaine, it was used to perform a study on asthma patients whom were on oral glucorticoids. It was noted that those patients who were given daily inhaled lignocaine, were able to tail down their glucocorticoid dosage over a period of time, and it proves that lignocaine provides effective and safe therapy in patients in the mild to moderate category of asthma (Hunt *et al.*, 2004).

There were no other significant side effects being noted other than mild bronchoconstriction when lignocaine was used in the above studies, but this was easily prevented with addition of salbutamol to the lignocaine being nebulized. Furthermore, inhalational route of lignocaine provides adequate attenuation response of histamine-induced bronchoconstriction and were found that the serum levels of lignocaine were of safe level.

Intravenous lignocaine has profound effects on intracellular calcium level in smooth muscle. It causes relaxation of the smooth muscle by reducing the intracellular calcium level (Kai *et al.*, 1993). This local anaesthetic also causes inhibiton of neurally mediated acetylcholine release (Brown *et al.*, 2001), and therefore its use in asthma during anaesthesia is acceptable (Yamakage, 2002).

From the above studies, lignocaine proves to be promising bronchodilator drug as it can provide good attenuation of bronchoconstriction and mimics the effect of

corticosteroid effects on the airway. Apart from this two primary actions, it is also noted that inhaled lignocaine provides good response when given to patients with intractable cough (Udezue, 2001).

3. OBJECTIVES

3.1 GENERAL OBJECTIVES

3.1.1 To compare the result of relief of bronchoconstrictions in patients with acute asthma when they are given either combined nebulized lignocaine & salbutamol or salbutamol only.

3.1.2 To document the side effects of combined nebulized lignocaine and salbutamol.

3.2 SPECIFIC OBJECTIVES

3.2.1 To assess the difference of bronchoconstriction relief between patients nebulized with combination of lignocaine with salbutamol and salbutamol alone using the peak flow meter.

3.2.2 Other clinical improvements will be assessed by observing the difference of blood pressure, pulse rate, oxygen saturation level and respiration rate during the treatment.

3.2.3 To document the side effects of combined nebulized lignocaine and salbutamol.

4. METHODOLOGY

4.1 RESEARCH DESIGN (Figure 4.1)

A prospective randomized controlled single blinded trial was conducted on patients whom presented themselves to the emergency department and has been categorized as mild and moderate asthma.

4.1.1 VENUE

This study was conducted at the Department Of Emergency Medicine, Hospital Universiti Sains Malaysia from September 2005 to February 2006.

4.1.2 TIME FRAME

This study was conducted from September 2005 to February 2006.

4.1.3 APPROVAL

This study was presented and subsequently approved by the Research and Ethical Committee, Pusat Pengajian Sains Perubatan, Universiti Sains Malaysia, Kubang Kerian, Kelantan.

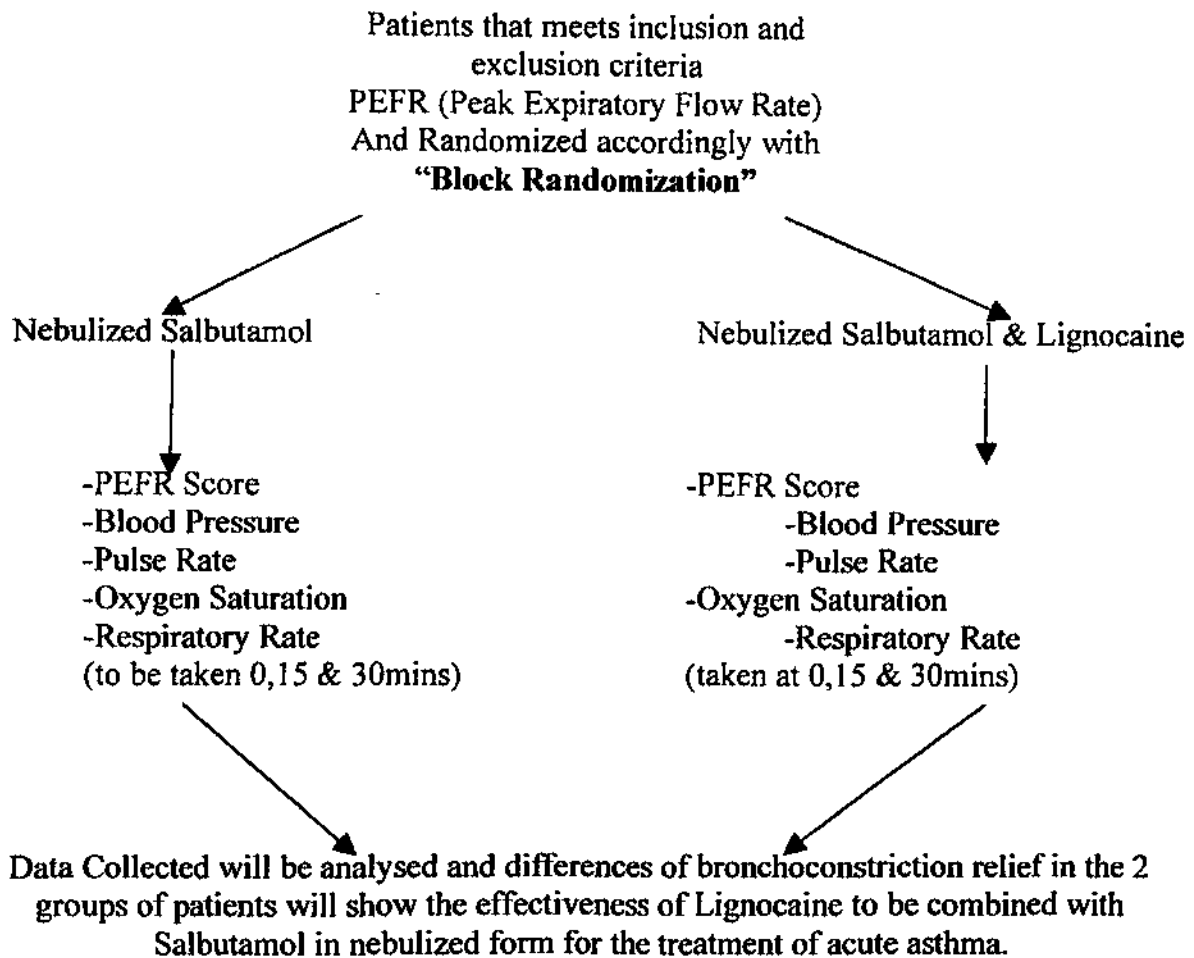


Figure 4.1 Conceptual Framework