

**ANALYSIS OF LARYNGOPHARYNGEAL REFLUXAT  
AMONG THE POST ELECTIVE SURGERY PATIENT  
AT WAHIDIN SUDIROHUSODO HOSPITAL MAKASSAR**

**(Comparative Study of Ranitidine and Omeprazole  
Premedication's Effect  
on Laryngopharyngeal Pepsin Content and pH)**



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**COMBINED DEGREE CONCENTRATION  
OTORHINOLARYNGOLOGY – HEAD AND NECK SURGERY  
BIOMEDIC POSTGRADUATE PROGRAM  
HASANUDDIN UNIVERSITY  
MAKASSAR  
2014**

**SUBMISSION PAGE**

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Thesis

One of the degree requirements for the degree of Master

Otorhinolaryngology –  
Head And Neck Surgery  
and Biomedic Program

Submitted and proposed by

**HILMIYAH SYAM**

to

**POSTGRADUATE PROGRAM  
HASANUDDIN UNIVERSITY  
MAKASSAR**

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**ENDORSEMENT**  
LAST EXAMINATION OF GRADUATE DEGREE

COMBINED DEGREE  
OTORHINOLARYNGOLOGY – HEAD AND NECK SURGERY  
BIOMEDIC POSTGRADUATE PROGRAM  
FACULTY OF MEDICINE HASANUDDIN UNIVERSITY

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**THESIS**

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Makassar, December 2013

Hilmiyah syam

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3. Dean and Staff of Medical Faculty Hasanuddin University.
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We realize, this work is very far from perfection, therefore we expect for more contribution and criticism in order to dedicate a better work and result.

Makassar, december 2013

Hilmiyah Syam

**ABSTRACT**

**HILMIYAH SYAM : ANALYSIS OF LARYNGOPHARYNGEAL REFLUXAT AMONG THE POST ELECTIVE SURGERY PATIENT AT WAHIDIN SUDIROHUSODO HOSPITAL MAKASSAR: Comparative Study of Ranitidine and Omeprazole Premedication's Effect on Laryngopharyngeal Pepsin Content and pH.**

(Supervised by Abdul Qadar Punagi, Riskiana Djamin, Arifin Seweng and Ramli Ahmad)

**Aim of study :** This study was performed to compare the effect of ranitidine and omeprazole premedication on laryngopharyngeal content.

**Methods :** Data were obtained from 97 elective surgical patients semi-randomly allocated to one of three groups, who received either omeprazole 20 mg orally then 40 mg injection, or ranitidine 150 mg orally then 50 mg injection, or neither, on the evening prior to and on the morning of surgery. Laryngopharyngeal pepsin and pH was measured after direct aspiration.

**Result :** The patient's characteristic baseline data shows there are no statistically significant difference among the three groups ( $p > 0,05$ ). There were significant differences in the levels of pepsin and pH among the three groups of subjects ( $p = 0.023$  and  $p = 0.009$  respectively). Premedication with omeprazole gave the higher pH than ranitidine or non-antacid premedication did, but non-antacid premedication gave the lowest pepsin level.

**Keywords:** omeprazole, ranitidine, laryngopharyngeal content, refluxat, acidity, pH, pepsin



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3.	Etichal Clearance Approval
4.	Explanations Text to obtain approval from the research subject
5.	Informed Consent Form
6.	Equipment and activity photographs

## ABBREVIATION LIST

Symbol/ Abbreviation	Meaning
%	Percent, ...of one hundred
°C	Temperature degree in Celsius
LPR	Laryngopharyngeal Reflux
EER	Extra Esophageal Reflux
pH	<i>Potentia Hydrogenii</i> , measure of the acidity or basicity of an aqueous solution. Solutions with a pH less than 7 are said to be acidic and solutions with a pH greater than 7 are basic or alkaline.
mL	milliliter, $10^{-2}$ liter
H <sup>+</sup> /K <sup>+</sup> -ATPase	hydrogen kalium/potassium ATPase
pg/mL	Picogram per milliliter, $10^{-12}$
ELISA	enzyme-linked immunosorbent assay

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## **CHAPTER I**

### **INTRODUCTION**

#### **A. BACKGROUND**

One of the most common symptoms during the post operative period is hoarseness, which may occur in anywhere from 14.4% to 50% of patients that underwent tracheal intubation. In the vast majority, this symptom is temporary and lasts on mean two to three days. However, in 10% of the cases, hoarseness becomes a permanent phenomenon, bringing changes in lifestyle for the patient, who had a normal voice before surgery.(Martins 2006, Jones 1992, Mencke 2003). Otolaryngologists are frequently asked to evaluate patients who are endotracheally intubated or have voice or airway complaints after being intubated.(Quinn 1999). Any physician being asked to evaluate a patient who is or has been intubated should be aware of both the acute and long term complications that may be encountered, as well as understand their diagnosis, prevention and management.

Gastroesophageal reflux and aspiration are common in critically ill patients. This repetitive bathing of the laryngeal structures with gastric acid causes a chemical irritation that adds to the local injury from the endotracheal tube(Quinn 1999, Lundy 1998).

Evidence suggests that in both healthy and patient populations, the refluxed gastric acid may come into contact with structures as high as the pharynx. Furthermore, several signs of laryngeal irritation, which are

generally considered to be signs of laryngopharyngeal reflux (LPR), were found to be present in a high percentage of asymptomatic individuals on laryngoscopic examination (Milstein 2005).

Failing to recognize laryngopharyngeal reflux (LPR) is dangerous, while overdiagnosis of laryngopharyngeal reflux (LPR) can lead to unnecessary costs and missed diagnosis. Inflamed laryngeal tissue affected by laryngopharyngeal reflux (LPR) is more easily damaged from intubation, has a high risk of progressing to contact granulomas, and may evolve to symptomatic subglottic stenosis (Maronian 2001).

It is generally agreed that patients with gastric contents of pH <2.5 and volume > 25 ml are at risk of pulmonary damage if aspiration occur (Power 1987). In adults, 30-50% of patients undergoing elective general surgery have gastric volumes greater than 25 ml and 64-82 % have a gastric pH less than 2.5. Thus patients undergoing surgery under general anaesthesia may benefit from the use of prophylactic agents which decrease gastric volume and increase gastric pH. H<sub>2</sub> receptor blockers increase gastric content pH by decreasing the production of gastric acid; ranitidine and famotidine have been used successfully for this indication. Omeprazole, a substituted benzimidazole, is the first of a new class of agents that inhibits gastric secretion by altering the activity of H<sup>+</sup>/K<sup>+</sup>-ATPase, the final common step in acid secretion by gastric parietal cells (Boulay 1994).

As many studies has been conducted, it suggests that in clinical study, proton pump inhibitors were superior to H<sub>2</sub> receptor antagonists in

terms of clinical efficacy. Dent J (1994) found that for patients who respond favourably to acute treatment with omeprazole 20 mg every morning, the drug is a safe and highly effective maintenance treatment for preventing relapse of reflux oesophagitis and its associated symptoms over 12 months. Yeomans ND et al (1998) suggest that In patients with regular use of NSAIDs, omeprazole healed and prevented ulcers more effectively than did ranitidine. But the clinical effectivity seems to depend on the dose, as Park et al (2005) has studied that BID PPI appears to be more effective than QD PPI in achieving clinical symptom response in suspected LPR. More response was achieved at 4 months compared with 2 months. Therefore, aggressive acid suppression with BID PPI for at least 4 months is warranted for treatment of LPR.

The role of gastroesophageal reflux in exacerbating laryngeal injury is not clearly known. Furthermore, the best methods for preventing or minimizing its effects need to be further investigated. This study was designed to compare the effects on laryngeal pepsin content and pH of ranitidine and omeprazole at recovery from general anaesthesia in patients undergoing elective surgery.

## **B. PROBLEM IDENTIFICATION**

Based on the background above, the research question could be formulated as : "How is the comparison of omeprazole and ranitidine and non-antacid premedication's effect on laryngeal pepsin content and pH

among the post elective surgery patient at Wahidin Sudirohusodo hospital Makassar?"

### **C. AIMS OF STUDY**

#### **1. General Purpose :**

Finding out the comparison of the clinical efficacy among ranitidine premedication and omeprazole premedication and non-antacid premedication in elective surgery patients.

#### **2. Spesific Purpose :**

- a. Determining pH of the preextubation laryngeal content of the patient whom premedicated with ranitidine
- b. Determining pH of the preextubation laryngeal content of the patient whom premedicated with omeprazole
- c. Determining pH of the preextubation laryngeal content of the patient whom premedicated without ranitidine and/or omeprazole
- d. Determining the value of pepsin in preextubation laryngeal content of the patient whom premedicated with ranitidine
- e. Determining the value of pepsin in preextubation laryngeal content of the patient whom premedicated with omeprazole
- f. Determining the value of pepsin in preextubation laryngeal content of the patient whom premedicated without ranitidine and/or omeprazole
- g. Comparing the pH and pepsin content among the three groups

#### **D. HYPOTHESIS**

1. The premedication effect on pH of laryngeal content will be best, better, good for omeprazole, ranitidine, none of both respectively.
2. There is no different of laryngeal pepsin content among the three groups.

#### **E. BENEFIT OF STUDIES**

1. Results of this study could be considered in the management of preoperative patients and also in our ENT outpatient clinic.
2. The results could be used as a baseline data in conducting further research.

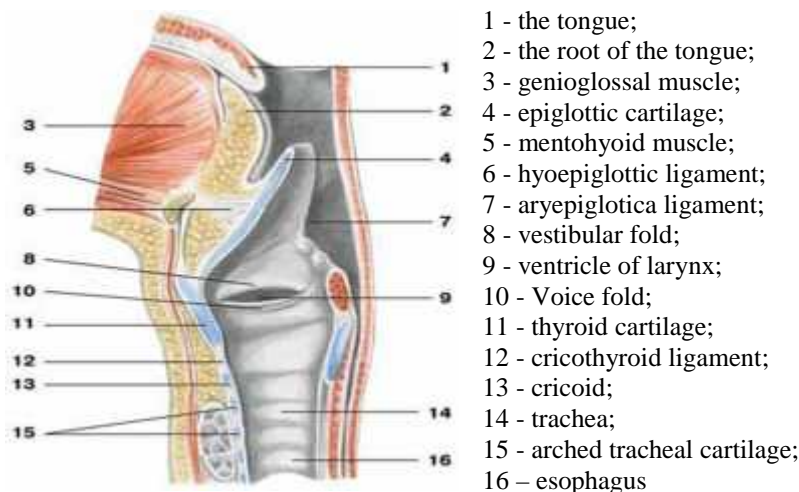
## CHAPTER II

### LITERATURE REVIEW

#### A. Literature Review

##### 1. Anatomical, Morphological And Physiological Aspects Of The Larynx

The larynx is a muscle-cartilaginous structure in which a delicate and intrinsic muscle structure interconnects with cartilages to promote the opening of the vocal folds during breathing and the closing of the folds during phonation and swallowing preventing food from entering airway. The innervation of the intrinsic muscles of the larynx is made up inferior laryngeal nerves and recurrent laryngeal nerves, which were branches of the vagus nerve. Only the cricothyroid muscle receives innervation from the superior laryngeal nerve. The epithelium that lines the vocal folds is of the stratified squamous variety and is made up of many layers of thin, flat cells and basic round cells. The cells of the more superficial layers are constantly renewing them selves and have microprojections. The epithelium lies above a basement membrane that separates the epithelium from the lamina propria. (Fechner 1992, Behlau 2001)



Modified from <http://anthropotomy.com>



The lamina propria is a laminar structure with some unique characteristics. Didactically speaking, it is made up of three layers. The superficial layer is known as the Reinke space and is composed of less dense collagen, few cells, some fibroblasts and very few capillaries. This space allows for the wave-like movement of the mucous above the superficial lamina, which is important in determining vocal quality. Some surgical procedures or even congenital epithelial irregularities may lead to the destruction, the atrophy or fibrosis of the Reinke space, which in turn may prevent adequate movement of the mucous layer over the superficial lamina which in turn have an important role in determining vocal quality. The intermediate and deep layers of the lamina propria are made up of dense collagen fibres and elastic fibre, they constitute the vocal ligament, located above the vocal muscle (thyroid arytenoid muscle). (Hirano 1993, Hirano 1974)

The vocal folds have very few lymphatic vessels, meaning that an edema on the inside will take long to be reabsorbed, thereby resulting, many times, in secondary lesions, such as vocal polyps. The structure of the glottis is V-shaped, where in the anterior portion, which is positioned obliquely at an angle, projects it self towards the cervical regions in front of the thyroid cartilage. The posterior region of the glottis is in close contact with the superior sphincter of the esophagus and, often times, is affected in patients with gastroesophageal reflux due to the constant acidic reflux in the region. (Martins, 2006)

## **2. Laryngeal Lesions: Causal Factors**

It is relatively common to see scientific articles aiming at many different complications involving tracheal intubation that are often the cause of symptoms related to the respiratory tract. In the literature, there are accounts of broken teeth, lesions in the mucous membranes of the lips, tongue, palate, floor of the mouth, uvula, esophagus, larynx and trachea, among other lesions (Holzki 1997, Molins 1998, Chandler 2002, Lacau

2003, Sue 2003). Consequently, the postoperative pharyngolaryngo tracheal symptoms such as throat aches, difficulty talking, coughing, secretions increase and pain upon swallowing are common. Hoarseness, however, is a very common symptom due to the high incidence of laryngeal lesions during tracheal intubation, especially when neuromuscular blockers are not used. The sensitive structures of the larynx may be affected for countless reasons(Mencke 2003)

The trauma during intubation may occur in emergency situations or situations in which the glottis is hard to expose, thereby resulting in lacerations and hematomas on the vocal folds, as well as luxations of the arytenoid cartilages and muscle disinsertions (Martins,2004). Another important factor that causes complications in the respiratory tract is the period that the tracheal cannula remains in contact with the mucous membranes of the larynx and trachea. The incidence of complications involving tracheal intubation is said to increase significantly after the seventh day of intubation, when the recommendation for the tracheotomy is put discussed. (Martins 2004, Walner 2001)

Holzki (1997) studied lesions in the respiratory tract related to intubation in children and found that they occur in 20% of cases, especially in children undergoing intubation for more than 25 days. This percentage increases if the caliber of the cannula is larger; in fact, according to the author, they are the main cause of laryngotracheal traumatism. Hence, the choice of the cannula's diameter is another important point to consider, seeing as, due to the V-shape of the glottis, the posterior of the larynx will be in close contact with the cannula. When one uses large-caliber tracheal cannulas, the region may suffer the consequences of an ischemia caused by compression of the cannula on the mucous layer. In these cases, one will observe necrosis and superficial ulceration of the mucous layer immediately following extubation. According to Holzki (1997), the most serious complication brought about by tracheal intubation is a necrosis on the circumference of the cricoid cartilage which evolves into subglottic stenosis.

The use of stainless steel spiral reinforced cannula in head and neck surgeries involving both oral and nasal intubation decreases the incidence of potential tracheal lesions because they are more malleable and do not result in compressions or folds. When tracheal cannula with cuffs are used, it is recommended that the pressure inside remain lower than the pressure of the capillary perfusion, that is, lower than 30 cmH<sub>2</sub>O (Nordin 1977, Castilho 2003).

Castilho et al.(2003), after a hystological analysis of the tracheal mucous of dogs in contact with the cuff, observed epithelial lesions when compared to normal respiratory epithelium, such as areas with superficial erosion and where cilium fall, even when using a very low pressure of 13 cmH<sub>2</sub>O. It is important to emphasize that a large part of these lesions are resolved naturally and spontaneously due to the epithelium's ability to renew it self. However, in some circumstances, the evolution of this process may cause greater damages and lead to laryngeal lesions of varying degrees of gravity, as is the case with patients who are diabetic or debilitated, which systemic infections or changes in hemodynamics.

Multiple risk factors for developing complications after intubation have been identified. Physical trauma incurred during the act of intubation is usually the result of abnormal anatomy and difficult laryngoscopy, multiple intubations or lack of skill of the operator. Abnormal larynges are more prone to injury, as in acute laryngotracheobronchitis where the inflammatory response already present within the larynx makes the mucosa more susceptible to pressure necrosis. Vocal fold immobility were seen more often after intubation for surgical reasons and had a significantly higher incidence of previous intubation and tobacco usage(Divatia 2005, Hagberg 2005, Quinn 1999, Lundy 1998)

Maronian (2001) also suggest that inflamed laryngeal tissue affected by laryngopharyngeal reflux (LPR) is more easily damaged from intubation, has a high risk of progressing to contact granulomas, and may evolve to symptomatic subglottic stenosis. Damage to cilia from refluxate that leads to

mucous stasis and chronic throat clearing and cough, with consequent symptoms of laryngeal inflammation and irritation.

### **3. Laryngopharyngeal Reflux and Laryngeal Injury**

Laryngopharyngeal reflux (LPR) also extraesophageal reflux disease (EERD) refers to retrograde flow of gastric contents to the upper aerodigestive tract, which causes a variety of symptoms, such as cough, hoarseness, and asthma, among others. Although heartburn is a primary symptom among people with gastroesophageal reflux disease (GERD), heartburn is present in fewer than 50% of the patients with LPR. Other terms used to describe this condition include atypical reflux and supraesophageal (or supra-esophageal) reflux. (Ford CN 2005, Postma GN 2008)

Major factors that have led clinicians to associate chronic supraesophageal disorders with reflux of gastric acid include the frequent lack of an etiology for some chronic laryngeal symptoms and findings, the recurrent or persistent nature of these disorders, and the benefit of empiric antireflux treatment as reported by multiple observational studies. However, the cause-effect relationship has been difficult to establish for several reasons including that GERD is a prevalent disorder, but only a small proportion of these patients have supraesophageal problems. However, most believe that the mucosa of the pharyngolarynx is not designed to handle the direct injury of acid or pepsin found in the refluxate. (Amirlak 2012)

Two hypotheses exist about how gastric acid precipitates extraesophageal pathologic response. The first purports direct acid-pepsin injury to the larynx and surrounding tissues. The second hypothesis suggests that acid in the distal esophagus stimulates vagal-mediated reflexes that result in bronchoconstriction and chronic throat clearing and coughing, eventually leading to mucosal lesions. These 2 mechanisms may

act in combination to produce the pathologic changes seen in laryngopharyngeal reflux (LPR) (Burton, 2005)

The role of gastroesophageal reflux in exacerbating laryngeal injury from intubation is not clearly known. Furthermore, the best methods for preventing or minimizing its effects need to be further investigated. Clearly, the presence of a nasogastric tube increases the likelihood of reflux and worsening the laryngeal injury. All patients with a nasogastric tube should be placed on H<sub>2</sub>-blocker therapy and this recommendation may be carried over to endotracheally intubated patients as well. (Quinn, 1999)

Boulay et al (1994) have studied, in 150 patients undergoing elective general surgery, the effect on gastric content of omeprazole 40 mg, ranitidine 300 mg and famotidine 40 mg, given orally the night and the morning before surgery. Volume and pH of gastric content were measured at induction and recovery from anaesthesia. Gastric volumes did not differ between groups. The median gastric pH was lower with omeprazole compared with ranitidine and famotidine at intubation (5.11, 7.05 and 6.99, respectively) ( $P < 0.001$ ) and extubation (6.41, 6.98 and 6.96) ( $P < 0.001$ ). The proportion of patients with gastric pH  $< 2.5$  at induction was 40% for omeprazole, 12% for famotidine and 10% for ranitidine ( $P < 0.02$ ); the proportion did not differ significantly at extubation.

However, as many studies has been conducted, it suggests that in clinical study, proton pump inhibitors were superior to H<sub>2</sub> receptor antagonists in terms of clinical efficacy. Dent J (1994) found that for patients who respond favourably to acute treatment with omeprazole 20 mg every morning, the drug is a safe and highly effective maintenance treatment for preventing relapse of reflux oesophagitis and its associated symptoms over 12 months. Yeomans ND et al (1998) suggest that In patients with regular use of NSAIDs, omeprazole healed and prevented ulcers more effectively than did ranitidine. But the clinical effectivity seems to depend on the dose.

#### 4. Pepsin

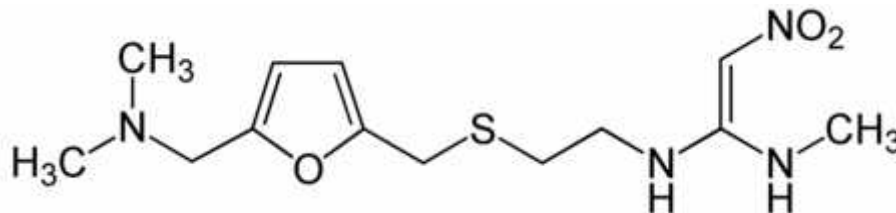
Pepsin is an enzyme whose zymogen (pepsinogen) is released by the chief cells in the stomach and that degrades food proteins into peptides. It was discovered in 1836 by Theodor Schwann who also coined its name from the Greek word *pepsis*, meaning digestion (*peptein*: to digest). It was the first enzyme to be discovered, and, in 1929, it became one of the first enzymes to be crystallized, by John H. Northrop. Pepsin is a digestive protease, a member of the aspartate protease family. Pepsin is one of three principal protein-degrading, or proteolytic, enzymes in the digestive system, the other two being chymotrypsin and trypsin. During the process of digestion, these enzymes, each of which is specialized in severing links between particular types of amino acids, collaborate to break down dietary proteins into their components, i.e., peptides and amino acids, which can be readily absorbed by the intestinal lining. Pepsin is most efficient in cleaving peptide bonds between hydrophobic and preferably aromatic amino acids such as phenylalanine, tryptophan, and tyrosine. (Dunn 2001, Guyton 2006, Johnston 2007)

Pepsin is most active in acidic environments ( optimum pH between 1,8 – 3,5) and is inactive at pH 5 and above, however pepsin is not fully denatured or irreversibly inactivated until pH 8.0. (Guyton 2006, Johnston 2007)

#### 5. Ranitidine

Ranitidine is a histamine H<sub>2</sub>-receptor antagonist that inhibits stomach acid production, can also be coadministered with NSAIDs to reduce the risk of ulceration. Ranitidine can be administered preoperatively to reduce the risk of aspiration pneumonia. The drug not only increases gastric pH, but also reduces the total output of gastric juice. Ranitidine may have an antiemetic effect when administered preoperatively. It can be administered

intravenously in intensive care units to critically ill patients (particularly geriatric ones) to reduce the risk of gastric bleeding.



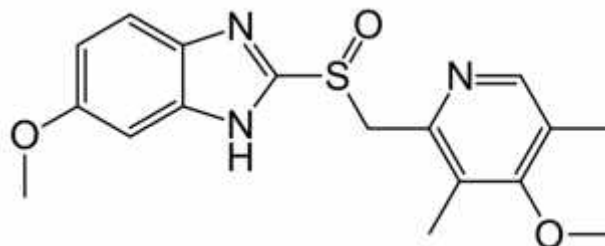
*N*-(2-[(5-[(dimethylamino)methyl]furan-2-yl)methylthio]ethyl)-*N'*-methyl-2-nitroethene-1,1-diamine

The usual dose of ranitidine is either 150 mg twice a day or 300 mg once every 24 hours, usually at night. For ulcer treatment, a 300-mg night-time dose is especially important - as the increase in gastric/duodenal pH promotes healing overnight when the stomach and duodenum are empty. Conversely, for treating reflux, smaller and more frequent doses are more effective. Ranitidine used to be administered long term for reflux treatment, sometimes indefinitely. However, PPIs have taken over this role.

In some patients with severe reflux, up to 600 mg of ranitidine can be administered daily, usually in four lots of 150 mg. Such a high dose was not unusual in the past, but nowadays a once-a-day PPI is used instead - both for convenience and because they are more effective in raising gastric pH. (VanZyl 2000, Brunton 2005)

## 6. Omeprazole

Omeprazole is a specific inhibitor of H<sup>+</sup>,K<sup>(+)</sup>-ATPase or 'proton pump' in parietal cells. This enzyme is responsible for the final step in the process of acid secretion; omeprazole blocks acid secretion in response to all stimuli. Single doses produce dose-dependent inhibition with increasing effect over the first few days, reaching a maximum after about 5 days.

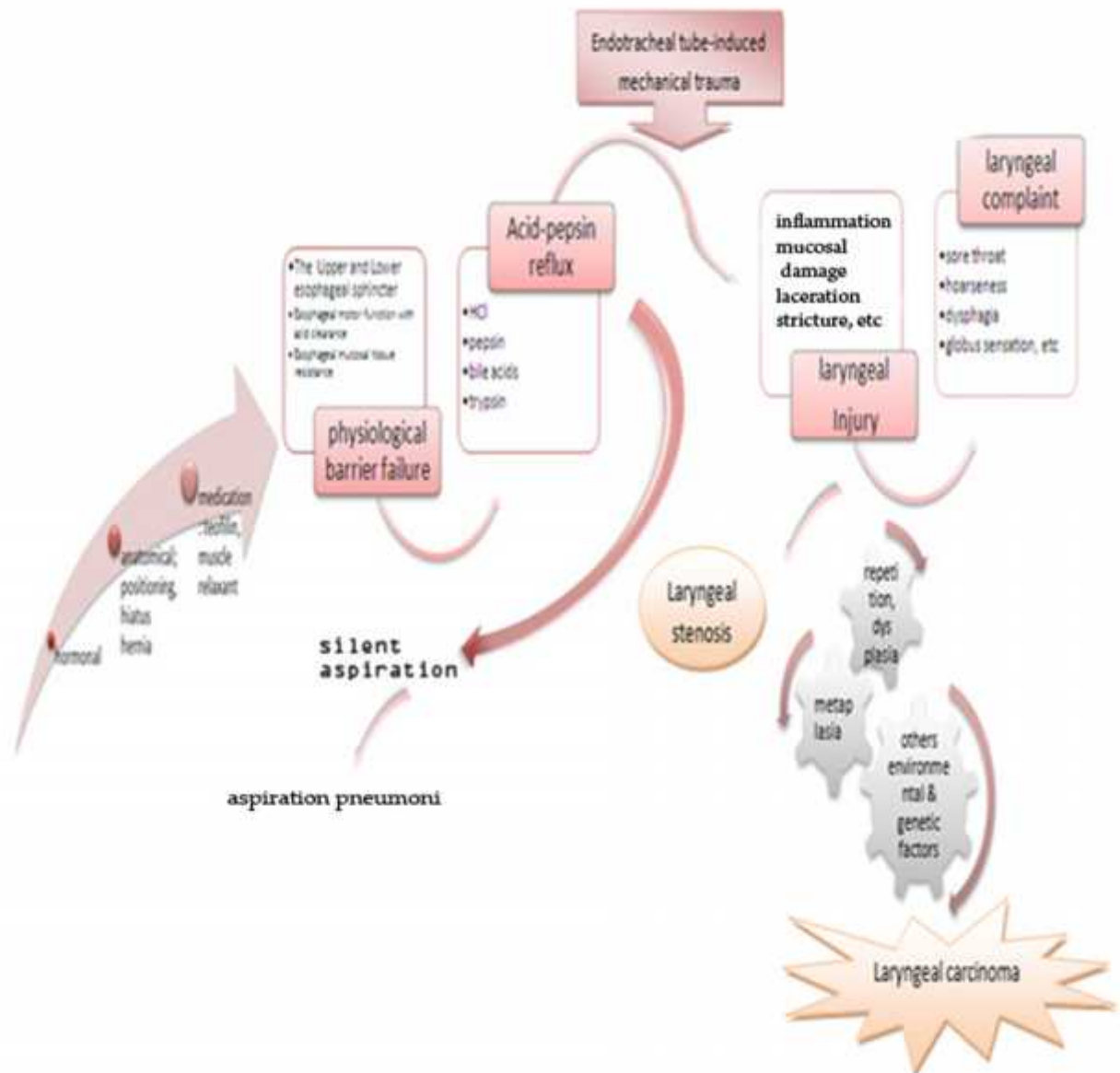


(*RS*)-5-methoxy-2-((4-methoxy-3,5-dimethylpyridin-2-yl) methylsulfinyl)-1*H*-benzo[*d*]imidazole

Doses of omeprazole 20mg daily or greater are able to virtually abolish intragastric acidity in most individuals, although lower doses have a much more variable effect. Omeprazole causes a dose-dependent increase in gastrin levels. Omeprazole must be protected from intragastric acid when given orally, and is therefore administered as encapsulated enteric-coated granules. Absorption can be erratic but is generally rapid, and initially the drug is widely distributed. It is highly protein-bound and extensively metabolised. Its elimination half-life is about 1h but its pharmacological effect lasts much longer, since it is preferentially concentrated in parietal cells where it forms a covalent linkage with H<sup>+</sup>,K<sup>(+)</sup>-ATPase, which it irreversibly inhibits. Omeprazole binds to hepatic cytochrome P450 and inhibits oxidative metabolism of some drugs, the most important being phenytoin. Omeprazole has produced short term healing rates superior to the histamine H<sub>2</sub>-receptor antagonists in duodenal ulcer, gastric ulcer and reflux oesophagitis.(Howden 1991, McTavish 1991)

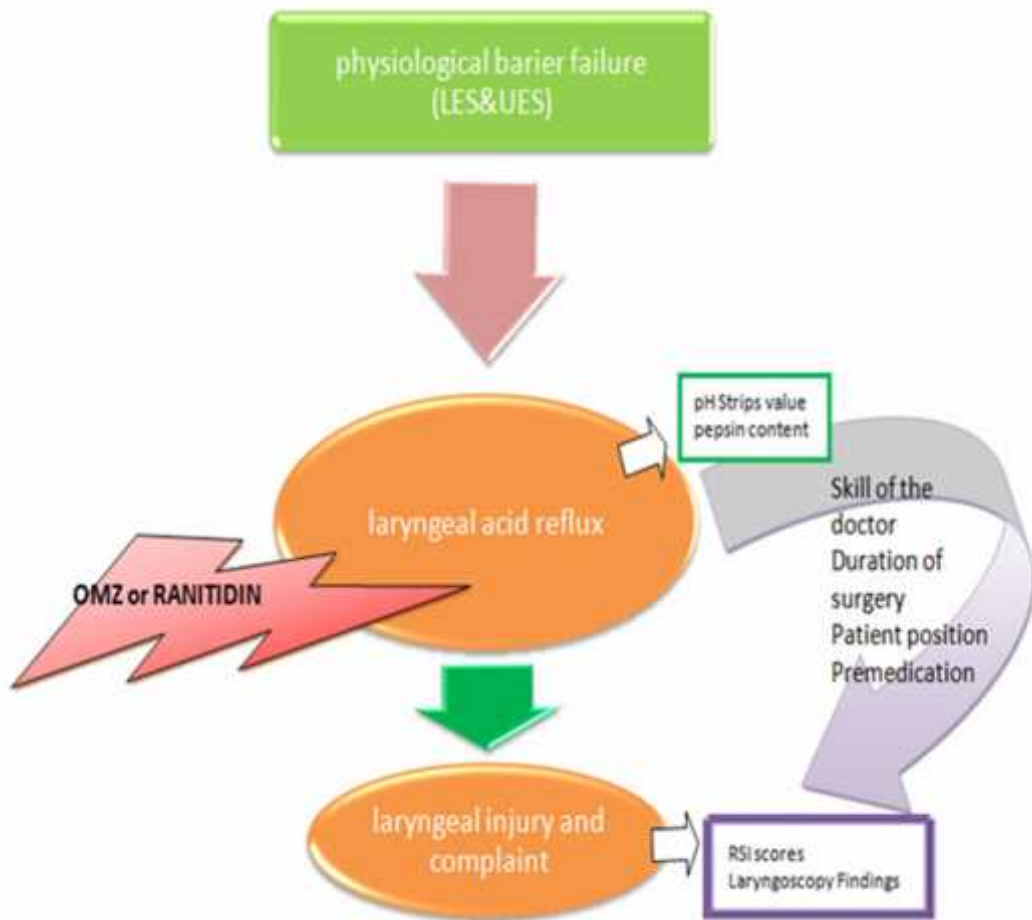


## B. Theoretical Framework



Modified from :Quinn 1999, Lundy 1998, Divatia 2005, Hagberg 2005

**C. Conceptual Framework**



**Keterangan :**



: independent variable



: controlled variable



: intermediate variable



: dependent variable



: not examined variable

#### D. Operational Definition and Objective Criteria

- Laryngopharyngeal content/ refluxat/ liquid sample** : fluid contained in the laryng and collected just prior to extubation by using a disposable 50 cc syringe connected to a no.7 suction catheter.
- Laryngopharyngeal content pH/ acidity** : acidity of the laryngeal fluid measured by strips test, the range of pH value determined by the color change of the stripes which compared againts the indicator chart on the packanging. Mentioned in numbers : 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14



- Laryngopharyngeal pepsin presence** : the presence of pepsin in the laryngopharyngeal content, determined by ELISA test, and mentioned in (+) or (-). Pepsin (+) if the value is more than “blank” standad (360pg/mL).
- Laryngopharyngeal pepsin content/pepsin level/value** : mentioned in “pg/mL”, the value of pepsin in the laryngeal fluid which determined by SEA632Hu 96 Tests ELISA Kit for Pepsin (PP), a Cloud Clone Group Production.



5. **Premedication** : omeprazole 20mg tablet that given orally at night followed by injection of 40mg omeprazole 1 hour before surgery, or ranitidine 150 mg tablet, given orally at night and followed by injection of 50 mg ranitidine. Premedication are chosen according to patient condition and given by anesthesiologist (or residence) at night before surgery and 1 hour before surgery.
6. **Elective surgery patient** : patients whom will undergoing surgery procedures with general anesthesia using endotracheal tubes.
7. **Fasting duration** : hours (h) : duration of fasting time of patient from beginning until the laryngopharyeal content/fluid collected.
8. **Age** : age of patient mentioned in “years”
9. **Time of secretion taken** : duration time, from injection of omeprazole or ranitidine untill we collect the laryngopharyngeal fluid.  
Mentioned in (hours)
10. **Clinical Efficacy** : ability of antacid agents to reduce the acidity (increasing the pH) of stomach juice.
11. **Ranitidine group/ R group** : patients who received ranitidine premedication

**12. Omeprazole group/ O group** : patient who received omeprazole premedication

**13. None/ N/ non-premedication/ non antiacid premedication group** : patient who did not receive ranitidine (H2 reseptor blockers) or omeprazole (PPI) premedication

**14. ELISA/ enzyme-linked immunosorbent assay** : is a test that uses antibodies and color change to identify a substance, in this study we use SEA632Hu 96 Tests ELISA Kit for Pepsin (PP), a Cloud Clone Group Production.