

A Comparison of Phospholipase A2 Levels- An Inflammatory Marker for Endotracheal Intubation via Direct & Video Laryngoscope in Patients Undergoing Cardiac Surgery

Dr Pooja Neogi¹, Dr Vishwas Sathe², Dr Robin Gupta³

¹Junior Resident, Department of Anaesthesia MGM Medical College & Hospital Kamothe, Navi Mumbai, Maharashtra, India

²Professor, Department of Anaesthesia MGM Medical College & Hospital Kamothe, Navi Mumbai, Maharashtra, India

³Senior Resident, Department of Anaesthesia MGM Medical College & Hospital Kamothe, Navi Mumbai, Maharashtra, India

Abstract: *The role of inflammatory response to pathogenesis of atherosclerosis has been topic of intense research. Several markers of inflammatory response have shown predictive value for first and recurrent coronary events in patients with established Coronary Heart Disease (CHD). Among these markers, lipoprotein associated Phospholipase A2 mass and activity appears to be associated with increased risk for CHD, in general population and in patients with pre-existing CHD. The aim of study is to measure and compare Lipoprotein associated Phospholipase A2 activity, a selective inflammatory marker of CHD in patients undergoing cardiac surgery during endotracheal intubation via direct and video laryngoscope*

Keywords: lipoprotein associated phospholipase A2, Coronary Heart Disease, Inflammatory response, direct laryngoscope, Video laryngoscope

1. Introduction

Phospholipase A2 (PLA2) is one of a family of phospholipases, enzymes that hydrolyse phospholipids. One of which, lipoprotein-associated PLA2 (LpPLA2) is also known as platelet activating factor acetyl hydrolase (PAF-AH). Lipoprotein-associated PLA2 promotes the hydrolysis of oxidized phospholipids in lipoproteins, generating lysophospholipids and proinflammatory oxidized fatty acids.

This reaction is of the utmost importance in the context of cellular signalling; since it constitutes the main pathway by which arachidonic acid (AA) is liberated from phospholipids. Free AA is a precursor of compounds known as the eicosanoids, which includes the cyclooxygenase-derived prostaglandins and the lipoxygenase-derived leukotrienes¹.

The importance of the eicosanoids and platelet-activating factor as key mediators of inflammation as well as other pathophysiological conditions is now universally accepted [1]. Furthermore, sPLA2s promote cytokine and chemokine production from macrophages, neutrophils, eosinophils, monocytes, and endothelial cells. Hence it might play an important role in the initiation and amplification of the inflammatory reaction.²

Inflammatory processes play a significant role in initiation, progression, and rupture of atherosclerotic plaques (3). Recent studies show lipoprotein-associated phospholipase A₂ (Lp-PLA₂) as an emerging marker of cardiovascular risk^{4, 5, 6, 7, 8, 9, 10}. Lp-PLA₂ is a highly specific vascular inflammatory marker^{4, 5, 9}. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is bound predominately to

low-density lipoprotein and has been implicated as a risk factor for coronary artery disease (CAD)¹¹

Airway management hold utmost importance during delivery of general anaesthesia. Since anaesthetised patients are unable to maintain adequate airway on their own, hence artificial devices for management of the airway is inevitable.¹²

Endotracheal intubation is a method of airway protection that results in local inflammation and in some cases tracheal injury that may progress to subglottic stenosis¹³ Although these inflammatory responses carry risk for all patients who are receiving anaesthesia, it is more significant in patients who have underlying coronary artery disease.

Modification of instruments and utilization of various other intubating devices may be tried to dampen these inflammatory responses.

Direct visualisation of larynx and its structure is a prerequisite for conventional intubation with Macintosh laryngoscope which provides only a narrow field of vision and can get worsened with repeated attempts. . The Video Laryngoscope provides enlarged and enhanced video image of structure of airway, facilitating better expertise.

Hence this study is aimed at comparing the alteration in inflammatory marker phospholipase A2 level during and after endotracheal intubation with conventional laryngoscope and video laryngoscope.

Inclusion Criteria

- 1) Age: range 20 – 80 yrs.
- 2) ASA physical status grade III and grade IV patients

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- 3) Patients who gave informed written consent.
- 4) Elective cardiac surgery
- 5) Either gender

Exclusion Criteria

- 1) Patient refusal
- 2) Emergency cardiac surgery
- 3) MPC III and IV (difficult intubation) (anticipated difficult intubation or history of difficult intubation, and limited nuchal range of motion)
- 4) Failure to intubate after three attempts and duration more than 3 minutes were excluded from the study (an attempt is defined as time from introduction of laryngoscope into oral cavity until its removal)
- 5) Parturient and lactating women
- 6) Poor left ventricular function (LVEF < 35%), conduction abnormality and on permanent pacemaker
- 7) Less than 20 years

Source of Data

- a) Study Site:
MGM Medical College, Kamothe, Navi Mumbai.
- b) Study duration:
December 2018 to November 2019.
- c) Study design:
Prospective randomized comparative study.
- d) Sample size:
40 patients would be included in this study.

2. Material and Method

After obtaining informed written consent from patients, patients were randomly divided into 2 groups. Sequentially, numbered sealed opaque envelopes were used for allocation concealment.

Group 'A': – 20 patients: intubated by using direct laryngoscope
Group 'B': – 20 patients: intubated by using video laryngoscope

All intubation were performed by senior experienced anaesthetist who had an experience of using video laryngoscope. All patients will be kept fasting overnight. Tablet Alprazolam 0.5mg and Tablet Pantoprazole 40 mg were given to patients on day before surgery during pre-anaesthetic evaluation. On entering the operation theatre, one wide bore intravenous cannula along with 7 french central line and femoral line were inserted 15 min prior to induction of anaesthesia

The following monitors will be attached for continuous monitoring and baseline values recorded

- 1) Pulse Oximeter
- 2) Capnography
- 3) Electrocardiography (ECG)
- 4) Continuous arterial pressure recording through femoral arterial line
- 5) Continuous central venous pressure recording through central line

Patients were preoxygenated and premedicated- Inj. Midazolam 0.05mg/kg and Inj. Fentanyl 2mcg/kg and

induced with IV inj. Etomidate (0.3 – 0.4 mg/kg). After confirming for check ventilation using bag and mask ventilation (i.e. visible chest rise) neuromuscular blockade was achieved using IV inj. rocuronium (0.4-0.6mg/kg). After three minutes of assisted ventilation as per the group, endotracheal tube was inserted by using conventional laryngoscope (Macintosh blade) in one group (consisting of 20 patients each) and video laryngoscope in another group. After successful attempt cuff of the endotracheal (ET) tube was inflated and correct placement was confirmed by auscultation (i.e. air entry B/L equal) and end tidal carbon dioxide (EtCO₂) values. Patient was maintained on oxygen, air and sevoflurane.

Blood samples for the determination of serum phospholipase levels were taken after discarding 5ml of blood at each time point from Central venous catheterisation.

Blood samples were taken according to the following timetable:

- 1) Time point 1: 5 min prior to the administration of any induction agent, for the measurement of baseline plasma levels of phospholipase A₂ [pre - induction & pre - intubation]
- 2) Time point 2: 15 min post tracheal intubation

All blood samples were drawn into precooled tubes (2-8°C) and immediately transferred to the laboratory and centrifuged in a refrigerated centrifuge at 0°C. The separated serum was stored at - 70°C until processing. Lp-PLA₂ activity was measured with Diazyme's PLAC® Test. All assays were analysed at GENOMICS Lab, with laboratory personnel blinded to all clinical data. Lp-PLA₂ index, an integrated measure of mass and activity, expressing enzymatic properties, were calculated.

Assay Principle

The PLAC Test for Lp-PLA₂ Activity is an enzyme assay. Lp-PLA₂, in plasma or serum, hydrolyzes the sn-2 position of the substrate, 1-myristoyl-2-(4-nitrophenylsuccinyl) phosphatidylcholine, producing a colored reaction product, 4-nitrophenol. The rate of formation of 4-nitrophenol is measured spectrophotometrically and the Lp-PLA₂ activity is calculated from the rate of change in absorbance. A set of five Lp-PLA₂ calibrators is used to generate a standard curve fit of change in absorbance versus Lp-PLA₂ activity level in nmol/min/mL from which the sample Lp-PLA₂ activity is derived¹⁴

3. Observation and Results

Null Hypothesis (H₀): There is variance in means (readings of Lipoprotein associated Phospholipase A₂ activity, a selective inflammatory marker of CHD) between group of patients undergoing cardiac surgery during endotracheal intubation via direct and video laryngoscope

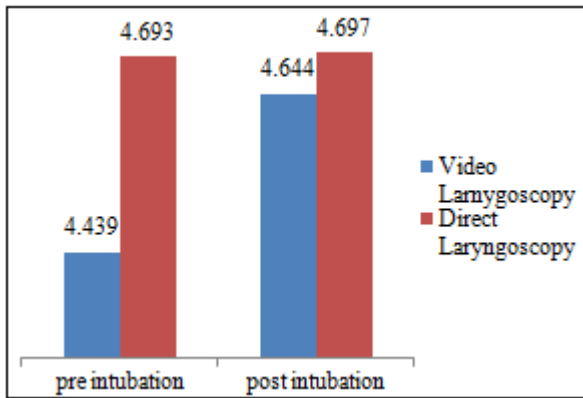


Figure 1: Mean values between groups (Lp-PLA2 activity level in nmol/min/mL)

Readings of Lp-PLA2 activity was compared between Group A (administered using Direct Laryngoscopy) & Group B (administered using Video Laryngoscopy) using two tail T test, which was used to determine if there is a significant difference between the means of two groups.

In the course of the study, it has been found that there is no statistical difference ($p > 0.05$) in mean serum phospholipase level in Group A & Group B. However, it has been observed, that mean values of Lp-PLA2 is higher in Group A versus Group B, but no statistical inference can be drawn.

4. Discussion

In the present study, we investigated the association between PLA2 and inflammatory response to direct and video laryngoscopy in patients undergoing cardiac surgery. We report that PLA2 activity was associated with significant inflammatory response to intubation via direct and video laryngoscope.

Because Lp-PLA2 activity levels were predictive of CAD for both groups, we performed different analysis to determine whether Lp-PLA2 activity would independently contribute to inflammatory response to endotracheal intubation beyond traditional risk factors. There was no significant statistical difference in mean serum phospholipase level in patients undergoing endotracheal intubation with both direct laryngoscope and video laryngoscope.

Tracheal inflammation secondary to ETT presence was previously documented in a similar study done by Carlos *et al* in which tracheal subglottic samples obtained from patients provided documentation that PMN recruitment and cytokine and C5a level elevation occurred during endotracheal intubation. The total number of PMNs per sample increased significantly, over the period of intubation¹³

5. Limitations

Since the study was conducted in a small group of 40 patients, hence further studies with large sample size with different inflammatory markers would have given different outcome and requires further evaluation.

6. Conclusion

PLA2s are emerging as a novel class of mediators of inflammation and immune responses. These molecules are found in biologic fluids in a variety of systemic inflammatory, allergic, and autoimmune disorders.

However, Null hypothesis of (H_0): There is variance in means (readings of Lipoprotein associated Phospholipase A2 activity, a selective inflammatory marker of CHD) between group of patients undergoing cardiac surgery during endotracheal intubation via direct and video laryngoscope is **REJECTED**.

In conclusion, it can be inferred from this study, that using Direct or Video Laryngoscopy has no effect on variation of Lipoprotein associated Phospholipase A2 activity.

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References

- [1] Jesús Balsinde, Edward A. Dennis, in Handbook of Cell Signaling (Second Edition), 2010
- [2] Secretory phospholipases A2 in inflammatory and allergic diseases: Not just enzymes. Triggiani, Massimo et al. Journal of Allergy and Clinical Immunology, Volume 116, Issue 5, 1000 - 1006
- [3] Ross R 1999 Atherosclerosis—an inflammatory disease. N Engl J Med 340:115–126
- [4] Packard CJ, O'Reilly DS, Caslake MJ, McMahan AD, Ford I, Cooney J, Macphee CH, Suckling KE, Krishna M, Wilkinson FE, Rumley A, Lowe GD 2000 Lipoprotein-associated phospholipase A2 as an independent predictor of coronary heart disease. West of Scotland Coronary Prevention Study Group. N Engl J Med 343:1148–1155
- [5] Caslake MJ, Packard CJ 2003 Lipoprotein-associated phospholipase A2 (platelet-activating factor acetylhydrolase) and cardiovascular disease. Curr Opin Lipidol 14:347–352
- [6] Koenig W, Khuseynova N, Löwel H, Trischler G, Meisinger C 2004 Lipoprotein-associated phospholipase A2 adds to risk prediction of incident coronary events by C-reactive protein in apparently healthy middle-aged men from the general population: results from the 14-year follow-up of a large cohort from southern Germany. Circulation 110:1903–1908
- [7] Ballantyne CM, Hoogeveen RC, Bang H, Coresh J, Folsom AR, Heiss G, Sharrett AR 2004 Lipoprotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident coronary heart disease in middle-aged men and women in the Atherosclerosis Risk in Communities (ARIC) study. Circulation 109:837–842
- [8] Blake GJ, Dada N, Fox JC, Manson JE, Ridker PM 2001 A prospective evaluation of lipoprotein-associated phospholipase A(2) levels and the risk of future cardiovascular events in women. J Am Coll Cardiol 38:1302–1306

- [9] Lavi S, McConnell JP, Rihal CS, Prasad A, Mathew V, Lerman LO, Lerman A 2007 Local production of lipoprotein-associated phospholipase A2 and lysophosphatidylcholine in the coronary circulation: association with early coronary atherosclerosis and endothelial dysfunction in humans. *Circulation* 115:2715–2721
- [10] Blankenberg S, Stengel D, Rupprecht HJ, Bickel C, Meyer J, Cambien F, Tiret L, Ninio E 2003 Plasma PAF-acetylhydrolase in patients with coronary artery disease: results of a cross-sectional analysis. *J Lipid Res* 44:1381–1386
- [11] Anuurad E, Ozturk Z, Enkhmaa B, Pearson TA, Berglund L. Association of lipoprotein-associated phospholipase A2 with coronary artery disease in African-Americans and Caucasians. *J Clin Endocrinol Metab.* 2010;95(5):2376–2383. doi:10.1210/jc.2009-2498
- [12] Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon heart. *The Journal of surgery, gynecology and obstetrics* 1940;70:157-62.
- [13] Puyo, Carlos & Dahms, Thomas. (2012). Innate Immunity Mediating Inflammation Secondary to Endotracheal Intubation. *Archives of otolaryngology--head & neck surgery.* 138. 854-8. 10.1001/archoto.2012.1746.
- [14] <http://www.diazyme.com/lipoprotein-associated-phospholipase-a2-activity>