CASE REPORT

CASE REPORTS OF TRANSIENT AUTONOMIC DYSFUNCTION IN COPD PATIENTS UNDERGOING MAJOR SURGERIES

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ABSTRACT: Chronic Obstructive Pulmonary Disease (COPD) is a systemic disease which has been shown to negatively affect the cardiovascular and autonomic nervous systems. In COPD patients the activity of sympathetic nervous system may be affected by recurrent hypoxemia, hypercapnia, increased intrathoracic pressure swings due to airway obstruction, increased respiratory effort, systemic inflammation, oxidative stress and the use of beta sympathomimetics. These case reports are to emphasize the importance of pre anaesthetic evaluation and risk assessment of COPD patients coming for major surgeries.

KEY WORDS: COPD, transient autonomic dysfunction, hypoxemia, increased intrathoracic pressure swings.

INTRODUCTION: There is increasing evidence, indicating that COPD is more complex and is not only involving airflow obstruction. It has been recognized that COPD is a systemic disease which has been shown to negatively affect the cardiovascular and autonomic nervous system (1,2).

The insight into sympatho vagal imbalance as a pathological phenomenon in COPD may be important in understanding the pathophysiology of COPD and may have a potential clinical importance for improving risk stratification and treatment of patients with COPD.

Patients with COPD have functional alterations of cardiac autonomic modulation as reflected in elevated resting heart rate, reduced baroreflex sensitivity, reduced heart rate variability (HRV)(3,4), reduced respiratory sinus arrhythmia(RSA)(5), a direct increase in muscle sympathetic nerve activity (6,7) and abnormal heart rate recovery(HRR) following exercise (8).

Enhanced sympathetic tone at rest and disruption of autonomic reflexes give rise to a self-perpetuating cycle that contributes to the pathogenesis of COPD and possibly play an important role regarding the mortality in these patients (9, 10).

CASE REPORT 1: A 52 year old gentleman, case of carcinoma larynx with tracheostomy tube insitu, assessed under ASA3 (COPD with moderate obstruction, malnourished, major surgery) posted for total laryngectomy with radical neck dissection. Patient was premedicated with Inj. Glycopyrrolate 0.2mg and Inj. Morphine 6mg IV. Induced intravenously with Inj. Thiopentone 250mg and Inj. Vecuronium 5mg. Anaesthesia maintained through tracheostomy tube with Nitrous oxide (3L/MIN), Oxygen (1.5l/min) and Sevoflurane (0.6 to 2%) and controlled ventilation. Patient was stable for the initial three hours after which ST segment depression was noticed in the ECG monitor followed by ventricular ectopic beats which was managed with preservative free lignocaine 2% (3 ml) IV later he developed bradycardia which responded to Inj. Atropine (0.6 mg) IV. Surgical handling as the cause was ruled out. Patient was stable for the next three hours. Again he developed ST segment depression in the ECG followed by ventricular ectopics, responded to Inj preservative free lignocaine 2% (3 ml). The procedure lasted for about 8 hours. At the end of the procedure patient was reversed,

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recovered well and shifted to the postoperative ward with spontaneous ventilation via tracheostomy tube.

Patient was evaluated postoperatively by a cardiologist. Diagnosed to have transient autonomic dysfunction. Pre operative and post operative ECHO reports were normal.

CASE REPORT 2: A 70 year old male patient had come for left parotid swelling diagnosed as poorly differentiated adenocarcinoma in histo-pathological examination. His hemoglobin was 5.8 g/dl. After two transfusions and iron therapy, hemoglobin improved to 11.1g/dl. Total parotidectomy was planned. On anaesthetic assessment he was found to have bilateral wheeze and emphysematous changes in the chest x ray. His ECG was within normal limits.

His blood sugars, electrolytes, renal function tests and liver function tests were normal. X ray neck was normal. Chest physician opinion was requested and cardiology workup was also done. Cardiologist opinion was that ECG and ECHO were within normal limits. Pulmonary function tests showed severe obstructive lung disease.

Inj. Deriphylline IV BD, inj. Solumedrol 125mg IV BD and Asthalin+ Ipratropium+ Budecort nebulization TDS was started as per pulmonologist opinion. He was taken up for surgery with high risk consent under ASA III. His 12 lead ECG on the morning of surgery showed sinus arrhythmia, short PR interval, HR 96/min and few premature ventricular contractions. His pre-op BP was 160/110 mm Hg and HR 108/minute. ECG on table showed multiple VPCs >14/minute. After premedication with inj. Midazolam 1mg, inj. Glycopyrrolate 0.2mg and inj. Morphine 6mg IV, his BP was 140/100 mm Hg and HR 98/minute with ECG showing VPCs. As patient was hemodynamically stable induction with inj. Thiopentone 175mg, and inj. Vecuronium 5mg was done and oral intubation with ET size 8.0 flexometallic tube after 2ml Xylocard injection IV. Controlled ventilation with Tidal Volume 500ml, RR- 12/min and I: E ratio 1: 2 was maintained and Etco2 was maintained normal throughout the procedure. Analgesia was provided with intermittent Morphine 1mg/hour IV. Thirty minutes after induction ECG was normal with no ectopics. Two hours later VPCs started appearing initially at 5 per minute and went upto 26 per minute with other vitals remaining stable. They settled spontaneously in 15 minutes and reappeared for a short time three hours later. The surgery was completed in 6 hours with extubation being uneventful. Postoperatively patient was hemodynamically stable with HR-89/min and BP-150/100 mm Hg spo2- 100%. Reflexes were good and speech coherent. Patient was shifted to post operative ward. Post operative ECG and Echo were within normal limits. Patient was evaluated postoperatively by a cardiologist and diagnosed to have transient autonomic dysfunction.

Causes of autonomic dysfunction in these patients: Surgical handling as cause was ruled out. There were no episodes of hypoxemia intraoperatively.

Intra operative MI was ruled out after evaluating cardiac enzymes for the 1st patient. Also post operative ECHO reports were normal with no organic pathology.

Probable causes in these patients are COPD and nutritional deficiency.

DISCUSSION: In COPD persistent hypoxemia may be associated with autonomic dysfunction. Disruption of autonomic reflexes with increased sympathetic tone, loss of parasympathetic tone and altered baroreceptor sensitivity are major risk factors for cardiac morbidity and mortality.

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Patients with COPD have elevated resting heart rate, reduced baroreflex sensitivity, reduced respiratory sinus arrhythmia, a direct increase in muscle sympathetic nerve activity and abnormal heart rate recovery (HRR) following exercise. Enhanced sympathetic tone at rest and disruption of autonomic reflexes contributes to the pathogenesis of COPD and possibly play an important role regarding the mortality in these patients.

This is to emphasize the importance of preoperative assessment of COPD patients planned for major surgeries. Malnourished, cachectic, carcinoma patients with COPD should be evaluated for autonomic dysfunction by simple tests in PAC itself so that peri operative untoward cardiac events like cardiac arrhythmias, sudden cardiac arrest can be anticipated and increased risk stratification can be done.

Anaesthetic management can be planned as discussed below so that untoward events due to existing symptoms can be prevented.

COPD seems to induce a generalized attenuation of excitatory pathways regulating respiratory, cardiac autonomic and cardiovascular systems. Since these three systems share identical control mechanisms, mutual interference of these systems is likely to occur in response to alterations affecting one system (11). The abnormality of autonomic function in patients with COPD may affect stimulus reception, afferent nerve conduction, central processing, efferent nerve conduction, and neuromuscular response. The sensory receptors that might play a significant role in autonomic dysfunction in patients with COPD are arterial and cardiac baroreceptor, metabolic and pulmonary stretch receptors, bronchopulmonary C-fibres and arterial chemoreceptors.

Type II respiratory failure in COPD is defined by co-existing hypoxemia and hypercapnia. It is likely that these two conditions have different effects on the autonomic nervous system; hypoxemia is acting mainly on peripheral chemoreceptors while hypercapnia is mainly stimulating central chemoreceptors.

The effect of chronic hypoxemia on autonomic dysfunction however, is difficult to predict as the sensitivity of arterial chemoreceptors may change over time. Furthermore, an interaction between arterial baro receptors and the chemoreceptor reflex has been demonstrated; an increase in baroreceptor activation causes an inhibition of the chemoreceptor reflex (12). Saito et al have demonstrated that the degree of hypoxemia correlates with the degree of sympathetic muscle nerve activity (13).

Several studies have suggested that hypercapnia leads to increased sympathetic tone (14) and that combined hypercapnia and hypoxemia synergistically increase sympathetic activity through impaired baroreceptor-cardiac reflex control in healthy humans (12, 15).

Patients with COPD have reduced baroreflex sensitivity to transient rise of blood pressure (BRS) (3, 4). It has been demonstrated, that impaired baroreflex sensitivity leads to an increase in sympathetic activity through inhibitory afferents (16, 17). Besides mechanical influences, other factors are discussed as possible causes of the reduced baroreflex sensitivity in patients with COPD. There is considerable evidence of interactions between peripheral chemoreceptor and arterial baroreceptor reflexes (18). Hypoxemia, but not hypercapnia, alters the baroreflex sensitivity (19). Furthermore it has been demonstrated, that elevated pulmonary arterial pressure alters baroreflex sensitivity in patients with COPD (20).

Eckhart and colleagues found evidence that the respiratory pattern influences autonomic output by inhibiting the ability of baroreceptor inputs to modulate the activity of autonomic

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motoneurons (21). The influence of the respiratory pattern on cardiac autonomic modulation is well known: the magnitude of parasympathetic induced heart rate variability has been shown to depend on both the lung hyperinflation (tidal volume VT) and respiratory rate (22, 23). Different patterns of activity of cardiac autonomic modulation are influenced by the extent to which lung hyperinflation (tidal volume VT) and respiratory rate changes occur in COPD patients. Slow breathing reduces sympathetic activity quickly, tends to increase baroreflex sensitivity and reduces chemoreflex sensitivity (17, 24) in COPD patients. Higher respiratory rate above a characteristic frequency causes sympathetic activation and vagal withdrawal (16, 25). However, it should be stressed, that breathing at lower respiratory rates does not lead to a normalization of baroreflexes and sympathetic activity in patients with COPD (16). Furthermore, no causal link has been found between breathing pattern, altered baroreflexes and heightened sympathetic activity in COPD (16). Instead, it is reasonable to suggest that a number of other synergistic mechanisms, including lung inflation reflexes, contribute to sympathetic activation in COPD. It may be postulated, that the development of a rapid shallow breathing pattern during an exacerbation or exercise probably is a contributor to autonomic dysfunction in patients with COPD.

The increased work of breathing due to severe obstructive and restrictive breathing in patients with chronic lung disease could lead to sympathetic activation through stimulation of local metaboreceptors. Oxygen radicals and products of ischemic metabolism generated during muscular contraction (e.g., isometric exercise) have been shown to stimulate local receptors and cause increases in heart rate, arterial pressure, and sympathetic activity (26, 27).

Clinical evaluation: The clinical picture associated with pathology of the autonomic nervous system

The autonomic nervous system contains three main components -

1. The Hypothalamic-Pituitary axis,
2. The Ascending pathways in the brain from the basal ganglia
3. The Descending autonomic sympathetic and parasympathetic pathways from the hypothalamus to the viscera.

Symptoms, signs and treatment:

- Orthostatic hypotension – Sleeping with head up position full length elastic stockings, Volume expansion with Fludrocortisone.
- Resting Tachycardia HR > 90/min
- Absent variation in heart rate with deep breathing
- Cardiac dysrhythmias
- Asymptomatic hypoglycemia
- Postural dizziness - elastic stockings, ephedrine, tyrosine, beta-blockers, mineralocorticoid e.g. fludrocortisone 0.1-0.3mg daily.
- Reflux oesophagitis and delayed gastric emptying - metoclopramide 10mg before meals.
- Nocturnal diarrhoea - metoclopramide 10mg 8 hourly, a short course of tetracycline may be of benefit to the patient.
- Post gustatory sweating - anticholinergics - propantheline hydrobromide before meals.

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- Bladder dysfunction and urinary retention - regular voiding and antibiotics for infections.
- Impotence - counseling, pharmacological erections and penile implants.
- Cardiorespiratory arrest - maintain high FiO₂ at all times.
- Pupillary abnormalities – sluggish reaction
- Thermal irregularities – inability to control body temperature
- Skin colour abnormalities.

Tests for autonomic dysfunctions (28):

1. Parasympathetic System :

- a. Parasympathetic Heart rate response to a Valsalva maneuvers. The seated subject blows into a mouthpiece (while maintaining a pressure of 40mmHg) for 15 seconds. The Valsalva ratio is the ratio of the longest R-R interval (which comes shortly after release) to the shortest R-R interval (which occurs during the maneuver) Normal value-Ratio of >1.21
- b. HR response to standing: HR is measured as the subject moves from a resting supine position to standing. A normal tachycardic response is maximal around the 15th beat after rising. A relative bradycardia follows that is most marked around the 30th beat after standing. The response to standing is expressed as a 30: 15 ratio and is the ratio of the longest R-R interval around the 30th beat to the shortest R-R interval around the 15th beat. Normal value-Ratio of >1.04
- c. HR response to deep breathing: The subject takes six deep breaths in 1 minute. The maximum and minimum heart rates during each cycle are measured, and the mean of the differences (maximum HR – minimum HR) during three successive breathing cycles is taken as the maximum-minimum HR. Normal value- Mean difference >15 beats/min. Heart rate variation during quite inspiration and expiration is lost with autonomic dysfunction.

2. Sympathetic System :

- a. Postural hypotension- BP response to standing. The subject moves from resting supine to standing, and standing SBP is subtracted from supine. Normal value-SBP Difference <10 mm Hg, pathological is when the difference is >30mmHg.
- b. Blood pressure response to sustained handgrip. The subject maintains a handgrip of 30% of the maximum handgrip squeeze for up to 5 minutes. BP is measured every minute, and the initial DBP is subtracted from the DBP just before release. Normal value-Difference >16 mm Hg.

Pre-operative history should elicit the causes for neuropathy and co-morbid conditions.

The examination is directed at finding evidence of cardiac decompensation and concomitant peripheral neuropathy. A thorough airway evaluation is necessary. Bed side examination for autonomic dysfunction generally involves finding postural hypotension and noting the heart rate response to a Valsalva manoeuvre. Investigations are aimed at determining the degree of renal dysfunction, checking the degree of myocardial ischaemia and cervical spine X rays for ligament laxity.

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Premedication:

- Decrease the amount of residual gastric volume - Metoclopramide 0.1mg/kg IV 90 minutes before induction.
- Increase the pH of the residual gastric volume - Ranitidine 2mg/kg IV HS and 90 minutes before induction. Combined with 0.3 Molar sodium citrate, 30ml orally 30 minutes prior to induction

Intra-operative Anaesthesia technique:

Induction: Good pre-oxygenation followed by a rapid sequence intubation with a cuffed oral tracheal tube. If a difficult laryngoscopic view is anticipated then endotracheal intubation must be secured while the patient is awake. Centro neuraxial anaesthesia is complicated due to fluctuations in blood pressure. Controlled level of block with epidural anaesthesia is preferred to prevent sudden fall in BP. Acute hypotension should be promptly corrected with vasoconstrictors like ephedrine 6mg increments IV. The presence of peripheral neuropathy must be well documented prior to any regional procedure.

Maintenance: Inhalational anaesthesia with Nitrous oxide, oxygen and a volatile agent, in view of the prolonged duration of surgery, preferably Sevoflurane as it has less effect on CVS should be used. Opioid supplementation with Inj. Fentanyl 25µg increments IV in case of short procedures or Inj. Morphine 1mg increments IV in case of long duration procedures can be used to avoid sudden drops in blood pressure and post operative respiratory depression. Non depolarising muscle relaxants like Inj. Vecuronium 1mg IV to be used as and when patient has respiratory attempts.

Monitoring apart from Routine

- ECG for ischaemia and rhythm abnormalities.
- Arterial line should be inserted before induction and should remain connected throughout positioning of patient for monitoring beat to beat variations of blood pressure. Quick aggressive correction of hypotension with Inj. Phenylephrine 50 mg boluses should be done.
- Central venous pressure and urine output for optimal fluid balance.
- Temperature probe.

Positioning and padding: Slow controlled positioning is necessary to avoid sudden blood pressure changes. These patients are at an increased risk of iatrogenic nerve injuries so excellent attention must be paid to padding vulnerable areas.

Emergence: Complete reversal of any non-depolarising muscle relaxant to ensure excellent airway control. Extubate the patient only when fully awake and in the recovery position with good suction available.

Post operative: Supplemental oxygen (40%) and close respiratory monitoring along with close haemodynamic monitoring with correction of hypotension should be done for at least 24 hours. Good post operative analgesia like - patient controlled analgesia or regional analgesia along with anti-emetics like Inj. Ondansetron 4mg IV should be provided.

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