INTRODUCTION

About one third of the population of industrial countries is at least 20 % overweight and the prevalence of obesity is steadily ***(Kuczmarski et al., 1994).*** Obese patients have an impaired respiratory function and are prone to develop post operative respiratory complications ***(Luce et al., 1980).*** During general anesthesia and mechanical ventilation, lung are compressed by a cranial diaphragmatic shift, leading to formation of compression atelectasis ***(Tokics et al., 1987).*** The use of laparoscopic techniques in general surgery is increasing in popularity due to combination of factors, the small limited incisions, the benefit of faster recovery compared to open laparotomy, health care cost may be decreased by diminishing length of postoperative hospital stay and by reducing the need for postoperative analgesia and less impairments of post operative respiratory function compared to open surgery ***(Ellstrom et al., 1998).***

Laparoscopic surgeries required the formation of a working area within the peritoneal cavity. This achieved by gas insufflation into the peritoneal space. The peritoneal gas insufflation increases intra abdominal pressure, determined by the compliance of the abdominal cavity and the volume of insufflated gas. Pneumoperitoneum causes cephalad displacement of the diaphragm resulting in decreased lung volume, including functional residual capacity (FRC), decreased pulmonary compliance, increased resistance and

ventilation -perfusion mismatch ***(Safran et al., 1994).*** The overall decrease may reduce the functional residual capacity below the closing volume which predisposes to airway closure and atelectasis. Laparoscopy is not a benign procedure .It is associated with major and minor surgical and non surgical complications. The anaesthesiologist goals during laparoscopic surgery are haemodynamic and respiratory stability, appropriate muscle relaxation, control of diaphragmatic excursion, intra operative and post operative proper patient analgesia and a quick post - anesthesia recovery. Nevertheless, general anesthesia which tends to provoke respiratory dysfunction, is conventionally used for laparoscopic surgery ***(Sydow et al 1989).*** In open surgery, epidural anesthesia has been shown to relieve post operative pain, improve diaphragmatic function, and reduce the probability of hypoxemia, with a consequent reduction of post operative respiratory morbidity compared with general anesthesia ***(Rawal et al., 1984).*** However the advantages of epidural anesthesia observed in open surgery can not be translated to laparoscopic surgery due to particular maneuvers inherent in laparoscopic surgery, which include pneumo peritoneum, factors affecting cardiovascular and respiratory functions ***(Lewis et al., 1972).***

AIM OF THE WORK

We investigate the usefulness of thoracic epidural anesthesia in obese patients undergoing laparoscopic cholecystectomy compared with general anaesthesia focusing on the perioperative respiro-circulatory function and complications. We also compare pain status including post operative analgesic requirements between both groups.

OBESITY

Obesity is associated with increased morbidity and mortality and a wide spectrum of medical and surgical diseases ***(Adams et al., 2000).*** A measure of obesity is the body mass index (BMI) ***(Morgan et al., 2006).*** Calculation of body mass index = $\frac{\text{weight (kg)}}{[\text{height (meters)}]^2}$

Body mass index (BMI) which is defined as weight in kilograms divided by height in meters squared (kg/m^2), has been established as a useful standard measure of overweight and obesity. Although BMI does not directly measure body fat, it provides a reasonable estimate of adiposity which, in turn, also predicts risks for current or future medical complications of obesity ***(Dietz and Robenson, 1998).***

BMI (kg/m^2) between 22 and 25 is considered normal, more than 30 is considered obese, between 25 and 30 is considered overweight but at minimally increased risk of morbidity and mortality and more than 35 is considered morbid obesity. A BMI more than 40 kg/m^2 reflects extreme obesity, while that of more than 55 kg/m^2 is considered a upper extreme obesity ***(Quetelet, 1994).***

Obesity is a complex and multifactorial disease, but in simple terms, occurs when net energy intake exceeds net energy expenditure over a prolonged period of time. However it is not always easy to identify a single

explanation as to why this occur in some individuals and not others genetic predisposition, environmental influences, developmental factors, medical disorders and energy imbalance are main predisposing factors ***(Weigle, 1994).***

Physiologic disturbances associated with obesity:

Obesity has detrimental effects on multiple organ system including the patient respiratory and cardiovascular system.

Obesity related pathophysiology of respiratory system

Obstructive sleep apnea (OSA):

An obstructive apneic episode is defined as 10 seconds or longer of total cessation of airflow despite continuous respiratory efforts against a closed airway. Obstructive sleep apnea, characterized by frequent episodes of apnea or hypopnea during sleep, airway obstruction manifesting as snoring, dynamic somnolence due to repeated episodes of fragmented sleep during the night, and physiological changes that includes arterial hypoxemia, arterial hypertension, polycythemia, pulmonary hypertension, and right ventricular failure, is present in 2% to 4% of middle age adults, especially men ***(Adams et al., 2000 and Strollo et al., 1996).***

Obesity hypoventilation syndrome (OHS):

Obesity hypoventilation syndrome is the long term consequence of obstructive sleep apnea. Obstructive sleep apnea is initially limited to nocturnal sleep with correction of respiratory acidosis during waking hours. As the obesity hypoventilation syndrome develops there is evidence of nocturnal alterations in the control of breathing manifestations as central apneic events (apnea without respiratory efforts). These nocturnal episodes of central apnea reflect progressive desensitization of the respiratory centers to nocturnal hypercarbia. At its extreme, obesity hypoventilation syndrome culminates in the Pick-Wickian Syndrome, which is characterized by obesity, daytime hypersomnolence, arterial hypoxemia, polycythemia, hypercarbia, respiratory acidosis, pulmonary hypertension, and right ventricular failure ***(Stoelting et al., 2002).***

Lung volumes:

Obesity imposes a restrictive ventilation defect because of the weight added to the thoracic cage and the abdominal weight impending motion of the diaphragm, especially with assumption of the supine position. The results of this added weight and associated splinting of the diaphragm are decreasing functional residual capacity (FRC), expiratory reserve volume (ERV), and total lung capacity, with the FRC declining exponentially with increasing BMI ***(Adams et al., 2000).*** The FRC may be

decreased to the point that small airway closure occurs with resulting ventilation to perfusion mismatching, right to left shunting, and arterial hypoxemia. Anesthesia accentuates these changes such that a 50% decrease in FRC occurs in obese anesthetized patients compared with 20% decrease in nonobese individuals ***(Adams et al., 2000)***. The application of positive end expiratory pressure (PEEP) improves of the FRC and arterial oxygenation.

The decrease in FRC impairs the ability of obese patients to tolerate periods of apnea, such as during direct laryngoscope for tracheal intubation ***(Stoelting et al., 2002)***.

Lung compliance and resistance

Increasing BMI is associated with exponential decrease in respiratory compliance and resistance. These changes in lung compliance and resistance result in rapid, shallow breathing patterns and increased work of breathing that is most marked when obese individuals assume the supine position ***(Stoelting et al., 2002).***

Work of breathing:

Oxygen consumption and carbon dioxide production are increased in obese individuals as a result increased metabolic activity of the excess fat and the increased workload on supportive tissues. Normocapnia is maintained usually by increased minute ventilation, which results in

increased oxygen cost (work) of breathing. Obese patients typically breathe rapidly and shallowly, as this pattern results in the least oxygen cost of breathing ***(Stoelting et al., 2002).***

Pulmonary dysfunction:

Obese patients sustain a combination of mechanical and inflammatory mediated insults that result in pulmonary disability. The excess fat externally and internally compresses the thoracic cavity. Evidence suggests that fatty infiltration of the accessory muscles of breathing can decrease compliance of the chest wall. Central adiposity can increase intra abdominal pressure causing cephalic displacement of the diaphragm. This displacement results in a chronic abdominal compartment syndrome resulting in diminished lung volumes and suboptimal pulmonary dynamics. Obesity also leads to increased pulmonary blood volume which competes for space in the chest cavity, further decreasing lung volumes ***(Davis et al., 2007).***

The large amount of work it takes to move an obese body combined with the decreased compliance of the chest wall can lead to a subjective sensation of dyspnea, commonly seen in obese patients. To make matters worse, evidence suggests that this continued battle to breathe can lead to respiratory muscle weakness as evidenced by decreases in maximum inspiratory pressure in a comparison with no obese subjects ***(Weiner et al., 1988; Chlif et al., 2005).*** For these reasons, it is not hard to understand that,

with weak muscles, poor chest wall compliance, and a large body habitus, exercise tolerance is poor in the severely obese patient ***(Fantuzzi et al., 2005).***

Evidence suggests that mechanical forces are not the only insult of obesity on respiratory function; there are also patho-physiologic changes at the molecular level. Obesity can be characterized as a disease of systemic inflammation. C-reactive protein, tumor necrosis factor, and interleukin-6 can all be elevated in the obese patient and can affect airway reactivity ***(Fantuzzi et al., 2005).*** In addition, leptin, which is produced by adipocytes and thereby elevated in the obese patient, may increase airway reactivity ***(Maffei et al., 1995).***

Obesity related pathophysiology of the cardiovascular system

Obesity affects the cardiovascular system in multiple ways. Obese individuals have an increased total blood volume to meet the perfusion needs of the increased adipose tissue. Increase are seen in both intracellular and extracellular fluid and are associated with increased stroke volume, although resting heart rate remains unchanged. The increased stroke volume increases resting cardiac output and left ventricular (LV) work ***(Marik and Varon, 1998).***

Cardiac and stroke work indices remain normal in normotensive obese individuals. The increase in cardiac output is also accompanied by a decrease in systemic vascular resistance in normotensive obese individuals. Because of increased LV workload, oxygen consumption is also increased; the oxygen consumption increase linearly with the increase in body weight ***(Marik and Varon, 1998).***

Cardiovascular system dominates the morbidity and mortality in obesity and manifests itself in the form of ischemic heart disease, hypertension and cardiac failure.

Mild to moderate hypertension is seen in 50-60% of obese patients and severe hypertension in 5-10%, with 3-4 mmHg increase in systolic and a 2 mmHg increase in diastolic arterial pressure for every 10 kg of weight gained ***(Adams and Murphy, 2000).***

Hyperinsulinaemia, which is a characteristic of obesity, can contribute by activating the sympathetic nervous system and by causing sodium retention. In addition, insulin resistance may be responsible for the enhancement in pressor activity of norepinephrine and angiotensin 2 ***(Mikhail et al., 1999).***

Hypertension per se leads to concentric left ventricular hypertrophy and a progressively non compliant left ventricle which, when added to the increased blood volume, increase the risk of cardiac failure. Weight loss has

been shown to reduce hypertension in the obese ***(Alpert et al., 1995).***

Obese individuals tend to have increased values of fibrinogen, factor 7, factor 8 (von Willibrand factor), and plasminogen activator inhibitors as well as decreased levels of antithrombin 3 and circulating fibrinolytic activity ***(Marik and Varon, 1998).***

Polycythaemia may also develop as a result of chronic hypoxia ***(Gleason, 1987).***

These hemostatic and fibrinolytic changes, when combined with decreased mobility and venous stasis, place obese individuals at increased risk for thromboembolic disease, especially deep vein thrombosis. ***Marik and Varon (1998)*** reported that obesity is the single most important risk factor for pulmonary embolism.

It is generally accepted that obesity is an independent risk factor for ischemic heart disease ***(Duflou et al., 1995)*** and is more common in those obese individual with a central distribution of fat Other factors such as hypertension, diabetes mellitus, hypercholesterolaemia and reduced high density lipoprotein levels, which are all common in the obese ***(Adams and Murphy, 2000).***

Interestingly, 40% of obese patients with angina do not have demonstrable coronary artery disease ***(Lean,***

1999) in other words, angina may be a direct symptom of obesity.

Arrhythmia may be precipitated in the obese by a number of factors: hypoxia, hypercapnea, electrolyte disturbance caused by diuretic therapy, coronary artery disease, increased circulating catecholamines concentrations, obstructive sleep apnea (OSA), myocardial hypertrophy and fatty infiltration of the conduction system ***(Valensi et al., 1995).***

There is a linear relationship between cardiac weight and body weight up to 105 kg, after which cardiac weight continues to increase, but at a slower rate. The increase in heart weight is a consequence of dilatation and concentric hypertrophy of the left and to a lesser extent, the right ventricle ***(Duflou et al., 1995).***

Otherwise healthy obese individuals demonstrate an increased cardiac output, elevated left ventricular end diastolic pressure (LVEDP) and left ventricular hypertrophy on echocardiography. Left ventricle systolic function is also impaired, when the ejection fraction rises to a lesser extent, and more slowly, than in lean individuals ***(Ferraro et al., 1996)***.

The pathophysiology of obesity induced cardiomyo-pathy is now well defined, largely as a result of studies in non hypertensive individuals awaiting bariatric surgery (of

some importance since the general extremely obese population may be somewhat less fit than preselected group ***(Murphy, 2000).***

The ventricular dilation results in increased left ventricle wall stress, leading to hypertrophy. Such eccentric left ventricular hypertrophy results in reduced compliance and left ventricular diastolic function, i.e., impairment of ventricular filling, leading to elevated LVEDP and pulmonary oedema ***(De Simone et al., 1996).***

The capacity of the dilated ventricle to hypertrophy is limited so, when left ventricular wall thickening fails to keep place with dilatation, systolic dysfunction ensues (obesity cardiomyopathy) ***(Alpert et al., 1995).***

Obesity is associated with an increase in blood volume and cardiac output, the latter rising by 20-30 mL per kilogram of excess body fat. The increase in cardiac output is largely a result of ventricular dilatation and an increase in stroke volume.

The problem is often compounded by superimposed hypertension and ischemic heart disease. Ventricular hypertrophy and dysfunction worsen with increasing duration of obesity and improve to some extent with weight loss ***(Alpert et al., 1995).***

As a result of the continuous pressure overload, increased blood viscosity, obesity related hypertension, and

concentric left ventricular hypertrophy (LVH) develop. In the absence of hypertension, the myocardium may also be damaged by the chronic fluid overload related to increased cardiac output, which may lead to LV dilatation and an eccentric LVH ***(Schunkert, 2002).***

Concentric and eccentric LVH increase the risk of developing both systolic and diastolic ventricular dysfunction, in the obese, systolic dysfunction is most evident. Increased LV end diastolic volume is often accompanied by decreased ejection fraction in the chronically obese, putting them at risk for congestive heart failure ***(Schunkert, 2002)*** and cardiac arrhythmias. The incidence of premature ventricular contractions is higher in individuals with concentric LVH. Because of dilatation of the atria related to increased fluid volume, the prevalence of atrial fibrillation and stroke is also higher in this population ***(Schunkert, 2002).***

Gastric emptying:

The obese patients are at increased risk for aspiration and development of aspiration pneumonitis based on increased intra-abdominal pressure, delayed gastric emptying, and the increased incidence of hiatus hernia and gastroesophageal reflux is questionable ***(Adams et al., 2000).*** In fact, obese patients without symptoms of gastroesophageal reflux have resistant gradients between the stomach and gastroesophageal junction similar to those in nonobese

individuals in both sitting and supine positions. Furthermore, although gastric volume is greater in obese individuals, gastric emptying may be more rapid in these subjects than in non obese subjects. Nevertheless, because of the larger gastric capacity, the residual volume is larger in obese individuals ***(Stoelting et al., 2002).*** Both the faster gastric emptying and the larger gastric volume can be partially reversed by weight loss ***(Tosetti et al., 1996).***

Diabetes mellitus:

Glucose tolerance curves are often abnormal, and the incidence of diabetes mellitus is increased several fold in obese patients. This finding is consistent with the resistance of peripheral tissues to the effects of insulin in the presence of increased adipose tissue. Indeed, obesity is important risk factor for the development of non-insulin dependent diabetes mellitus (NIDDM). In obese patients with NIDDM the catabolic response to the surgery may necessitate the use of exogenous insulin during the perioperative period ***(Stoelting et al., 2002).***

Hepatobiliary disease:

Abnormal liver function tests and fatty liver infiltrations are frequent findings in obese patients. Development evidence that volatile anesthetics are defluorinated to a greater extent in obese patients. There is no evidence of exaggerated anesthetics induced hepatic