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EFFECTS OF OBESITY ON ANESTHESIA

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Abstract:

Background: *Studies have shown that obesity among adults is rapidly increasing throughout the world, Due to its associated pathophysiology, obese individuals show varied response to many medication doses, including anesthetics. The effect of obesity on anesthetics is a narrowing of the therapeutic index.*
Methodology: *We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through* ***February*** *2017. The following search terms were used: anesthesia, obesity, airway management for obese patients, pharmacokinetics of anesthetics in obese patients, volume distribution*
Aim: *In this review, we aim to study how obesity affects anesthetic medication and airway management differently.*
Conclusion: *Anesthesia in obese adults needs careful considerations regarding changes in the PK and PD properties of many medications used in anesthesia. Physiological and anthropometric alteration, like increases in cardiac output, alterations in regional blood flow, and elevations in fat mass and lean mass affect PK properties. Additionally, respiratory pathophysiology such as the increased incidence of OSA, and fat deposition in the oropharynx and chest wall change PD characteristics of the anesthetic medications.*

Keywords: *anesthesia, MAC, obesity, volume distribution*

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INTRODUCTION:

Studies report that the prevalence of obesity in adults is increasing in the United States. The Centers for Disease Control and Prevention reports that more than 1/3 of US adult population are obese (around thirty five percent) **[1]**. Additionally, obesity's incidence has increased dramatically over the previous years. It is estimated that the number of states with an obesity rate of more than thirty percent had increased to 12 in 2010. Obesity has been well studied, it has been confirmed that it is a risk factors for both number of hospital admissions and length of hospital stay. The National Institutes of Health strongly recommended bariatric surgery as the mainstay management of morbid obesity in 1998 **[2]**. The number of bariatric surgeries has increased since then. Since 2006, this number has plateaued **[3]**. Studies described the increased risks of anesthesia among obese adults **[4]**. Obesity changes the normal physiology and anthropometric measurements which can influence the pharmacokinetics (PK) of anesthetic medications. Obesity is also associated with an elevated risk in cardiac output and in total blood volume, which could change the medication distribution, peak concentration and clearance. Additionally, elevates the fat- and lean-body mass and alters tissue perfusion. The pathophysiology linked with obesity, involves an elevated prevalence of obstructive sleep apnea and C02 retention, reduced functional residual capacity, and cardiac dysfunction. The end result is a narrowing of the therapeutic index of anesthetic medications **[5]**.

METHODOLOGY:

- **Data Sources and Search terms**

We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: anesthesia, obesity, airway management for obese patients, pharmacokinetics of anesthetics in obese patients, volume distribution

- **Data Extraction**

Two reviewers have independently reviewed the studies, abstracted data, and disagreements were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout.

The study was approved by the ethical board of King Abdulaziz University Hospital

Airway Management

Morbidly obese (MO) adults have a higher risk of difficult mask ventilation, laryngoscopy, and intubation. This is due to the obese patient's large tongue, redundant oropharyngeal tissue, atlantoaxial joint limitation due to cervical and thoracic fat pads, and parasternal fat deposits inhibit movement of the laryngoscope and increase the difficulty of direct laryngoscopy (DL). Risk factors like a higher Mallampati classification and neck circumference are suggestive of a difficult airway. The astute anesthesiologist integrates multiple historic and physical clues like thyromental distance, mouth opening, neck range of motion, and prognathism, to do the preoperative airway assessment and predict conditions for airway protection **[6]**.

After the assessment of the airway, the physician can reach one of the following: (1) endotracheal intubation will most probably be feasible by DL, so the airway could be secured after general anesthesia (GA) induction; or (2) endotracheal intubation will be hard by DL, so an awake intubation will be necessary. Luckily, most of the obese patients' airways can be protected sufficiently after GA induction **[7]**.

The position of the patient has to be adjusted according to the airway management. The head-elevated laryngoscopy position (HELP) utilizes preformed pillows to elevate the patient's upper body to maintain the external auditory meatus at the level of horizontal plane with the sternal notch, in order to compensate for the fixed flexion caused by cervical fat. The regular blankets and towels are also available in any operating room and could be used to achieve this same optimal positioning **[8]**.

In case of induction of GA prior to intubation, it is highly critical to preoxygenate or denitrogenate the obese patient in order to prepare for the unavoidable period of apnea and potential oxygen desaturation prior to protecting and securing the airway. When the obese patient becomes unconscious, the muscles of the pharynx and the tongue relax, which lead to occlusion of the airway. Oral and/or nasal airways are usually mandatory to keep a patent airway and to helps mask ventilation. Oral airways are recommended over nasal airways due to the latter could lead to bleeding that could obscure the visual field when intubation is needed. The sizing and placement of airways correctly are essential, because the in appropriate technique could worsen the obstruction.

One of the worst-case scenarios that could occur with an unexpected difficult airway in which both ventilation and intubation are difficult. In this case, the laryngeal mask airway (LMA) is highly recommended and can successfully rescue device for

the difficult to ventilate patient until a more definite airway can be obtained, which could include a surgical airway. Some societies like the American Society of Anesthesiologists reported guidelines for the proper management of the difficult airway **[9]**.

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is an important comorbidity of obesity that can often be not paid much attention on. It can be a cause of difficulty in correctly placing mask ventilation, lead to hypoxemic events, cause coronary artery blockage, arrhythmias, as well as sudden death. All of these unfortunate events get amplified in under effect of anesthetic drugs. The postoperative, period after extubating is the most critical time due to the residual pain and anesthetics medications which weaken the respiratory drive activated by hypoxemia and high carbon dioxide. The obstruction can worsen, and ultimately leading to decreased ventilation, causing adverse events. Many obese patients may already have OSA which was not diagnosed earlier. The American Society of Anesthesiologists' Checklist and STOP Questionnaire are can be used to identify patients with underlying undiagnosed OSA before proceeding to surgery. Patients known to have OSA those on home CPAP (continuous positive airway pressure) are advised to bring their device along with them for instant use after surgery. Furthermore, it is suggested to have a CPAP device on standby at the time of recovery from anesthesia for those patients with suspected OSA **[10; 11]**.

For the patient with OSA, minimizing the use of benzodiazepines, opiates, and other respiratory drive-suppressing drugs is the focus in management. Therefore, the major roles are taken by regional anesthesia and nonopioid substitutes. For surgery done in outpatient setting, the American Society of Anesthesiologists Practice Guidelines recommends a, additional 3-hour observation period on suspected OSA patients, and 7-hours period following last event of obstruction or hypoxemia, if there was one, before sending home. This guideline also indicates any event of oxygen desaturation, if it occurs, requires overnight observation **[10]**.

Cardiovascular

The MO patient has higher than average lean body mass and total body weight donating to amplified metabolic demands, resultant in a greater total blood volume. The greater volume of blood and the lower systemic vascular resistance, which is commonly seen in obese patients, cause higher cardiac output. Stroke volume rises but the heart rate stays almost unchanged. The increased volume leads to increased wall stress in the left ventricle, resulting in compensatory concentric hypertrophy and subsequent diastolic dysfunction over a period of time. Eventually it is followed by systolic dysfunction, which would lead to pulmonary hypertension. The MO patient are at risk for OSA, as discussed above, are further predisposed to high pressure in the pulmonary circulation, leading to right ventricle failure. This can consequently lead to atrial arrhythmias. For patients at risk of OSA, an electrocardiogram as along with a comprehensive cardiopulmonary history and functional status must be included in the preliminary screening. Additional studies including chest x ray, arterial blood gas analysis, and echocardiogram give more awareness into this pathophysiology, such that preoperative optimization and interventions to lower risk can be applied and assist the anesthesiologist tin designing the optimal perioperative plan for anesthesia **[10]**.

Pain Management

Efficient postoperative pain management must be compulsory in any surgical process. Accomplishing sufficient pain control in the obese patient population can be difficult to achieve. Opioids are the basis of pain control therapy in the post-operative period; nevertheless, they are concomitant with respiratory suppression and sedation, which when added to the obese patient's risks of OSA, dosing difficulties, and sensitization to the depressant effects of opioids lead repeatedly to insufficient management of pain. The most successful formulation for pain control includes multimodal techniques. This can be explained as for an open procedure, epidural analgesia with additional acetaminophen along with nonsteroidal anti-inflammatory drugs (NSAIDs) would provide effective pain control minus the adverse effects of opioids. Local anesthetics constantly delivered through catheters in the location of wound with complementary nonopioids can successfully provide sufficient analgesia while diminishing the use of opioids. Opioids in intravenous patient-controlled analgesia in a supervised setting as part of a multimodal method permits more constant blood levels of pain killers, and thus better control of pain. It can deliver effective control of pain in open surgeries as well as in laparoscopic procedures **[12]**.

Volume of Distribution and Clearance

Obesity was believed as just a pathology of high adiposity. Now, we understood that although all obese subjects have a common phenotype, the high adiposity is also linked to multi-organ system dysfunction. To understand how obesity affects the Pharmacodynamic and Pharmacokinetics of

anesthetic medications.

Obesity is linked to a high total body weight (TBW), lean body weight (LBW), and fat mass. LBW is responsible for about thirty percent of the high TBW in obese adults. But, with higher obesity, fat mass elevates greater extent than LBW, and the ratio of LBW to TBW lowers **[13]**. The elevation in fat mass is thought to elevate the volume of distribution of lipophilic medications. Central volume of distribution is the main pharmacokinetic parameter guaranteeing the proper selection of a loading dose. So, administer larger initial loading doses of the medications makes sense. But, plasma protein binding, cardiac output and tissue perfusion play a vital role in medication distribution **[14]**.

Though obesity has not been found to change medication binding to albumin and α-acid glycoprotein, there is an increase in cardiac output linked to obesity **[15]**. The elevation in cardiac output is thought to be related to the increase in LBW. Cardiac output is a major predictor of early distribution kinetics. It could be debated whether a loading dose can be administered based on TBW to reflect the increase in volume of distribution or administered based on LBW to reflect the alteration in cardiac output **[16]**.

The elevation in cardiac output linked to obesity leads to elevated hepatic and renal blood flow. Additionally, there are regional differences in the perfusion of adipose tissue. Abdominal and visceral fat get less blood flow than subcutaneous adipose tissue **[17]**. Obesity is linked with a higher in medication clearance. But, recently many studies are showing that the effect of obesity on drug metabolism and clearance is dependent on the metabolic pathway. Obesity lowers clearance of medications metabolized by the cytochrome P450 3A4 pathway, while medications metabolized by 2D6, 2E1, 1A2, and 2C9 show higher clearance in obese versus non-obese individuals **[18]**.

Factors affecting pharmacokinetics in obesity

The physiologic alterations that are produced by obesity could significantly affect the distribution, binding, and elimination of anesthetic medications, and serious side effects could happen if the medication dosing is based only on the body weight. Systemic absorption of oral medications does not appear to be remarkably influenced by obesity, though researchers concluded a delay in gastric emptying in the obese patient **[19]**.

Obesity can increase fat and lean masses of obese in comparison to nonobese adults of the same age, height, and sex. The elevation in lean body mass represents twenty to forty percent of total excess of weight; but, the percentage of fat mass per kilogram of TBW increases more than does the lean mass, leading to a relative decrease of the percentage of lean mass and water of obese in comparison to nonobese patients of the same age, sex, and height. These alterations in tissue distribution produced by obesity could significantly influence the apparent volume of distribution of the anesthetic medications. Moreover, there are other alterations produced by obesity that could influence the pharmacokinetic of the anesthetic medications, like the absolute elevation in total blood volume and cardiac output (CO) and changes in plasma protein binding. It should be illustrated that alterations in respiratory and cardiovascular functions due to obesity could affect the absorption and elimination of inhalation anesthetics, which is considered a major component in modern balanced anesthesia **[20]**.

Obesity-induced alterations in the hemodynamic status and regional blood flow could moreover influence anesthetic medications pharmacokinetics. Fat tissue gets around five percent of CO, while viscera and lean tissues get around seventy and twenty of CO, respectively. But it has been studied that blood flow per gram of fat is decreased in the obese in comparison to the nonobese patient, suggesting that blood flow could be proportionally decreases in fat than in lean mass in obese adults. Furthermore, the decrease in cardiac performance produced by obesity itself could further decrease tissue perfusion **[21]**.

The effects of obesity on drug binding to the plasma proteins are still unclear. It has been studied that the increased concentrations of triglycerides, lipoproteins, cholesterol, and free-fatty acids may inhibit protein binding of some medications, increasing their free plasma concentrations. While the elevation in concentrations of acute phase proteins, including α1-acid glycoprotein, noticed in the obese patient may also increase the degree of binding of other drugs, reducing their free-plasma concentrations **[22]**.

Lastly, the pharmacokinetic profile of anesthetic medications could be influenced by alterations in their elimination linked the obesity-induced alterations of liver and kidney functions. Obese patients usually have a fatty degeneration of the liver, which could degenerate in liver fibrosis. These alterations could potentially affect hepatic clearance. however, hepatic clearance is often normal or even elevated in the obese patient. Renal clearance elevates in obesity due to the increase in kidney weight, renal blood flow, and glomerular filtration

rate, and it has been shown that creatinine clearance is elevated in healthy obese subjects in proportion to the estimated fat-free mass. But, the alterations produced by obesity contribute with time in developing a more severe glomerular injury, leading to chronic renal disease **[23]**.

Effect of Obesity on Anesthetic Drugs' Pharmacokinetic Properties

Benzodiazepines are often used as a premedication and conscious sedation, and their loading dose should be adjusted on actual weight while maintaining doses have to be calculated on IBW. The medications mainly used for anesthesia induction are thiopental and propofol, and their regimen should be based on TBW with a reduced loading dose for thiopental only due to the higher sensitivity of the obese patient to the action of this medication. The loading dose of lipophilic opioids must be based on TBW while the maintaining dose should be decreased due to the higher sensitivity of the obese patient to the depressant effects of these agents. The new opioid, remifentanil, has interesting characteristics for anesthetic management of the obese patient.

Anti-emetics

A common complication of general anesthesia is post-operative nausea and vomiting (PONV) is, which is particularly disturning for the patient and can end up with slower recovery time and therefore prolonged hospital stay. Certain procedures such as manipulation of the upper stomach, for example in bariatric surgery, can cause sever nausea, therefore good anti-emetic therapy is extremely anticipated **[24]**.

5-hydroxytryptamine 3 (5-HT3) receptor antagonists are recommended by Guidelines on PONV published in 2013 as the first-line prophylactic agent in patients in the high-risk category. Ondansetron is the most commonly used, but its comparatively short duration of action suggests that this medication should be given near the end of the surgery. Meanwhile in high risk patients for high risk procedures, use of multiple anti-emetics is recommended, and the combination of a dexamethasone with 5-HT3 antagonist is a frequently chosen pairing. There is additional advantage to be gained with the use of triple anti-emetic therapy; some commonly used agents include cyclizine and metoclopramide **[25]**.

CONCLUSION:

Anesthesia in obese adults needs careful considerations regarding changes in the PK and PD properties of many medications used in anesthesia. Physiological and anthropometric alteration, like increases in cardiac output, alterations in regional blood flow, and elevations in fat mass and lean mass affect PK properties. Additionally, respiratory pathophysiology such as the increased incidence of OSA, and fat deposition in the oropharynx and chest wall change PD characteristics of the anesthetic medications. Surgery and anesthesia could be safely done in morbidly obese patients with normal cardiac, pulmonary, renal, and hepatic function. For the high-risk obese patients with severe multisystem disease, good outcomes are also possible, provided the entire perioperative team is well aware of the comorbidities of the patient and associated inherent risks of surgery and anesthesia, and they strive to work together toward the optimization of the patient's condition at every step of the process.

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