بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: ....

Efficacy of Dexamethasone in Attenuation of Postinduction Hypotension in Geriatric Patients Undergoing General Anesthesia: A Randomized Controlled Trial

Thesis

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List of Abbreviations

Abb.	Full term
AKI	*Acute kidney injury*
ASA	*American Society of Anesthesiologists*
AVN	*Avascular necrosis*
CNS	*Central nervous system*
CO	*Cardiac output*
eNOS	*Endothelial nitric oxide synthase*
ENT	*Ear nose and throat*
GABA	*γ-aminobutyric acid*
HR	*Heart rate*
IVI	*Intravenous infusion*
LV	*Left ventricular*
LV	*Left ventricular*
MAP	*Mean arterial pressure*
MI	*Myocardial infarction*
MINS	*Myocardial injury after noncardiac surgery*
NMBAs	*Neuromuscular blocking agents*
NO	*Nitric oxide*
PONV	*Post-operative nausea and vomiting*
PONV	*Postoperative nausea and vomitting*
PVR	*Peripheral vascular resistance*
PVR	*Peripheral vascular resistance*
SVR	*Systemic vascular resistance*
TKA	*Total knee arthoplasty*

INTRODUCTION

Nearly all intravenous anesthetics may produce arterial hypotension. Hence, the induction of general anesthesia may result in decreased systemic vascular resistance and depression of cardiac function, which result in arterial hypotension, particularly in elderly patients ***(Reich et al., 2005).***

Since cardiovascular reserves diminish with increasing ages, elderly patients are particularly prone to the development of post-induction hypotension ***(Sanders et al., 2009).***

Intraoperative hypotension may have serious effects on postoperative outcome in terms of vital organ system functions such as acute kidney and myocardial injury ***(Salmasi et al., 2017).***

Dexamethasone increases tissue peripheral vascular resistance (PVR) in rats ***(Tonolo et al., 1988)*** and humans by a variety of mechanisms, and there is a plethora of studies confirming its role in maintaining the integrity of circulation in situations of intense vasodilatation like septic shock ***(Fang et al., 2019)*** and anaphylaxis ***(Liyanage et al., 2017).***

The investigators will conduct this study to test the hypothesis of obtunding postinduction hypotension in geriatric patients undergoing general anesthesia for elective operations after receiving a single preoperative dose of dexamethasone 8 mg intravenous infusion (IVI).

Aim of the Work

This study will be conducted to evaluate the efficacy of a single preoperative dose of dexamethasone 8 mg IVI to attenuate the postinduction hypotension in geriatric patients undergoing general anesthesia for elective operations.

Chapter 1

GERIATRIC PHYSIOLOGY

Older adults (≥65 years of age) account for a disproportionately large fraction of all surgical procedures performed in the United States ***(Neuman and Bosk, 2019)***. Older age is a risk factor for perioperative mortality ***(Chung et al., 1999),*** but preoperative comorbidity and invasiveness of the surgical procedure are other important predictors of mortality in this age group ***(Turrentine et al., 2006).*** The American Society of Anesthesiologists (ASA) Physical Status score, indicating severe systemic disease, is an established predictor of adverse outcomes after surgery in patients of all ages but does not specify age as a factor ***(Sankar et al., 2014)***

Aging is associated with a progressive loss of functional reserve in all organ systems. However, there is considerable individual variability in the onset and extent of these changes. Nevertheless, even the healthy older adult has reduced physiologic reserve, and organ systems may be compromised during illness and/or surgical stress. The following physiologic changes specifically impact anesthetic care, in large part by increasing susceptibility to anesthetic drugs ***(Akhtar, 2018).***

1- Nervous system:

Age-related changes in the central and peripheral nervous system affect the older adult's response to anesthetics

and other medications, as well as the perception of pain. Central nervous system changes include reduction in brain size and neuronal density and widening of the sulci and ventricles. Regional reductions in neurotransmitters (eg, dopamine, serotonin, and acetylcholine) and neuroreceptors may occur ***(Nickalls and Mapleson, 2003)***

Pharmacodynamic sensitivity increases with age for all intravenous agents that act within the central nervous system (eg, propofol, fentanyl, and midazolam). Furthermore, there is an age-related decrease in the minimum alveolar concentration at 1 atmosphere preventing movement in 50 percent of patients exposed to a surgical incision (termed "MAC") for all volatile anesthetic agents ***(Lawrence et al., 2006***). In addition, a decrease in cholinergic receptor activity may explain the older patient's vulnerability to the anticholinergic side effects of medications such as diphenhydramine, meperidine, and scopolamine (***Nickalls and Mapleson, 2003)***

The normal ventilatory response of the central nervous system to hypercapnia, and especially to hypoxemia, is diminished with age. The respiratory depressant effects of opioids, benzodiazepines, and volatile anesthetics are exaggerated in older adults and may further impair the response hypercapnia and hypoxemia ***(Hasukić et al., 2002)***

Finally, although the mechanisms are not clear, it is known that postoperative central nervous system complications,

particularly postoperative delirium and postoperative cognitive deficits, are primarily a problem in older patients ***(Rooke, 2003)***

2- Cardiovascular system:

Normal changes in the older adult's cardiovascular system, such as vascular stiffening and autonomic changes, influence the physiologic response to anesthetic administration ***(Das et al., 2010).*** Labile blood pressure is common in the anesthetized older adult. The reasons are frequent use of diuretics due to pre-existing diseases, a reduction in the thirst response in the elderly.In addition, age-related renal function changes can aggravate the reduction of preload, increasing the sensitivity to volume status during episodes of hemodynamic instability. Thus, significant hypotension requiring treatment often develops in these patients ***(Phillip et al., 2003)***

Vascular stiffening in older age leads to a gradual increase in blood pressure and renders the vascular system less elastic. These vascular changes increase impedance to left ventricular (LV) outflow, causing an increase in LV work and, ultimately, LV hypertrophy. The myocardium becomes stiffer and diastolic filling is impaired. In fact, frank diastolic dysfunction is present in approximately half of patients over 65 years of age with a known diagnosis of congestive heart failure (***Groban, 2005***). These patients may be extremely dependent upon the atrial contribution to filling during diastole (the "atrial kick"). Thus, even brief episodes of atrial arrhythmias during

anesthesia may result in development of significant hypotension. Furthermore, diastolic dysfunction increases the risk of development of pulmonary edema during fluid administration. A ***(Sprung et al., 2006)***

Older adult patients also have autonomic changes, collectively referred to as the "dysautonomia of aging." Impaired beta receptor responsiveness limits the ability to increase cardiac output by increasing heart rate, so that the patient is more reliant on vascular tone and preload (***Dai et al., 2015)***

3- Respiratory system:

Normal aging of the pulmonary system decreases overall pulmonary reserve**.** Increased stiffening of the chest wall and decreased elasticity of the lung parenchyma are predictable changes, which increase the work of breathing. In addition, increased compliance of the smaller airways in older patients, as well as increased closing capacity, can lead to small airway collapse. Thus, there is a higher risk of atelectasis and consequent hypoxemia. In addition, impaired pharyngeal function predisposes some older patients to increased risk of aspiration and potential pulmonary complications (***Tran et al., 2018)***

The exaggerated respiratory depressant effects of opioids, benzodiazepines, and volatile anesthetics in older adults increase the risk of perioperative hypercapnia and hypoxemia, as well as postoperative apnea and/or respiratory

failure. This risk is exacerbated if reversal of neuromuscular blocking agents (NMBAs) is inadequate, if the patient is frail and more susceptible to fatigue, or has certain comorbidities (***Shafer, 2000)***

4- Hepatic system:

Age-related declines in hepatic mass and function, as well as decreased hepatic blood flow, result in slower metabolism of most intravenous drugs used in anesthesia ***(McLean and Le Couteur, 2004)***. In addition, diminished albumin levels may result in larger free-drug concentrations of highly protein bound drugs such as propofol ***(Akhtar, 2018)***.

5- Renal system:

Aging causes a variable decline in glomerular filtration rate, creatinine clearance, and renal functional reserve that may be underestimated by the serum blood urea nitrogen and creatinine alone ***(Giannelli et al., 2007).*** Thus, the plasma concentration of renally excreted intravenous agents may be increased**.** Comorbidities common in older adults (eg, diabetes, hypertension, and vascular disease) can cause further decline in renal function. In addition, functional changes in the kidney alter the patient's ability to maximally dilute urine; thus, the older patient has decreased ability to handle a salt or water load. Finally, the older kidney is more prone to nephrotoxic

effects of intravenous contrast or medications such as nonsteroidal antiinflammatory drugs (***Esposito et al., 2007)***

6- Volume of drug distribution:

Decreased total body water and increased adipose tissue in older adults result in changes in the volume of distribution and clearance of many anesthetics and other drugs ***(Akhtar, 2018).*** Thus, the effective concentration of anesthetic induction agents such as propofol is increased, due to a smaller initial volume of distribution. Increased body fat also results in a prolonged effect of lipid-soluble drugs due to slow release from the relatively large adipose reservoir ***(McLean and Le Couteur, 2004)***.