Comparative Study of Prophylactic Intravenous Ondansetron in the Attenuation of Post Spinal Hypotension versus Dexamethasone in Parturient undergoing Caesarean Delivery

Thesis

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List of Abbreviations

Abb.	Full term
5- HT$_3$	*5-hydroxytryptamine (serotonin)*
ASA	*American Soceity of Anesthesiologists*
BMI	*Body Mass Index*
BUN	*Blood urea nitrogen*
CNS	*Central Nervous System*
CYP	*Cytochrome P*
DEXA	*Dexamethasone*
ECG	*Electrocardiogram*
EGP	*Egyptian pound*
ENT	*Ear, Nose and Throat*
FDA	*Food and Drug Administration*
GI	*Gastro-Intestinal*
hr	*Hours*
IM	*Intra-Muscular*
IV	*Intra-Venous*
min	*Minutes*
N	*Number*
NK-1	*Neurokinin-1*
OND	*Ondansetron*
P	*Probability*
PACU	*Postanesthetic Care Unit*
PON	*Postoperative Nausea*
PONV	*Postoperative Nausea and Vomiting*
SD	*Standard Deviation*
VC	*Vomiting Center*
X^2	*Chi-square*
Yrs	*Years*

INTRODUCTION

Spinal anaesthesia (SA) is the preferred anaesthesia technique for Caesarean section. Hypotension and bradycardia are the most common side effects encountered and are more pronounced in pregnant patients, the incidence being as high as 52.6% and 2.5% in normal patients**.** The occurrence of hypotension can be dangerous as it compromises placental circulation and can have a detrimental effect on the foetus ***(Stewart et al., 2016).***

Maternal hypotension is the most common intraoperative complication after spinal anesthesia during cesarean delivery, with an incidence as high as 50-80%. Maternal hypotension may cause maternal nausea and vomiting as well as detrimental neonatal effects, such as apnea. Thus, some vasopressive drugs including ephedrine and phenylephrine have been widely used to prevent maternal hypotension. It has been demonstrated that ondansetron treatment preloading with crystalloid infusion reduces maternal hypotension in parturient women undergoing cesarean delivery ***(Ngan Kee, 2017).***

Causes of hypotension after administration of SA block in aparturient are numerous but the main causes are sympathetic blockade with a parasympathetic overdrive, aortocaval compression caused by the gravid uterus and the Bezold Jarisch reflex (BJR) Of these, the first two causes are unavoidable, however BJR, is a reflex mediated by serotonin

receptors within the wall of the ventricle in response to systemic hypotension ***(Lahsaei et al., 2012).***

It is thought that the stimulation of these peripheral 5‑hydroxytryptamine subtype 3 (5‑HT3) receptors results in increased parasympathetic activity and decreased sympathetic activity, resulting in bradycardia, vasodilatation, and hypotension ***(Wang et al., 2014).***

Ondansetron, a widely used antiemetic and serotonin antagonist, has been safely used to blunt the Bezold–Jarisch reflex, resulting in less bradycardia and hypotension in humans undergoing spinal anesthesia ***(Christofaki et al., 2014).***

Even though spinal anesthesia is a simple and safe procedure, rare complications such as unresponsive hypotension and bradycardia are real anesthetic challenges. It is preferred to prevent hypotension rather than treating it. Hence, in the recent past, most of the studies are focusing on prophylactic management of hypotension; ondansetron is such a drug gaining popularity in the prevention of hypotension in patients who underwent subarachnoid block.

Glucocorticoids are well known for their analgesic, antiinflammatory, immune-modulating, and antiemetic effects. The mechanism by which glucocorticoids alleviate nausea and vomiting is not fully understood, but the effects are probably centrally mediated via inhibition of prostaglandin synthesis or

inhibition of the release of endogenous opioids ***(Henzi et al., 2007).***

There is convincing evidence indicating that sodium retention with a resultant volume expansion is not a mechanism of dexamethasone-induced hypertension. Dexamethasone-induced hypertension is also associated with increased total peripheral resistance and heightened pressor response to vasoconstrictors but not raised sympathetic activity. The roles of endogenous vasoconstrictors and vasodilators in the pathogenesis of hypertenion assosiated with dexamethasone are variable, with possible links to nitric oxide, angiotensin II, arginine vasopressin, endothelin, catecholamines and atrial natriuretic peptide ***(Ferrario et al., 2008).***

Results from other studies suggested that corticosteroids act directly on blood vessels in potentiating norepinephrine vasoconstrictor actions, one of them showed that topical application of glucocorticoids resulted in increased sensitivity of conjunctival vessels to topical norepinephrine ***(Reis, 2007).***

The role of steroid hormones in supporting the vasoconstrictor actions of catecholamines began to appear as there are more data available on potentiation of catecholamine vasoconstrictors by corticosteroids than any other vasoconstrictor hormone.

Aim of the Work

The purpose of this study was to assess the efficacy of ondansetron versus dexamethasone in decreasing incidence of spinal induced hypotension in parturient undergoing cesarean surgery.

SPINAL ANETHESIA

The most bothersome and serious complications of spinal anesthesia:

The complications of spinal anesthesia range from the bothersome to the life-threatening. Broadly, the complications are those resulting from physiological excessive side effects, placement of the needle, and drug toxicity ***(Kleinman and Mikhail, 2013).***

1- Spinal Anesthesia induced Hypotension (SAIH):

Spinal anesthesia is one of the regional techniques commonly used in cesarean section to avoid most of the risks associated with general anesthesia. However, spinal anesthesia carries some risks also: the most common risk is hypotension due to almost complete sympathetic block as the level of block must be at T4 for adequate coverage plus the effect of gravid uterus on the venous return, Several studies were done in a trial to prevent undesired cardiovascular effects of spinal anesthesia like hypotension, which is considered one of the most risky effects ***(Glosten et al., 2000).***

Hypotension and bradycardia are common sequelae to spinal anesthesia. Estimates of the incidence of spinal anesthesia induced hypotension (SIH) are between 15% and 33% of cases. Prevalence varies because of individual patient history, comorbidities, and anesthetic technique. In addition, a

universal definition of hypotension does not exist but is commonly described in relation to systolic pressure ***(Yamano et al., 2000).***

During spinal anesthesia, neuraxial blockade reduces venous return. The reduction in preload triggers the BJR, which is mediated by the peripheral 5-HT3 type receptors. The BJR is an inhibitory cardiovascular response to noxious chemical substances and ventricular stretch sensed by the chemoreceptors and mechanoreceptors, which are primarily located in the wall of the left ventricle. The stimulation of the 5-HT3 type receptors increases parasympathetic activity and decreases sympathetic activity, resulting in the triad responses of bradycardia, vasodilation, and hypotension ***(Lupin´ski et al., 2011).***

The postulated mechanism for hypotension has been attributed to both venous and arterial Vasodilatation resulting from a local anesthetic induced sympathetic blockade that can extend 2 to 6 dermatomes cephalad from the initial sensory level of the spinal anesthetic. Because the blood in the venous system is approximately 75% of the total blood volume, venodilatation leads to venous pooling and reduction in venous return ***(Martinek, 2004).***

Activation of 5-HT3 receptors, which are G protein coupled, ligand-gated fast-ion channels, results in increased

efferent vagal nerve activity, frequently producing bradycardia ***(Somboonviboon et al., 2008).***

because most patients become tachycardic after induction of spinal anesthesia ***(Dyer et al., 2009)*** the incidence of bradycardia is believed to result from an increase in parasympathetic tone, blockade of the cardioaccelerator nerve fibers, and decreased baroreceptor activity. Recently, the Bezold Jarisch reflex (BJR) has been implicated as the most likely cause of bradycardia following spinal anesthesia ***(Campagna and Carter, 2003).***

Two major reviews with meta-analysis identified prevention and treatment options for SAIH. The goal of treatment is to restore preload, tighten peripheral vascular resistance, and improve cardiac output (CO). Multimodal treatment strategies include positioning, lower leg compression, loading and co-loading of crystalloids and colloids, and administration of pharmacologic vasopressors ***(Cyna et al., 2006).***

Current evidence-based practice uses the prophylactic administration of α- and β-adrenergic agonists, which have been shown to prevent and treat SAIH ***(Lin et al., 2012).***

2- Post-dural puncture headache (PDPH):

Post-dural puncture headache (PDPH) is the most common complication of spinal anesthesia. It occurs most frequently in young adults including obstetric patients, with an