Effect of intraoperative intravenous infusion of Dexmedetomidine - Ketorolac versus Fentanyl-Ketorolac on perioperative haemodynamics and postoperative analgesia in patients undergoing Mastectomy for breast cancer. A Comparative study.

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LIST OF ABBREVIATIONS

Abbreviation	Full name
AFOI	Awake Fiber Optic Intubation
BBB	Blood Brain Barrier
BMI	Body Mass Index
CBF	Cerebral Blood Flow
CNS	Central Nervous System
COX	Cyclooxygenase
CRPS	Complex Regional Pain Syndrome
CSF	Cerebrospinal Fluid
CYP	Cytochrome
DCIS	Ductal carcinoma in situ
DVT	Deep Vein Thrombosis
ECG	Electrocardiography
ETCO2	End-Tidal Co2
FDA	Food And Drug Administration
G_{DK}	Group Dexmedetomidine-Ketorolac
G_{FK}	Group Fentanyl-Ketorolac
HR	Heart Rate
IL	Interleukins
ICBN	Intercostobracial Nerve
ICP	Intracranial Pressure
ICU	Intensive Care Unit
IDC	Infiltrating Ductal Carcinoma

ILC	Infiltrating Lobular Carcinoma
IV	Intra Venous
LCIS	Lobular Carcinoma In Situ
LPN	Lateral Pectoral Nerve
LTN	Long Thoracic Nerve
MAC	Minimum Alveolar Concentration
MCN:	Medial Cutaneous Nerve Of The Arm
MODS	Multiple Organ Dysfunction Syndromes
MPN	Medial Pectoral Nerve
NIBP	Non-Invasive Blood Pressure
NRM	Nucleus Raphe Magnus
NSAID	Non Steroidal Anti Inflammatory Drugs
OAA/S	Observers's Assessment Of Alertness And Sedation
PACU	Post Anesthetic Care Unit
PE	Pulmonary Embolism
PGE2	Prostaglandins E2
PONV	Postoperative Nausea And Vomiting
RAS	Reticular Activating System
SpO2	Pulse Oximetry
SSR	Surgical Stress Response
TDN	Thoracodorsal Nerve
TNF-α	Tumor Necrosis Factor Alpha
VAS	Visual Analogue Scale
Vd	Volume Of Distribution
α2-ARs	Alpha2-Adrenergic Receptors

Abstract

This study Mean arterial blood pressure and heart rate significantly decreased in both groups after infusion of drugs, G_{DK} was statistically lower in MAP compared to the G_{FK} after intubation, extubation and at recovery time .No statistical significant difference in HR between groups throughout the procedure and the study has been conducted on 60 patients. The patients included in the study were divided into 2 equal groups (30 each); G_{DK}: The patients received Dexmedetomidine 1mcg/Kg over 10 minutes followed by continuous infusion at a rate of 0.5 mcg/kg/hr. and G_{FK}: The patients received Fentanyl 1mcg/kg followed by continuous infusion of 0.5 mcg/kg/hr. Anesthesia was induced by propofol 2 mg/kg iv and atracuronium at a dose of 0.5 mg /kg .Both groups received 30 mg IV Ketorolac 5 minutes after intubation. All patients have received the test drugs prior to intubation and infusion stopped before extubation.

Keyword:--

Dexmedetomidine
haemodynamics
Fentanyl-Ketorolac
Breast cancer

INTRODUCTION

The management of perioperative hemodynamics and pain is important to prevent potentially dangerous complications such as hypertension, tachycardia, arrhythmias and increased intracranial pressure.[1]

Such hemodynamic responses may be attenuated by several methods, including administration of intravenous (I.V) opioids, vasodilators, local anesthetics, β blockers or by deepening anesthesia. α2 adrenergic agonists decrease sympathetic tone and preoperative use of clonidine has been shown to blunt the hemodynamic responses to noxious stimulation and to prevent the overall hemodynamic variability.[2,3]

Dexmedetomidine is a highly selective α2-receptor agonist that was approved in 1999 by FDA as a sedative agent for adult patients in the Intensive Care Unit. [4,5] Previous clinical trials demonstrate how the use of Dexmedetomidine reduces the requirements of intravenous and inhalational agents, it provides haemodynamic stability and reduces the requirements of postoperative opioid analgesia.[6-10]

Dexmedetomidine has not been associated with respiratory depression despite of the profound levels of sedation. It decreases sympathetic outflow from the central nervous system.[11]

However, in certain types of pain in which opioid relief is suboptimal, such as in neuropathic pain, α2-agonists may offer specific advantages.[12]

As a result of these properties, Dexmedetomidine might be proven useful in the postoperative period for patients undergoing major surgical procedures which involve significant pain. The perioperative infusion of Dexmedetomidine has a

pivotal role in attenuating the incidence and severity of chronic pain also improving the quality of life in cases undergoing breast cancer surgery.[13]

Effective postoperative analgesia can diminish stress reactions following surgery. Recovery and physical mobilization are improved as a result of adequate treatment. The concept of balanced analgesia refers to the strategy of improvement of analgesic efficacy which is based on the result of drugs` combination with different local actions on nociception. The combination of systemic analgesics (Opioids in low dosages) with nonsteroidal analgesics (e.g. Diclofenac or Ketorolac) have been shown to be very effective.[14]

Fentanyl is 100 times more potent than morphine. While comparing it to intravenous morphine, the onset of analgesia with Fentanyl is immediate, thus makes it very effective in patients with severe acute pain and the duration of analgesia after a single bolus dose is 30-60 minutes.[15]

AIM OF THE WORK

The present study aims to compare the efficacy of intraoperative intravenous infusion of Dexmedetomidine-Ketorolac versus Fentanyl- Ketorolac on perioperative haemodynamics and postoperative analgesia in patients with breast cancer undergoing mastectomy.

Breast Cancer

Introduction

The breast is composed of two main types of tissues i.e., glandular tissues and stromal (supporting) tissues. Glandular tissues house the milk-producing glands (lobules) and the ducts (the milk passages) while stromal tissues include fatty and fibrous connective tissues of the breast. The breast is also made up of lymphatic tissue-immune system tissue that removes cellular fluids and waste.[16]

There are several types of tumors that may develop within different areas of the breast. Most tumors are the result of benign (non-cancerous) changes within the breast. For example, fibrocystic change is a non-cancerous condition in which women develop cysts (accumulated packets of fluid), fibrosis (formation of scar-like connective tissue), lumpiness, and areas of thickening, tenderness, or breast pain.[17]

Most breast cancers begin in the cells that line the ducts (ductal cancers). Some begin in the cells that line the lobules (lobular cancers), while a small number start in the other tissues. [18]

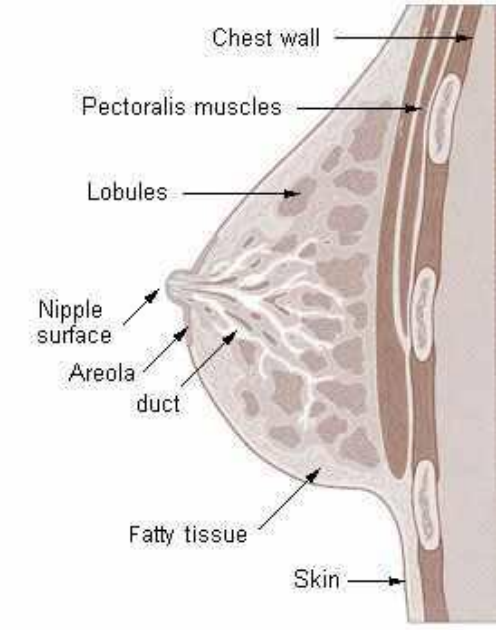

Figure 1 : "Anatomy of the Breast" [19]

Types OF Breast Cancer

According to Site:

Non-Invasive Breast Cancer

Cells that are confined to the ducts and do not invade surrounding fatty and connective tissues of the breast. Ductal carcinoma in situ (DCIS) is the most common form of non-invasive breast cancer (90%). Lobular carcinoma in situ (LCIS) is less common and considered a marker for increased breast cancer risk.

Invasive Breast Cancer

Cells that break through the duct and lobular wall and invade the surrounding fatty and connective tissues of the breast. Cancer can be invasive without being metastatic (spreading) to the lymph nodes or other organs. [20]

Frequently Occurring Breast Cancer:

Lobular Carcinoma In Situ (LCIS):

The term, "in situ," refers to cancer that has not spread past the area where it initially developed. LCIS is a sharp increase in the number of cells within the milk glands (lobules) of the breast.

Ductal Carcinoma In Situ (DCIS):

DCIS the most common type of non-invasive breast cancer, is confined to the ducts of the breast. For example, ductal comedocarcinoma.

Infiltrating Lobular Carcinoma (ILC)

ILC is also known as invasive lobular carcinoma. ILC begins in the milk glands (lobules) of the breast, but often spreads (metastatizes) to other regions of the body. ILC accounts for 10% to 15% of breast cancers.

Infiltrating Ductal Carcinoma (IDC):

IDC is also known as invasive ductal carcinoma. IDC begins in the milk ducts of the breast and penetrates the wall of the duct, invading the fatty tissue of the breast and possibly other regions of the body. IDC is the most common type of breast cancer, accounting for 80% of breast cancer diagnoses. [21,22]

Inflammatory Breast Cancer

Inflammatory breast cancer is the appearance of inflamed breasts (red and warm) with dimples and/or thick ridges caused by cancer cells blocking lymph vessels or channels in the skin over the breast. Though inflammatory breast cancer is rare (accounting for only 1% of breast cancers), it is extremely fast-growing.

Paget's Disease of the Nipple

A rare form of breast cancer that begins in the milk ducts and spreads to the skin of the nipple and areola, Paget's disease of the nipple only accounts for about 1% of breast cancers.

Phylloides Tumor

Phylloides tumors (also spelled "phyllodes") can be either benign (non-cancerous) or malignant (cancerous). Phylloides tumors develop in the connective tissues of the breast and may be treated by surgical removal. [23]

Less Commonly Occurring Breast Cancer [24]

Medullary Carcinoma: Medullary carcinoma is an invasive breast cancer that forms a distinct boundary between tumor tissue and normal tissue. Only 5% of breast cancers are medullary carcinoma.

Mutinous Carcinoma: Also called colloid carcinoma, mutinous carcinoma is a rare breast cancer formed by the mucus-producing cancer cells. Women with mutinous carcinoma generally have a better prognosis than women with more common types of invasive carcinoma.

Tubular Carcinoma: Tubular carcinomas are a special type of infiltrating (invasive) breast carcinoma. Women with tubular carcinoma generally have a

better prognosis than women with more common types of invasive carcinoma. Tubular carcinomas account for around 2% of breast cancer diagnoses.

Types of Breast Cancer Surgeries

Radical Mastectomy

This operation was developed by Halsted in the late 19th century .It involves removing the breast, skin and fat, pectoralis major and minor muscles of the chest, and all the lymph nodes under the ipsilateral arm. It is the most disfiguring breast cancer surgery, and exploration of other options began in the 1970s when it was realized that most breast cancer recurrences are not in the chest muscles. [25]

Modified Radical Mastectomy

Clinical trials conducted in the 1970s compared radical mastectomy with less extensive procedures. One was the modified radical mastectomy, in which the pectoralis muscles are not removed but all other aspects of radical mastectomy are retained. [26] Although removal of pectoralis minor was included with the initial modifications, it is now rarely performed.

Total (or Simple) Mastectomy

Removal of the entire breast, including the nipple, the areola, and most of the overlying skin.

Breast Conserving Surgery (Lumpectomy)

Breast-conserving surgical treatments have evolved rapidly and currently account for as much as 40% of breast cancer surgery.[25] Although commonly referred to as lumpectomy, these procedures have also been termed breast preservation, conservative breast surgery, wide local excision, partial mastectomy, segmentectomy, or tylectomy. [26] Lumpectomy involves removal of the primary tumor and a margin of normal tissue, and it is important to distinguish lumpectomy from lumpectomy with axillary node dissection and lumpectomy with sentinel node biopsy.

Patients who undergo only lumpectomy generally have earlier breast cancer (in situ disease) than those who require an axillary procedure.

Lumpectomy with Axillary Node Dissection

Outcomes of lumpectomy with axillary node dissection were first studied in the 1970s. The primary tumor and a margin of normal tissue are removed, and axillary node dissection is performed through a separate incision in the armpit. Post-operative radiation therapy is administered to the remaining breast and the tumor bed. When disease is found in the axillary nodes, post-operative chemotherapy administered. [25,26]

Lumpectomy with Sentinel Lymph Node Biopsy

This is the most recent and least invasive option. A sentinel lymph node (i.e. the first axillary lymph node to receive drainage from the breast tumor) is identified by injecting a dye or radiolabelled colloid into the area of the tumor before surgery and then the labeled node is identified and removed for pathologic examination. If no tumor is found within this node, the patient does not undergo axillary dissection. With sentinel node biopsy, only those patients with disease in the sentinel lymph node undergo axillary dissection, sparing many patients from axillary dissection and its complications. Post-operative breast radiation therapy is administered to patients.