

Efficacy of Granisetron for Prevention of the Postoperative Nausea and Vomiting after Laparoscopic Surgery in Adults

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(... رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ
وَأَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ وَأَدْخِلْنِي
بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ)

صدق الله العظيم

النمل.. آية رقم ١٩



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List of Abbreviations

<i>Abbr.</i>	<i>Full term</i>
5-HT	: 5-hydroxy tryptamine
ANOVA	: Analysis of variance
ASA	: American Society of Anesthesiologists
BMJ	: British Medicine Journal
CINV	: Chemotherapy induced nausea & vomiting
CNS	: Central nervous system
CO₂	: Carbon dioxide
CSF	: Cerebro-spinal fluid
CTZ	: Chemoreceptor trigger zone
CYP	: Cytochrome P
D	: Dopamine
ECG	: Electrocardiography
FDA	: Food and Drug Administration
GIT	: Gastro-intestinal tract
H	: Histamine
h	: Hour
IV	: Intravenous
N₂O	: Nitrous oxide
NK₁	: Neurokinin ₁
NVP	: Nausea & vomiting of pregnancy
PACU	: Postanesthesia care unit
PDNV	: Post discharge nausea and vomiting

List of Abbreviations *(Cont...)*

PETCO₂	: Partial end-tidal CO ₂
PINV	: Radiation induced nausea & vomiting
PONV	: Postoperative nausea and vomiting
RINV	: Radiation induced nausea and vomiting
SD	: Standard deviation
SP	: Substance P
SSRIs	: Selective serotonin receptor inhibitors
STN	: Solitary tract nucleus
T¹/₂	: Half life
VAS	: Visual analogue scale
VC	: Vomiting center

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Introduction

Postoperative nausea and vomiting (PONV) after laparoscopic surgeries remains a significant problem. The incidence of this distressing adverse effect can be reached up to 79% (*Apfel et al., 2009*).

Nausea is defined as the subjectively unpleasant sensation associated with awareness of the urge to vomit. Retching is defined as the laboured, spastic, rhythmic contraction of the respiratory muscles without the expulsion of gastric contents. Vomiting is defined as the forceful expulsion of gastric contents from the mouth (*Fujii and Tanaka, 2006*).

Most commonly used antiemetics occasionally cause undesirable effects, such as excessive sedation, hypotension, dry mouth, dysphoria, extrapyramidal syndrome and prolonged QT syndrome with droperidol (*McCormick, 2002*).

Granisetron, a selective serotonin type 3 receptor antagonist is effective for the treatment and prevention of PONV, radiation induced nausea and vomiting (RINV) and it is the most effective antiemetic drug in chemotherapy induced nausea and vomiting (CINV) (*Roila and Fatigoni, 2006*).

Aim of the Work

This study was performed to evaluate the efficacy and potency of granisetron in the prevention of PONV after laparoscopic surgery in adults.

I. Pathophysiological Pathway of Nausea and Vomiting

The Centers and Afferent Pathway:

Vomiting centers involve two functionally distinct medullary centers: the vomiting center and the chemoreceptor trigger zone. The act of vomiting is integrated by the vomiting center, which is located in the dorsal portion of the reticular formation of the medulla near the sensory nuclei of the vagus (the subnucleus gelatinosus and nucleus tractus solitarius). The chemoreceptor trigger zone is located in a small area on the floor of the fourth ventricle called area of postrema, where it is exposed to both blood and cerebrospinal fluid. It is thought to mediate the emetic effects of blood-borne drugs and toxins (*Carol, 2007*).

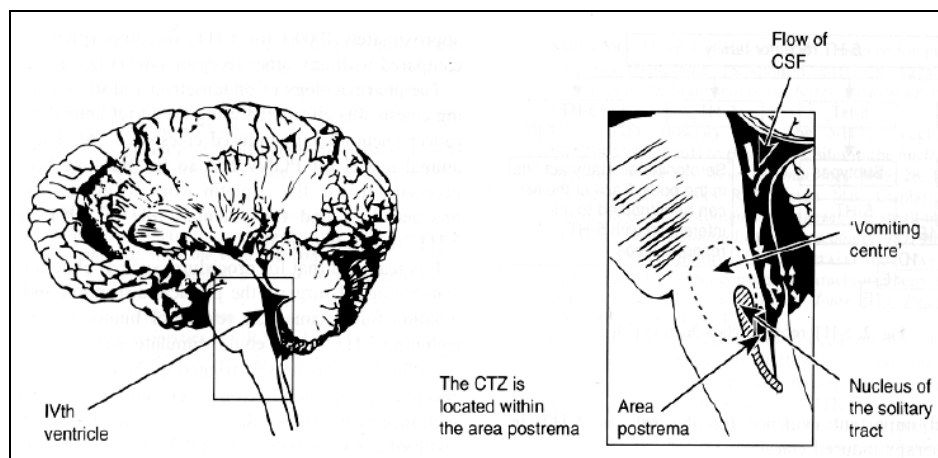


Figure (1): The anatomical location of the area postrema and the region of the vomiting center (*Janicki, 2005*).

There are different ways in which the vomiting centers are stimulated:

- (1) Irritation of upper GI mucosa is a common cause of vomiting by luminal stimuli (e.g. hypertonic solutions, copper sulphate) but the in-series tension receptors in the muscle could also be implicated if luminal stimuli evoked reflex motility changes via the enteric nervous system (**Grundy, 2006**).
- (2) Vomiting can also be initiated through the gag reflex by physical stimulation of the back of the throat. These afferent impulses reach the vomiting center through the IX and X cranial nerves (**Sabyasachi, 2008**).
- (3) Blood_borne emetics which include emetic drugs & toxins. Emetic drugs like apomorphine and ipecac can trigger vomiting. These stimulate the chemoreceptor trigger zone. Impulses from the chemoreceptor trigger zone are relayed to the vomiting center. The neurons in the chemoreceptor trigger zone appear to be dopaminergic and serotonergic. Dopamine and serotonin antagonists are therefore effective antimetic drugs. The vomiting that occurs in uremia and in radiation sickness is also mediated through the chemoreceptor trigger zone and occurs due to the endogenous production of emetic substance.
- (4) Motion sickness is associated with vomiting. The stimulus causing such vomiting originates in the vestibular apparatus. The afferent impulses relay in the vestibular nuclei in the cerebellum and then in the chemoreceptor trigger zone before finally reaching the vomiting center.