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**Research Article**

# ROLE OF DEXAMETHASONE,GRANISETRON AND HALOPERIDOL IN PATIENTS WHO HAVE UNDERGONE LAPAROSCOPIC SURGERIES

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**ABSTRACT**

Laparoscopic surgeries are associated with increased incidences of postoperative nausea and vomiting. There are variety of drugs which have been used for postoperative nausea and vomiting prevention which includes butyrophenones such as droperidol, 5HT3 antagonist ondansetron, dolasetron and corticosteroids decrease the incidence of PONV, none of these drugs either alone or in combination reduce incidence of PONV to 0%. These drugs have been tried together as combinations in their groups and also individually.

**Results:** Many studies established the antiemetic property of dexamethasone. There are very few studies which have compared granisetron and haloperidol for their efficacy as antiemetics. Also most of those studies have evaluated the drugs in combination. Hence the efficacy of each drug as agent for control of nausea and vomiting is not clear.



## INTRODUCTION

Incidence of post operative nausea and vomiting (PONV) is 20-30%. Nausea and vomiting is the second commonest complication for the surgeries done under general anesthesia[1] . Vomiting occurring after the surgery is usually self-limiting, if persistent results in morbidity and increases the duration of hospital stay. Vomiting and nausea are slightly higher in the population undergoing laparoscopic surgeries. It is higher especially in laparoscopic cholecystectomies[2] .There are increased incidences of PONV after laparoscopic surgeries which is due to creation of pneumoperitoneum which causes distension in the abdominal cavity leading to raised intraabdominal pressure resulting in altered physiology. [3] The risk factors for PONV are the type of anesthesia used , duration of surgery, female gender, age, obesity, use of volatile anesthetics, use of opioids and adverse drug reactions(ADR)[4] .Increased wound tension, high venous pressure, water electrolyte disorders, acid base imbalance, aspiration, asphyxia are the complications resulting from PONV and hence prevention and treatment are mandatory[5] . Nausea and vomiting can be very unpleasant to the patients more than pain. Treatment of vomiting and nausea improves patient's satisfaction and well being. It has been proved that incidence of PONV in regional anesthesia are less common as compared to general anesthesia.

There are different antiemetic drugs in practice for prevention and treatment of nausea and vomiting. These drugs act on different receptors like cholinergic, dopaminergic, serotonergic, antihistaminics and corticosteroids[6]. Corticosteroids like dexamethasone are well known for their analgesic, antiinflammatory, immunemodulatory and antiemetic effects and are often used for prevention of PONV.[7] It has been proved to be more effective than metoclopramide, droperidol, granisetron in prevention of PONV associated with chemotherapy[8].

Dexamethasone either alone or in combination with other antiemetics is effective in decreasing the incidence of PONV[9] . Haloperidol belongs to the class of butyrophenones and has a similar structure to droperidol. It blocks the effect of dopamine and is given prophylactically for PONV. It is the drug with minimal toxicity and is effective for prevention of PONV when given during gastroenterological procedures in the dose of 2mg intravenously (IV)[10] . It's a major tranquiliser and acts as a D2 receptor antagonist. It has been proven to be effective for prophylaxis of PONV.[11] Both these drugs i.e. haloperidol and droperidol have been compared for prevention of PONV in

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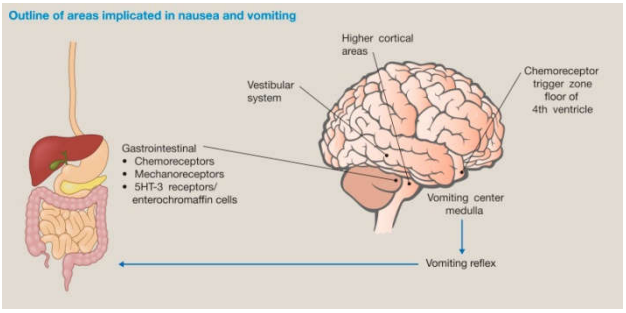
laparoscopic surgery and were equally effective in preventing PONV. Granisetron belongs to the class of serotonin 3 receptor antagonist. Drugs belonging to this class include granisetron, ondansetron, ramosetron and palonosetron. They produce block of 5HT3 receptors and is irreversible, which accounts for their longer duration of action. In patients with higher risk of PONV, granisetron with other antiemetics reduces the incidence of PONV[12]. Evaluation of ondansetron and granisteron is being done in preventing PONV in laparoscopic surgery and it is proved that granisetron is more effective than ondansetron in reducing the incidences of nausea and vomiting[13] . Although a variety of drugs, including droperidol, ondansetron, dolasetron decrease the incidence of PONV, none of these drugs either alone or in combination reduce incidence of PONV to 0%. These drugs have been tried together as combinations in their groups and also individually. There are very few studies which have compared granisetron and haloperidol for their efficacy as antiemetics. Hence the efficacy of each drug as agent for control of nausea and vomiting is not clear. To our knowledge the three drugs, dexamethasone,granisetron and haloperidol have not been compared against each other for laparoscopic surgeries. Hence we conducted the study to review the efficacy of these agents in prevention of PONV in laparoscopic surgeries.

## METHODS

An extensive search for articles on pubmed, google scholar database using the keywords laparoscopic surgeries, incidence of PONV, butyrophenones, 5 HT3 antagonist, granisetron, steroids, haloperidol, antiemetics published between May1992 to Dec2018. Articles written in English and available as free full text were selected for review. Related articles were extracted. Also credible reports and statistical figures from WHO were investigated.

### *Physiology of Nausea and Vomiting*

The physiology of ponv is unclear. Borison and wang have described two mechanisms of nausea and vomiting. Peripheral mechanism is through stimulation of vagus nerve in gastrointestinal tract.(GIT). Central mechanism is through stimulation of multiple emetogenic receptors such as Chemoreceptor trigger zone (CTZ), Nucleus tractus solitarius (NTS). Stimulation of the emetic centre in the medulla oblongata causes vomiting. Multiple pathways are involved in the cessation of vomiting. The CTZ which is located at the caudal end of the fourth ventricle in the area postrema and NTS is located in the area postrema in the lower pons. CTZ can detect emetogenic toxins, metabolites, drug in the blood. CTZ receives input from vagal afferents in GIT and throat. It projects neurons to NTS, which receives input from vagal afferents and also from limbic and vestibular systems. NTS induces vomiting by stimulating rostral nucleus, nucleus ambiguous and ventral respiratory group. PONV can be triggered by volatile anesthetic agents, opioids, anxiety, and adverse drug reactions through the neurotransmitters involved in physiology of nausea and vomiting. The communication between CTZ and NTS is via dopamine (D2) receptors. Anxiety induced nausea and vomiting originate in cerebral cortex. Antiemetic drugs have been developed that are effective against 5HT3, D2, H and ACH receptors.




### *Physiology of Vomiting*

### *Mechanism of Postoperative nausea and vomiting in laparoscopic surgeries*

The mechanism of it has not been understood clearly . But it is agreed that few factors like, longer periods of co2 insufflation contribute to PONV in laparoscopic surgery. CO2 is insufflated into the peritoneal cavity at a rate of 4-6 l/min and a pressure of 10-20 mmHg is to be maintained throughout the surgery. Constant gas flow at a rate of 200-300ml/minute is kept to maintain the pneumoperitoneum . The raised intraabdominal pressure and CO2 absorption leads to alteration in the physiology of different systems.

### *Physiology of Pneumoperitoneum*

Insufflation of carbon dioxide during laparoscopic surgery leads to increase in intraabdominal pressure (IAP) and subsequent absorption of carbon dioxide. This can result into various changes in different systems.

Effects on cardiovascular system Creating a pneumoperitoneum causes increased intraabdominal pressure which reduces myocardial function, venous return and increases systemic vascular resistance (SVR). Pooled blood from splanchnic circulation results in increased venous return and increased cardiac output. Further increase in increased IAP results in compression of inferior vena cava and reduction in venous return which causes decreased cardiac output. SVR is increased because of increased IAP and also because of increased release of circulating epinephrine and norepinephrine.

Effect on respiratory system Pneumoperitoneum causes cephalad shift of the diaphragm which reduces functional residual capacity (FRC) and causes airway collapse, ventilation/perfusion mismatch, atelectasis.

Effects on renal system Increased IAP reduces urine output and renal function due to increase in renal vascular resistance and decreased glomerular filtration rate secondary to decreased cardiac output.

Effects on gastrointestinal system Regurgitation of the gastric contents occurs as a result of increased intrabadominal pressure and hence laparoscopic surgeries are associated with the risk of pulmonary aspiration.

Effects on nervous system Due to increased intra-abdominal pressure there is also an increase in intracranial pressure which can reduce cerebral perfusion pressure.

### *Established Risk Factors for PONV*

i. Females three times more prone than males

ii. Prior history of motion sickness or PONV Non-smokers
iii. Pediatric patient: 3–16 years
iv. Concomitant medical problems such as diabetes mellitus, intestinal obstruction etc.)
v. State of hydration like hypovolemia and hypotension
vi. Inhalation anesthetic agents Nitrous oxide Opioid analgesics
vii. Laparoscopic procedures Mastoid ,inner ear and breast surgeries Intra-abdominal surgeries, procedures on testicles/scrotum
viii. Strabismus repair Tonsillectomy Oral, plastic and nasal procedures (swallowing of blood) Patient movement (vestibular changes)
ix. Patients with H/O orthostatic hypotension
x. H/O of migraine
xi. Preop anxiety.

Female gender is three times more likely to suffer from PONV than males. Non – smoking status doubles the risk of PONV. Its mechanism of action is not clear. Patients with history of motion sickness are susceptible for PONV due to stimulation of CN VIII and acoustic vestibular nerve. Metabolic causes of nausea and vomiting are diabetes mellitus, Uremia, Electrolyte disturbances, Hormonal variations like estrogen, progesterone changes occurring during pregnancy. Use of volatile anesthetic agents increases the risk of vomiting. It is the single most important factor for predicting emesis in first 2 postoperative hrs. PONV decreases the serum levels of anandamide (Cannabinoid neurotransmitter that acts on cannabinoid 1 and transient receptor potential vanilinoid 1 receptor to supress nausea and vomiting). Similarly use of inhalational gases such as N2O , opioids also increases the risk of PONV. Duration of anesthesia depicts exposure to emetogenic stimuli and thus more the duration, more is the incidence of PONV.

***Risk Score – Different Types of Risk Scores are Used for Evaluation of Ponv***

Apfel Simplified score is based on four factors. First, female gender ,second h/o of postoperative nausea and vomiting, third non smoking status , and fourth as postop use of opioids. The risk is 0% when no factor is present. It is 10% with presence of one factor,20% with two factors,30 % with three factors and 40% with four factors. Different groups of drugs have been studied for their role in prevention and treatment of postoperative emesis.

***Drugs Currently in Practice for Prevention and Treatment***

**First line drugs**: Different drugs which have been tried for postoperative nausea and vomiting such as antihistaminics, anticholinergics, dopamine receptor antagonist, 5HT3 receptor antagonist. These drugs have similar efficacy against postoperative nausea and vomiting. Granisetron , dolasetron have side effects as headache, constipation and dizziness when compared with ondansetron. Granisetron also associated with Qtc prolongation. Dexamethasone at low doses is effective against postoperative nausea and vomiting and postsurgical pain.

**Second line drugs**: Metoclopramide is a D2 receptor antagonist. Lesser dose of 10 mg does not have any effect on postoperative nausea and vomiting. Dose of 25-50mg has similar efficacy compared to other antiemetics. Haloperidol and droperidol are butyrophenones also act on D2 receptor and have proven for antiemetic action.

***5ht3 Receptor Antagonist***

These drugs are beneficial for chemotherapy or radiotherapy induced nausea and vomiting. Drugs belonging in this class are ondansetron, dolasetron, ramosetron ,granisetron,tropisetron. The agents which have been tried in prevention of nausea and vomiting. Ondansetron was the first 5HT3 antagonist which was approved for treatment of vomiting by IV and oral route in adults and children.8mg dose was effective when given orally 2 hours prior to induction of anesthesia. Most potent of all 5HT3 anatagonist is tropisetron has been found useful in controlling vomiting in patient undergoing breast and gynecological surgeries with a dose of 5 mg IV.

***Few Other Drugs that Have Been Tried for Prevention of Nausea and Vomiting***

Ephedrine -Intramuscular ephedrine in the dose of 0.5mg/kg have antiemetic effectiveness similar to droperidol in the dose of 0.04mg/kg in minor gynecological procedures .Ephedrine has similar efficacy as propofol in dose of 0.25mg/kg iv for the treatment of vomiting in laparoscopic surgeries. Intramuscular ephedrine is effective drug for control of vomiting especially when it is related to hypovolemia and hypotension.

***Propofol***

The mechanism of antiemetic action of propofol is not known. Propofol used intraoperatively is equally effective as 4mg of ondansetron IV in treating nausea vomiting during first six hours. Subhypnotic dose of propofol that is 0.5mg/kg is found to be effective in control of PONV in middle ear surgery. A subhypnotic dose of propfol is most effective in controlling vomiting after sevoflurane anesthesia than desflurane anesthesia in laparoscopic cholecystectomy cases. Vomiting was less with a 16 postoperative infusion with propofol in dose of 0.1mg/kg/hr IV as compared to 10% intralipid placebo.

***Neurokinin 1 Antagonist***

These compounds inhibit the effect of Substance P in brainstem. These drugs are found to be useful in delayed vomiting related to chemotherapy,in women undergoing major gynecological procedure and abdominal surgeries.

***Benzodiapines***

Benzodiazepines Have sedative,amnestic and anxiolytic properties. Drugs belonging to this class diazepam ,midazolam. These drugs decrease the anxiety related to anesthesia and surgery and result into reduction in PONV. Midazolam in a dose of 75 mcg/kg have shown to reduce incidence of nausea and vomiting in children who underwent tonsillectomy . Lorazepam in a dose of 10mcg/kg has shown antiemetic action when given prophylactically in strabismus surgery. Lorazepam has less chances of postoperative agitation when compared to droperidol in children. Benzodiazepines decrease anxiety by reducing catecholamine production.

***Anticholinergics***

These are the oldest first generation class of antiemetics. These drugs inhibit muscarinic and cholinergic emetic receptors in the cerebral cortex and pons. M3 and M5 receptors have selective antagonistic activity against motion sickness. Scopolamine and

atropine both are effective against motion induced vomiting. Scopolamine has better antiemetic properties compared to atropine. Anticholinergics are used for treatment of vomiting and nausea associated with opioids. These drugs can have side effects like sedation, blurred vision,dry mouth, dysphoria, confusion and restlessness.

***Mechanism of Action of Drugs***

***Dexamethasone***

The mechanism for its antiemetic action is unknown. Proposed mechanisms are tryptophan depletion, decreased in serotonin level, anti-inflammatory and membrane stabilising. Chronic treatment with larger doses can result in postoperative infection and delayed wound healing. Adverse reactions of iv doses are cutaneous flushing, perineal itching. Plasma half life of dexamethasone is 4-4.5 hrs. Effective dose for postoperative nausea and vomiting is 8-10mg . Dexamethasone administered before induction was effective in preventing postoperative nausea and vomiting upto 2hrs in PACU and also 2-24hrs.

***Granisetron***

It is a 5HT3 receptor antagonist. It is a commonly used drug for the control and treatment of PONV. 5HT3 receptor antagonist have a similar chemical structure as that of serotonin. It has 6 ring carbon and 5 ring nitrogen based nucleus . 5HT3 antagonist are considered to be the major advances for the treatment of nausea and vomiting. Most common side effects are headache and dizziness. Peak plasma concentration by oral route occurs in 60-30 min, by IV route in 30 min. Elimination half life is 6.3hrs. It is metabolised by CYP3A P450 and is excreted 49% and 36% in urine and feces repectively. Intravenous dose is more effective in prevention and treatment of PONV than oral route. The optimal dose of granisetron for prevention of PONV is suggested as 1mg IV.

***Haloperidol***

It is a butyrophenone. It blocks D2 receptors at the area postrema. It is also an alpha receptor blocker. Side effects include sedation, anxiety, restlessness, hypotension and extrapyramidal syndrome. It has a longer plasma half life than droperidol. Onset of action at D2 receptors is more rapid than droperidol.

**Wang and huang *et al*,** evaluated the prophylactic effect of low dose haloperidol 1mg in postoperative nausea and vomiting in ambulatory laparoscopic surgery and found that it was equally effective in reducing the incidences of postoperative nausea and vomiting in ambulatory laparoscopic surgery similar to droperidol in the dose of 0.625mg[24.]

**Huang *et al***, evaluated the prophylactic effect of low dose dexamethasone in preventing postoperative vomiting in patients undergoing ambulatory laparoscopic surgery. 5mg dexamethasone was compared with 10mg metoclopramide and normal saline. It was concluded that preeoperative low dose 5 mg dexamethasone was useful in preventing postoperative complications in patients undergoing ambulatory laparoscopic surgery[16.]

**Sunil *et al***, compared the prophylactic antiemetic efficacy of haloperidol, granisetron, for the prevention of postoperative nausea and vomiting followed by laparoscopic surgeries. 2mg haloperidol and 1mg granisetron was used and it was observed that both drugs had similar effects and were equally effective in PONV prevention[45.]

## CONCLUSION

Postoperative nausea and vomiting is multifactorial in origin and requires combination drug therapy for its prevention and treatment, especially patients undergoing laparoscopic surgeries and high risk patients. Prevention and management of PONV requires multimodal approach and further meta-analysis are required to establish the efficacy of newer antiemetics in the market.

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## References

1. Millers, Christian C Apfel. Postoperative nausea and vomiting. Textbook Millers Anesthesia Volume 2, 8th edition. Page 2947-2973.
2. Naguib, M., Bakry, A.K.E., Khoshim, M.H.B. Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron and metoclopramlde in patients undergoing, laparoscopic cholecystectomy: a randomized, double-blind comparison with placebo. Can J Anesth 1996; 43: 226
3. Sabir N, Ramachandra V Decontamination of anesthestic equipment. Continuing education in anesthesia and critical care and pain. 2004; 4:103-106.
4. Pierre S, Whelan R .Nausea and vomiting after surgery. Continuing education in anesthesia and critical care and pain. August 2012;13:28-32.
5. Tsang Y, Poon C, Lee K, Leong H . Predictive Factors of Long Hospital Stay After Laparoscopic Cholecystectomy. *Asian journal of surgery*. 2007;30:23-28.
6. Apfel C, Kortilla K, Abdalla K, Kerger H, Turan A ,Vedder I *et al* A factorial trial of six intervention for prevention of postoperative nausea and vomiting. N Engl J Med. June 2004;350(24):2441-2451.
7. Henzi I ,Walder B, Tramber M .Dexamethasone for the Prevention of Postoperative Nausea and Vomiting: A Quantitative Systematic Review. Anesth Analg 2000;90:186–94
8. Sekine I, Nishiwaki Y ,Kakinuma R, Kubota K , Hojo F ,Matsumoto T *et al* Phase II study of high-dose dexamethasone-based association in acute and delayed high-dose cisplatin-induced emesis. *British Journal of Anesthesia*. 1997;76(1):90-2.
9. Oliveira GS, Alves LJS, Ahmad S, Kendall MC, Mccarthy RJ Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Review Anesthesia and Analgesia . Dexamethasone to prevent postoperative nausea and vomiting: an updated meta-analysis of randomized controlled trials 2013; 116(1): 58-74
10. Buttner M, Walder B, Elm E,Tramer M Is low dose haloperidol a useful emetic? Anesthesiology. January 2005; 101(6):1454-63.
11. Aouad , M.T, Siddik S, S.M.,Taha, S.K *et al* Haloperidol vs. ondansetron for the prevention of

postoperative nausea and vomiting following gynecological surgery. European *journal of anesthesiology*. February 2007;24:171-178.
12. Newberry NR, Watkins CJ, Sprosen TS ,BRL 46460 potently antagonizes neural responses activated by 5HT3 receptors.Neuropharmacolgy 1993;32:729- 735.
13. Gauchan S ,Thapa C ,Shakya P, Bhattarai R , Shakya S Ondansetron and Granisetron for prevention of postoperative nausea and vomiting following laparoscopic cholecystectomy. JNMA J Nepal Med Assoc 2014; 52(193):682-6.
14. Watcha MF *et al* Anesthesiology1992;72:162.
15. Wang J , Ho S.T., Liu Y.H ,Lee S.C , Liu Y.C ,Liao YC *et al* Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. British journal of anesthesia. November 1999 ;83:772-7.
16. Huang J, Sheih J ,Tang C ,Tzeng J ,Chu K, Wang J *et al* Low-dose dexamethasone effectively prevents postoperative nausea and vomiting after ambulatory laparoscopic surgery. CAN J ANESTH 2001;48:973-977.
17. Fuji Y , Tanaka H , Kawasaki T A randomized, double-blind comparison of granisetron alone and combined with dexamethasone for post–laparoscopic cholecystectomy emetic symptom. Curr Ther Res Clin Exp September 2003;64 (8): 514–521
18. Biswas B , Rudra N Comparison of granisetron and granisetron plus dexamethasone for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Acta anesthesiologica scandinavika January 2003 ; 47:79-83.
19. Fujii Y, Tanaka H, Kawasaki T Effects of granisetron in the treatment of nausea and vomiting after laparoscopic cholecystectomy: a dose-ranging study. Clinical therapeutics. 2004, 26(7), 1055-1060 .
20. Laiq N , Khan MN , Qureshi FA , Khan S , Jan AS Dexamethasone as antiemetic during gynecological laparoscopic surgery. *Journal of the college of physicians and surgeons*. December 2005; 15(12):778-781.
21. Khan M , Kohli M , Kumar G.A , Singh V Granisetron and granisetron dexamethasone combination for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: A double blind, placebo controlled study. *Journal of anesthesiology and pharmacology*. July 2006; 22(3):261-265 ·
22. Bridges D, Nettle B, Duggirala J, Suda J, Garey W Low dose granisetron for prevention of postoperative nausea and vomiting.Journal of applied research. 2006;6.
23. Moussa AA, Oregan PJ Prevention of postoperative nausea and vomiting in patients undergoing laparoscopic bariatric surgery--granisetron alone vs granisetron combined with dexamethasone/droperidol. Prevention of postoperative nausea and vomiting in patients undergoing laparoscopic bariatric surgery--granisetron alone vs granisetron combined with dexamethasone/droperidol. Middle East J Anesthesiol June 2007; 19(2):357- 671.
24. Wang TF , Liu YH , Chu CC, Sheih JP, Tzeng JI , Wang JJ *et al* Low-dose haloperidol prevents post-operative nausea and vomiting after ambulatory laparoscopic surgery. Acta Anesthesiol Scand. February 2008; 52(2):280-4.
25. Sriraman R, Indu S , Chari P Is granisetron-dexamethasone combination better than ondansetron-dexamethasone in the prevention of postoperative nausea and vomiting in outpatient gynecological laparoscopy. *Journal of Anesthesiology and Pharmacology*. October 2007; 23(4):365-372. 75
26. Erhan Y, Erhan E, Aydede H ,Yummus O, Yentur A Ondansetron granisetron and dexamethasone compared for the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Surg Endosc June 2008;22(6):1487-92.
27. Chu CC ,Sheih JP ,Tzeng JI, Chen JY, Lee Y ,Ho ST *et al* The prophylactic effect of haloperidol plus dexamethasone on postoperative nausea and vomiting in patients undergoing laparoscopically assisted vaginal hysterectomy . Anesth analog. May 2008; 106(5):1402-6.
28. Karanicolas PJ, Smith S, Kanbur B, Davies E, Guyatt GE The impact of prophylactic dexamethasone on nausea and vomiting after laparoscopic cholecystectomy: a systematic review and meta-analysis. Annals of surgery. November 2008; 248(5):751-62.
29. Khan M , Singh V ,Kumar M , Singh B , Kapoor R,Bhatia V *et al* Prophylactic Antiemetic Therapy Using Combinations Of Granisetron, Dexamethasone And Droperidol In Patients Undergoing Laparoscopic Cholecystectomy. *The Internet Journal of Anesthesiology*. 2008;21.
30. Gupta V, Wakhloo R, Mehta A, Gupta S Prophylactic Antiemetic Therapy with Ondansetron, Granisetron and Metoclopramide in Patients Undergoing Laparoscopic Cholecystectomy Under GA. Department of Anesthesiology and ICU, Government Medical College, Jammu, J&K. June 2008;2(10)
31. Dabbous AS , Jabbous SI , Nasr VJ ,Moussa AA, Zbeidy RA, Khouzam NE *et al* Dexamethasone with either granisetron or ondansetron for postoperative nausea and vomiting in laparoscopic surgery. Middle east J anesthesiol. February 2010; 20(4):565-70.
32. Dhurjoti B, Dawn S, Nayak S, Roy P ,Acharya A, Dey R *et al* Efficacy of granisetron and palonosetron to prevent PONV in patients undergoing laparoscopic cholecystectomy. *Journal of anesthesiology of clinical pharmacology*. 2010;6:480-483.
33. Wang B, Hua KH ,Jiang Bi, Chao L Effect of prophylactic dexamethasone on nausea and vomiting after laparoscopic gynecological operation: meta-analysis. October 2011; 21(3):397-402.
34. Hessami M, Yari M Granisetron Versus Dexamethasone in Prophylaxis of Nausea and Vomiting After Laparoscopic Cholecystectomy. Anesthesiology and pain medicine. September 2012; 2(2): 81–8
35. Bernardo W, Aires F *et al* Efficacy of dexamethasone in the prophylaxis of nausea and vomiting during the postoperative period of laparoscopic cholecystectomy. Rev Assoc Med Bras. 2013;59:387-91 - Vol. 59
36. Ramaswamy S, Narendra, Upadya M Haloperidol vs granisetron for prophylaxis of postoperative nausea and

vomiting-A double blind prospective randomized study. *International journal of scientific research*.September 2013;2:293-295. 77

37. Bernado W , Aires F Efficacy of dexamethasone in the prophylaxis of nausea and vomiting during the postoperative period of laparoscopic cholecystectomy. Rev. Assoc. Med. Bras. August 2013;59.
38. Benevides M, Oliveira S,Nasimento J . The Combination of Haloperidol, Dexamethasone, and Ondansetron for Prevention of Postoperative Nausea and Vomiting in Laparoscopic Sleeve Gastrectomy: a Randomized Double-Blind Trial. OBES SURG (2013) 23:1389–1396.
39. Asdollah S, Vahadat M, Yazdkhasti P,Nirkavan N The influence of dexamethasone on postoperative nausea and vomiting in patients undergoing gynecological laparoscopic surgeries. Turkish journal of Obstetrics and gynecology. 2014 december 15;11(4)219-223. 40. Joo J, Park Y ,Baek J,Moon Y Haloperidol dose combined with dexamethasone for PONV prophylaxis in high-risk patients undergoing gynecological laparoscopic surgery: a prospective, randomized, double-blind, dose-response and placebo-controlled study. BMC Anesthesiology 2015; 15:99
40. Doyle B Is Dexamethasone 4mg a More Effective Anti-Emetic than Dexamethasone 8mg for the Prevention of Early Post-Operative Nausea and Vomiting in Women Undergoing Laparoscopic Gynecological Surgery. Doctoral projects . December 2015.
41. Jehan N, Ahmad M, Charak D, Ommid M, Shifat F Prevention of PostOperative Nausea and Vomiting Following Laparoscopic Cholecystectomies - Comparative Evaluation of Some Common Anti-Emetics. *Journal of Dental and Medical Sciences*.March 2015;14:34-39.
42. Wakasugi M, Tori M ,Shimuzu J,Kim Y,Noda T, Dono K *et al* Efficacy of preoperative dexamethasone for postoperative nausea and vomiting after laparoscopic cholecystectomy: a large-scale, multicenter, randomized, doubleblind, placebo-controlled trial in Japan. J Hepatobiliary .Pancreat Sci 2015; 22:802–809
43. Ying- X, Wi -Lu, Li –Xiu ,Li-B,Zou –Y. Dexamethasone combined with other antiemetics for prophylaxis after laparoscopic cholecystectomy. *Asian Journal of surgery*. 2015 Jan ;38:21-27.
44. Sunil B, Bhat S Comparison Of Prophylactic Antiemetic Efficacy Haloperidol and Granisetron For the Prevention of Postoperative Nausea and Vomiting Followed by Laparoscopic Surgeries. J. Evolution M. Dent September 2016;5: 2278-4478.
45. Rao K, Swarnalatha U Comparison of Granisetron versus Granisetron plus Dexamethasone after Laporoscopic Surgery. *International Journal of scientific research*. November 2016;5:275-277.
46. Wadaskar D,Magar J, Tendolkar B A study of comparing single dosegranisetron with combination of granisetron with dexamethasone in preventing postoperativenausea vomiting in laparoscopic cholecystectomies. Int J Res Med Sci. 2016 Aug;4(8):3191-3197
47. Zhu M, Zhou C,Huang B,Ruan L,Liang R Granisetron plus dexamethasone for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgery: A meta-analysis. *Journal of international medical research*. March 2017. ;45(3):904-911 79
48. Chapparo L, Gallo T, Gonzalez N, Rivera M ,Peng P Effectiveness of combined haloperidol and dexamethasone versus dexamethasone only for postoperative nausea and vomiting in high-risk day surgery patients: a randomized blinded trial. European Journal of Anesthesiology 2010, 27:192– 195.
49. Rudra A, Chakravorty K, Das S, Halder R, Rudra P , D.E.P *et al* Combination of granistron-dexamethasone in the prophylaxis of postoperative nausea and vomiting after thyroidectomy:comparison with granisetron alone. *Indian journal of anesthesia*.2005;49(5):391-394.
50. Nethra N, Gurudatt C A comparative study of ondansetron and granisetron in combination with dexamethasone in prevention of postoperative nausea and vomiting (PONV) in total abdominal hysterectomy cases performed under general anesthesia. *International journal of pharmacology and therapeutics*.2014;4(1).
51. Wilson A, Diemunsch P, Lindeque G, Scheinin S, Hansen H, Kroeks M , Kong K *et al* Single-dose i.v. granisetron in the prevention of postoperative nausea and vomiting. *British Journal of Anesthesia* 1996; 76: 515–518.
52. Janknegt R, Pinckaers R, Rohof M, Ausems M, Arbouw M, Velden R *et al* Double-blind comparative study of droperidol, granisetron and granisetron plus dexamethasone as prophylactic anti-emetic therapy in patients undergoing abdominal, gynecological, breast or otolaryngological surgery. Clinical efficiency of antiemetics following surgery. Anesthesia, 1999; 54:1059–1068. 80
53. Rusch D, Arndt C, Martin H, Kranke P The addition of dexamethasone to dolasetron or haloperidol for treatment of established postoperative nausea and vomiting. Anesthesia, 2007; 62: 810–817.
54. Mane M, Patil Divakar ,Paranjape J ,Thote R Role of Inj. Dexamethasonefor prevention of postoperative nausea and vomiting in laparoscopic Surgeries. *Med Pulse International Journal of Anesthesiology* August 2017; 3(2): 85-87.
55. Bisgaard T, Klarskov B, RN, Kehelet N, Rosenberg J Preoperative Dexamethasone Improves Surgical Outcome After Laparoscopic Cholecystectomy A Randomized Double-Blind Placebo-Controlled Trial. Annals of surgery November 2003;238: 651–660.
56. Abraham J, Upadhayay K Comparison of granisetron and granisetron plus dexamethasone for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy.2007