EFFICACY OF DEXAMETHASONE AND MIDAZOLAM AND THEIR COMBINATION FOR REDUCING POSTOPERATIVE NAUSEA AND VOMITING DURING AND AFTER SPINAL ANESTHESIA FOR CESAREAN SECTION.

A Thesis submitted to faculty of medicine for partial fulfillment of Master Degree in Anaesthesia & Surgical Intensive care

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LIST OF CONTENT

LIST OF ABBREVIATIONS

ASA	American society of anesthesiologists.
ANOVA	Analysis of variance .
ACH	Acetyl choline .
BP	Blood pressure.
CSF	Cerbrospinal fluid.
ECG	Electrocardiography.
BBB	Blood brain barier.
CTZ	Chemoreceptor trigger zone.
D2	Dopamine type2 receptor.
EPSs	Extrapyramidal symptoms.
GI	Gastrointestinal.
H1	Histamine type 1 receptor.
IONV	Inraoperative nausea and vomiting.
MBP	Mean blood pressure.
M1	Muscarinic cholinergic type1 receptor.
NK1	Neurokinin type1 receptor.
NTS	Nuclei tractus solitarii.
PONV	postoperative nausea and vomiting.
TIVA	Total intra venous anesthesia.
VC	Vomiting center.
VRS	Verbal rating scale.
5-HT3	Serotonin type 3 receptor.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is a common unpleasant experience. Although improvement of various anesthetics and the identification of patient- anesthesia and surgery-related risk factors for PONV have helped to develop many preventive strategies in recent years, the overall incidence of PONV in the adult population still remains at 20-30% [1, 2].

The incidence of nausea and vomiting is affected by the type of surgery; for example it is 30% - 65% after cesarean section [3] , 53% - 75% after laparoscopic cholecystectomy [4], 62% - 80% after middle ear surgery [5] and 40% -70% after tonsillectomy and adenoidectomy [6]. Emesis is highly troubling: it is not only results in delayed discharge from the hospital, leading to lavishing medical resources, but also reduces patient satisfaction [2,7] .

A variety of antiemetic drugs have been used for the prevention of PONV during 0-24 hours after anesthesia with varying degrees of success including traditional antiemetics (e.g. droperidol, metoclopramide, scopalamine, dixyradine, dimenhydrinate, and aprepitant), non-traditional antiemetics (e.g. dexamethasone, propofol, clonidine, midazolam, and lidocaine), and antiserotonins (e.g., ondansetron, granisetron, ramosetron, tropisetron, dolasetron, and ramosetron). Non-pharmacological techniques include acustimulation, acupressure, and acupuncture [8]. However, the traditional and antiserotonin antiemetics may produce undesirable adverse effects, such as drowsiness, restlessness, dystonic reactions, and extrapyramidal signs [8, 9].

Postoperative nausea and vomiting (PONV) can lead to serious complications such as aspiration, dehydration, electrolyte disturbances and disruption of incision site. The causes of PONV are multiple, including pharyngeal stimulation, gastrointestinal distention, abdominal distention, abdominal surgery, anaesthetic

agent, pain, opioids,hypoxia, hypotension ,vestibular disturbances and psychological factors [10].

Since the mid of 1980s, studies have shown that dexamethasone can reduce vomiting in patients after chemotherapy [11,12]. Subsequent studies have also found that dexamethasone can effectively prevent PONV [13,14] induced by epidural morphine used to reduce postoperative pain [15]. A decade ago, results from meta-analysis have further suggested that the preventive effect of dexamethasone against PONV is similar to ondansetron [16]. Because of its low cost and safety in use, dexamethasone may well be the first drug of choice in preventing PONV [16,17].

Physiology and pharmacology of nausea and vomiting:

- **Nausea** is defined, as a subjectively unpleasant sensation associated with awareness of the urge to vomit does not necessarily do so.
- **Retching** is defined as the laboured, spasmodic, rhythmic contraction of the respiratory muscles, including the diaphragm, chest wall and abdominal wall muscles without expulsion of gastric contents.
- **Vomiting** is defined as an objective physical motion characterized by contraction of the abdominal muscles, descent of the diaphragm, and opening of the gastric cardia, resulting in forceful expulsion of stomach contents from the mouth[18].

Physiology: Nausea and vomiting should be considered two separate entities and assessed independently. Nausea is mediated by neural pathways, whereas vomiting is initiated and coordinated by the vomiting center and the chemoreceptor trigger zone (CTZ) [19,20].

Two areas of the brain are important in the action of vomiting; these are the vomiting centre (VC) and the CTZ, figure-1.

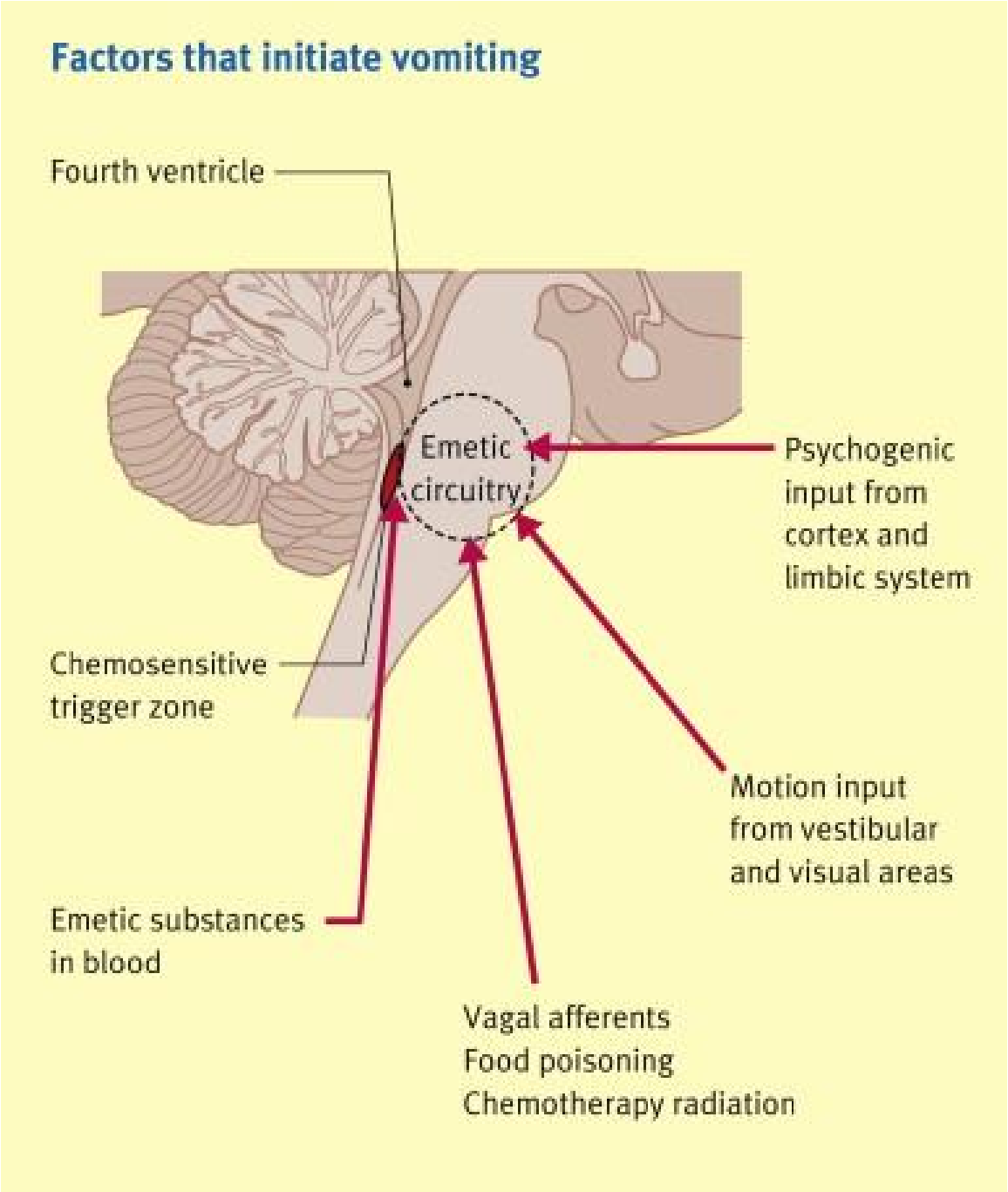

Figure-1. Vomiting centre (VC) outputs are via the vagus, hypoglossal, glossopharyngeal, trigeminal and facial nerves to the upper gut and spinal nerves to the diaphragm and abdominal muscles [(21)].

The VC is found in the lateral reticular formation of the brainstem and functions to coordinate the actions of the smooth and striated muscles involved in vomiting. The CTZ is in the area prostrema in the floor of the forth ventricle [21].

A multitude of neurotransmitters are involved in the vomiting pathways, the important ones being histamine (via H1 receptors), dopamine (via D2), serotonin(via 5-HT3) and acetylcholine (via muscarinic receptors). Other newly discovered transmitters such as neurokinin-1 (Substance P) may also play a role in the emetic reflex. Opioids also have a direct effect. Their integration and main sites of action are shown in figure-2.

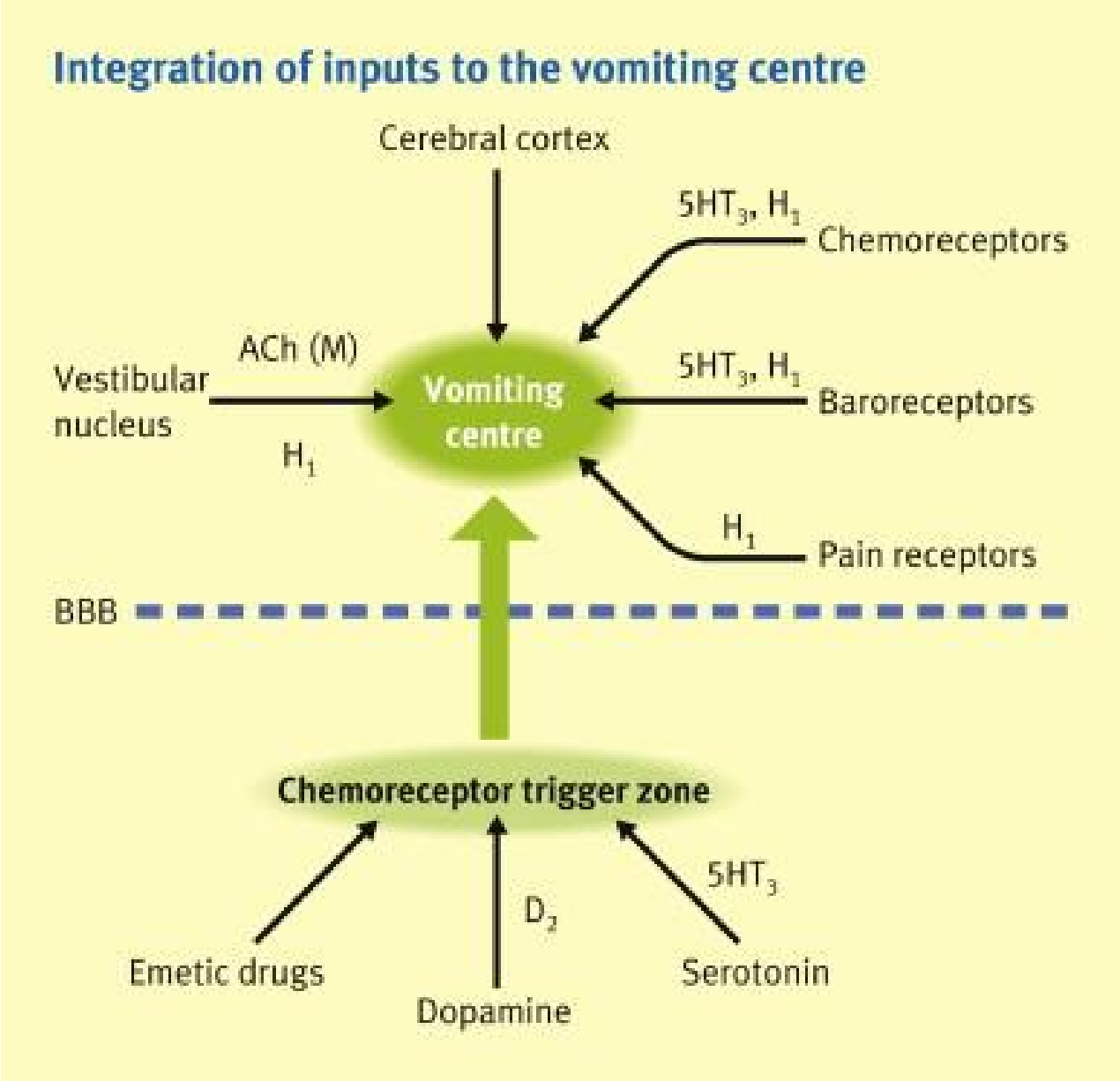

Figure -2. Chemoreceptor trigger zone (CTZ) lies outside the bloodebrain barrier and is sensitive to chemical stimulation such as drugs [(21)].

Anti-emetic drugs are antagonists at one of these receptors:

1- **Dopamine type-2 (D_2) receptors** are located in the stomach, the nuclei tractus solitarii (NTS), and the CTZ. D_2-receptors in the stomach appear to mediate the inhibition of gastric motility that occurs during nausea and vomiting, and they participate in reflexes that relax the upper portion of the stomach and delay gastric emptying. Hence, emesis have promoted by conditions that slow gastric emptying. D_2-receptors have also implicated in emetic signaling at the CTZ and in the NTS.

2- **Serotonin acting at the serotonin type-3 (5-HT_3)-receptors;** it is an important neurotransmitter in the afferent pathways from the stomach and small intestine, as well as centrally in the CTZ, area postrema, and NTS.

3- **Histamine type-1 (H_1) receptors and muscarinic cholinergic type-1 (M_1) receptors** are concentrated in the NTS, CTZ, and vestibular system, figure3.

The CTZ, area postrema, and nucleus of the solitary tract are located in the medulla and are jointly identified as the CTZ. NK_1-receptors are located in the brainstem and GI vagal afferent nerves [22].

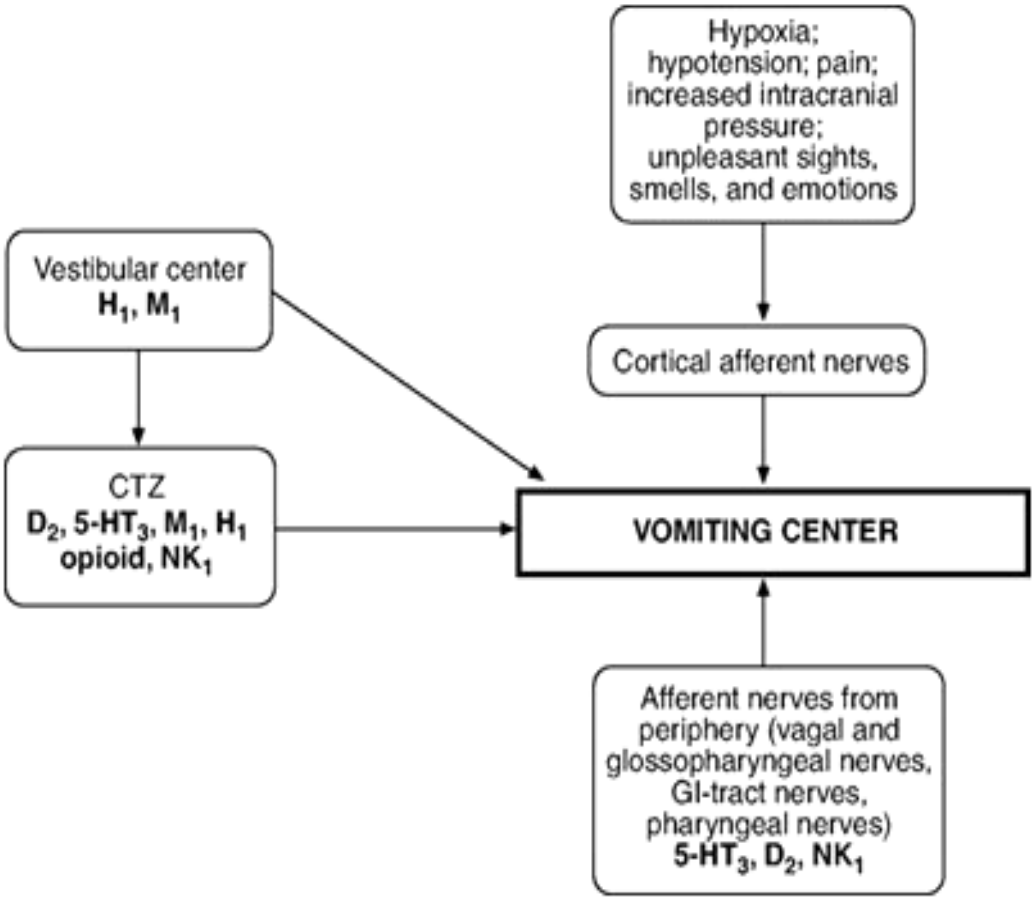

Figure-3. Pathways and neurotransmitters involved in postoperative nausea and vomiting. H_1 = histamine type-1 receptor, M_1 = muscarinic cholinergic type-1 receptor, CTZ = chemoreceptor trigger zone, D_2 = dopamine type-2 receptor, 5-HT_3 = serotonin type-3 receptor, NK_1 = substance P neurokinin type-1 receptor, and GI = gastrointestinal[22].

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High risk patients:

Identification of patients at increased risk for intraoperative (IONV) and PONV enables targeting prophylaxis to those who will benefit most from it.

Emesis prophylaxis is not appropriate for all patients; current agents, the practice would not be cost-effective, would be unlikely to benefit patients at low risk for emesis, and would put such patients at risk for the potential side effects of antiemetic agents. Patient-, anesthesia-, and surgery-related risk factors have been identified [23]. Spinal anaesthesia has been shown to be an easy, rapid and safe technique for cesarean section[24]. Nevertheless, it has some minor side effects, including IONV in more than 66% of the cases [25, 26].

Anesthesia-related risk factors include the use of volatile agents [23], nitrous oxide (which increases the risk for postoperative vomiting) [25], opioids [23, 26], and increased doses of neostigmine (>2.5 mg) for the reversal of neuromuscular blockade [27]. Patient-related factors include female sex,[28, 29] history of PONV or motion sickness,[28-30] and nonsmoking status [28, 29].

Increased levels of anxiety and postoperative pain, especially of pelvic or visceral origin, may also be associated with a greater incidence of PONV [31, 32]. Longer surgical procedures (each 30-minute increase in duration increases PONV risk by approximately 60% from baseline[29] and certain types of surgery also carry a greater risk of PONV [29,32,33].

In adults, greater incidences of PONV are found after ‘‘open’’ gastrointestinal surgery, major gynecologic surgery, laparoscopic surgery, breast surgery, craniotomy, or eye and otorhinolaryngologic surgery.

Pediatric surgical diagnoses and operations associated with greater risk for PONV include strabismus, adenotonsillectomy, hernia, orchidopexy, penile surgery, and middle ear procedures [34, 35].

The risk factors may be summarized as the following:

1. The patient-specific factors.
2. The type of surgery performed.
3. The anesthetic technique used.
4. The postoperative factors.

1. Patient-specific factors: The following groups had identified as having a greater requirement for postoperative anti-emetic drugs:

- Female patients.
- Patients with a history of motion sickness.
- Patients with a previous history of PONV.
- Patients who are non-smokers[28, 36].

2. Surgical Factors: The following types of surgery are associated with a higher incidence of PONV:

- Gynecology
- ENT
- Strabismus surgery
- Breast surgery
- Laparoscopy
- Laparotomy
- Craniotomy
- Orthopedic
- Surgical duration of > 60 minutes[37].

3. Anesthetic Factors: The following anesthetic techniques are associated with an increase in PONV:

- The administration of opioids intra and postoperatively.

- The use of nitrous oxide.
- The use of volatile inhalational anesthetics (e.g. ether).
- Some intravenous anesthetics (e.g. ketamine and etomidate).
- Spinal anesthesia by effect on BP(reducing BP).

4. **Postoperative factors:** Pain, anxiety, hypotension and dehydration, and using opioids postoperatively all contribute to nausea and vomiting. [28]

TREATMENT OF PONV:

A) Pharmacological treatment:

Once it is determined that a patient is at moderate to high risk of PONV, a strategy for prevention should be incorporated into the anesthetic plan. Because D_2-, M_1-, H_1-, and 5-HT_3-receptors have implicated in nausea and vomiting, the administration of prophylactic antiemetic agents to block one or more of these receptors in a patient at moderate to high risk is warranted. It is interesting to note that of the drugs generally referred to as anti-emetics and used in the management of PONV, some have more anti-nausea and less anti-vomiting effects, whilst others have less anti-nausea and more anti-vomiting effects. Before administering an anti-emetic in the immediate postoperative period, the clinician should rule out other causes of PONV, such as blood in the throat and gastric obstruction [38,39].

I. Monoantiemetic therapy:

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1. Dexamethasone:

Dexamethasone has been shown to be effective when given prophylactically at the start of surgery and decrease the risk of PONV by 26% [40].

The mechanism of dexamethasone-induced antiemetic activity is not fully understood, but may involve central inhibition of prostaglandin synthesis, and a decrease in 5-HT turnover in the central nervous system or changes in the permeability of the blood CSF barrier to serum proteins. Another hypothesis is that steroids could act to liberate endorphins [2].

Henzi and colleagues analyzed 17 trials involving 1946 patients that compared prophylactic dexamethasone with placebo for preventing PONV[16]. There were no reports of adverse effects from a single dose of dexamethasone. Eberhart et al also

performed a meta-analysis of dexamethasone and found it to be superior to placebo,[41]. Dexamethasone also effectively prevents opioid-induced nausea and vomiting [42].

Dexamethasone may be more effective in women with a history of motion sickness than in those without such a history[43]. The antiemetic effects of dexamethasone for preventing PONV are comparable to those of traditional antiemetics (specifically 5-HT_3- and D_2-receptor antagonists) [41].

Dexamethasone may offer additional benefits over traditional antiemetics in improving surgical outcomes. Compared with placebo, dexamethasone phosphate 8 mg i.v. given 90 minutes before laparoscopic cholecystectomy has demonstrated to significantly reduce postoperative fatigue, pain, total opioid requirements, and levels of C-reactive protein, in addition to reducing the frequency of PONV. Although time in the post-anesthesia care unit and the hospital did not differ between the groups, patients who received dexamethasone resumed recreational activities sooner (after a median of one day, versus two days for the placebo group. No adverse effects had attributed to dexamethasone [44].

Although 8 mg i.v. is probably the most common adult dose of dexamethasone phosphate for preventing PONV, the optimal dose has yet to be defined. One dose-finding study observed 2.5 mg to be the minimum effective dose for preventing postoperative vomiting in patients undergoing major gynecological surgery, [45] whereas subsequent studies found 5 mg to be the minimum effective dose in patients undergoing thyroidectomy[46] and in patients, experiencing nausea and vomiting associated with epidural morphine [47].

2.Midazolam:

Midazolam is a short-acting benzodiazepine with a rapid onset of action. In recent years, midazolam has been reported to be effective for prophylaxis of PONV by bolus administration before or after induction of anaesthesia or postoperative continuous infusion[48,49].

The suggested mechanism of action of midazolam as an antiemetic is by decreasing dopamine input at the CTZ in addition to decreasing anxiety. This leads to an adenosine-mediated reduction in the synthesis, release, and postsynaptic action of dopamine at the CTZ [50, 51] It may also decrease the adenosine reuptake (also decrease the dopaminergic neuronal activity and (5-HT) release by binding to the alpha-aminobutyric benzodiazepine complex [52] Apart from the IV administration of midazolam, it has also been administered sublingually, intranasally, and IM to alleviate PONV and has been found to be relatively successful [53]. Midazolam has been studied as an antiemetic mostly in small patients undergoing strabismus surgery [54].

Recently some authors [55] evaluated the effects of infusion of midazolam for prevention of PONV in parturients undergoing cesarean delivery performed under regional anesthesia, and they found a similar result to that of infusion of propofol. However, it seems that the infusion of midazolam or propofol is not an effective method for prevention of nausea and vomiting at the beginning of the operation.

Tarhan et al, reported an incidence of 66% nausea, 10% retching, and 10% vomiting in the group of patients undergoing cesarean section under spinal anesthesia who received the infusion of midazolam, compared with the incidence of 60% nausea, 3.3% retching, and 6.6% vomiting in the group of patients who received the infusion of propofol as antiemetic, compared with the incidence of 96% nausea, 43.3% retching, and 46.6% vomiting in the control groupThe results of their study show that

the incidence of nausea is higher in the beginning of the operation: 53.3% nausea before delivery versus 10% nausea after delivery in the midazolam group[55].

Midazolam is also an effective antiemetic in patients having chemotherapy[56]. Unlugenc et al, reported that midazolam was effective for treatment of established PONV. They also suggested that antiemetic effect of midazolam lasted longer than that of the sedative effect[57].

lee et al, compared the prophylactic anti-emetic efficacy of midazolam 2mg and ondansetron 4 mg in 90 patients scheduled for minor gynaecological surgery. They did not find a significant difference between the incidence of nausea and vomiting between the two groups[58].

3. Anticholinergics:

Scopolamine antagonizes M_1-receptors in the cerebral cortex and pons and H_1-receptors in the hypothalamus and vomiting center [59,60] . The noradrenergic system is also suppressed, [60] resulting in a less intense response and improved adaptation to vestibular stimulation. The pharmacologic effects of scopolamine make it a very effective agent for preventing and treating motion sickness [61].

Stimulation of the vestibular system by a surgical procedure, increased vestibular sensitivity from opioid administration, and movement following surgery can cause PONV. Because scopolamine can block H_1- and M_1-receptors activated by these vestibular causes of PONV, many researchers have studied scopolamine's effectiveness for preventing PONV[62].

4. Antihistamines:

Both histamine H1 and muscarinic receptors are present in the vomiting centre and the vestibular nucleus. The antihistamine drugs that are used to treat nausea and vomiting also have antimuscarinic activity; therefore it is unclear which property is more important for their anti-emetic action. Cyclizine has been used extensively to treat PONV and most reports demonstrate efficacy with few side effects such as sedation. Promethazine is a markedly sedative drug and has been used by anaesthetists to premedicate children, but whether its efficacy is due to its sedative or anti-emetic effect is debatable. Oral dimenhydrinate given at least 1 h before surgery has also been used to prevent PONV. Second-generation antihistamines (e.g. terfenadine, astemizole) are not effective anti-emetics because they do not cross the bloodebrain barrier[(63)].

Kranke et al, analyzed the results of 18 trials in 3045 patients that compared dimenhydrinate with placebo for prophylaxis of PONV. Dimenhydrinate was an effective antiemetic in patients at moderate to high risk. Dimenhydrinate had no more serious adverse effects than placebo. The most frequent complaints in the perioperative setting are likely to be dizziness, drowsiness, and headache[(64)].

5. 5-HT_3-receptor antagonists:

5-HT is released by cytotoxic agents and contributes to nauseaand vomiting by actions in the gastrointestinal tract and the brain. In addition, dopamine antagonists may be ineffective in severe chemotherapy-induced emesis. These observations prompted the successful trial of 5-HT3 antagonists (e.g. ondansetron) in chemotherapy-induced emesis. Subsequently, oral ondansetron was found to be effective in PONV, a finding that has been confirmed, using both the oral and intravenous routes, in many post-operative situations. Generally, the adverse effects of ondansetron were mild and no signs of the extrapyramidal symptoms or dry mouth seen with alternative anti-emetics were reported. Granisetron and palonosetronare also

effective in PONV. Other 5-HT3 antagonists, such as dolasetron and tropisetron, have been used in only a few trials of PONV, in which they were significantly better than placebo. Tropisetron metabolism involves the cytochrome P-450II-D6 enzyme system, which may be absent in a minority of patients, resulting in poor metabolism of the drug in those individuals. Comparative studies between individual 5-HT3 antagonists in PONV have not been carried out, but there are some reports of comparisons with other anti-emetics. Most clinical trials involving ondansetron used single doses and the equivalence of the dose of comparator (i.e. the standard drug with which ondansetron is compared) may be questioned[65].

In general, the 5-HT3 antagonists appear to be more effective and to exhibit fewer adverse effects than alternative anti-emetics used for PONV. However, the cost of treating all patients at risk of PONV with these relatively new agents must be considered[64].

6. Phenothiazines:

Prochlorperazine, promethazine, and perphenazine are phenothiazines that exert an antiemetic effect by blocking D_2-receptors in the CTZ and other areas of the brain [66].

Promethazine also has significant antihistamine and anticholinergic activity. Compared with placebo, promethazine hydrochloride (25 mg i.v. given at induction of anesthesia) effectively reduced the frequency of PONV in adults undergoing middle-ear surgery (from 39% to 79%) [67].

Prochlorperazine has a faster onset of action and causes less sedation than promethazine [68]. Compared with ondansetron 4mg i.v., prochlorperazine 10 mg (as the edisylate salt) i.m. administered at the end of surgery more effectively reduced postoperative nausea (56% versus 81%) and the need for rescue antiemetics (27% versus 46%) in adults undergoing total hip or knee replacement[69].

In patients undergoing tympanoplasty, prophylactic prochlorperazine 0.02 mg/kg i.m. administered at the end of surgery was as effective as ondansetron 0.06 mg/kg i.v. for reducing PONV [(70)].

Prochlorperazine has routinely been administered in a dose of 10 mg every 4 to 6 hours intra muscularly or 25 mg every 6 hours rectally to provide optimal antiemetic efficacy[(71)].

When administered before induction of anesthesia, perphenazine is as effective as ondansetron or droperidol in preventing PONV in women undergoing total abdominal hysterectomy[(72)]. In adult patients undergoing laparascopic cholecystectomy, perphenazine is as effective as droperidol plus ondansetron or droperidol plus metoclopramide administered after induction of anesthesia[(73)]. Although sedation may occur with perphenazine, it was not problematic in these two studies.

Because these agents are phenothiazines, extrapyramidal symptoms (EPS), such as akathisia (motor restlessness) and dystonia (e.g., oculogyric crisis), can occur. In fact, it had reported that 16% of patients developed akathisia and 4% dystonia after the administration of prochlorperazine in the emergency department[(74)].

7. Butyrophenones:

Haloperidol and droperidol exert their antiemetic effect by blocking central D_2-receptors in the CTZ and area postrema. Haloperidol (1 mg) has been shown to treat PONV effectively [(75)] and with a faster onset and shorter duration of action than droperidol [(76)]. Droperidol was the prime drug of this class and the most effective drug of all PONV. It was withdrawn in the UK due to an excess of cardiovascular side effects but may soon be re-introduced, may also cause hypotension but problems are uncommon at the low doses used for PONV[(21)].

8. Benzamides:

Metoclopramide is a central D_2-receptor antagonist and a prokinetic agent, hastening esophageal clearance, accelerating gastric emptying, and shortening bowel-transit time[66]. When used in a commonly administered dose of 10 mg i.v., metoclopramide does not effectively prevent PONV[77]. Metoclopramide is less effective than ondansetron in reducing postoperative vomiting. Although the difference is not statistically significant, ondansetron also tends to be more effective than metoclopramide for preventing postoperative nausea. Droperidol is also more effective than metoclopramide in reducing PONV[78].

Adverse effects of metoclopramide include sedation, dizziness, and drowsiness. EPS are not common but can occur. Symptoms can occur as feelings of weakness, anxiety, agitation, and motor restlessness[79]. Slow i.v. administration of metoclopramide and administration of a preoperative anxiolytic-sedative are important strategies for reducing the risk of akathisia from the administration of i.v. metoclopramide [80].

9 .Propofol:

Total iv anesthesia (TIVA) with propofol is associated with a lower incidence of PONV compared with inhalational agents[81, 82]. In one study, this technique was equally efficacious to ondansetron 4 mg in the prevention of PONV[33]. The antiemetic effect of propofol is most pronounced in the early postoperative period. It is not useful for PONV prophylaxis if given only as a bolus for induction of anesthesia [83].

More recently, continuous subhypnotic propofol infusion and the use of patient-controlled antiemesis with propofol were also found to be effective in the treatment of PONV [84,85]. The effective plasma concentration of propofol for the 50% reduction in nausea scores has been found to be 343 ng/ml. This is much lower than the range required for sedation (900–1,300 ng/ml) and anesthesia (3,000–10,000 ng/ml) [86].

Some authors used infusion of propofol with a subhypnotic dose (1.0 mg/kg/hr) and found that it was effective in the prevention of emetic symptoms during spinal anesthesia for cesarean section [87].

Although the precise mechanism of propofol's antiemetic effect has not been elucidated, several mechanisms have been proposed, including a direct depressant effect on the CTZ, the vagal nuclei, and other centers implicated in PONV. In animal models, propofol has been show to decrease synaptic nerve transmission in the olfactory cortex [88] and to decrease serotonin levels in the area postrema [89].

II. Combination Antiemetic Therapy:

As discussed previously, there are at least four major receptor systems involved in PONV. Combination antiemetic therapy was first introduced in 1988 for chemotherapy- induced vomiting [90]. Its success prompted similar research in the field of PONV.

More than 50 randomized, controlled trials have been published comparing the relative efficacy of combination versus single-agent antiemetic prophylaxis. Most of these studies report that two or more antiemetics acting at different receptors are more effective than monotherapy [91, 92]. In a meta-analysis, Habib et al, found no statistically significant difference in the incidence of PONV when a 5HT3 receptor antagonist was combined with either droperidol or dexamethasone. Both combinations provided significantly better PONV prophylaxis than the 5HT3 receptor antagonist alone [93].

Dexamethasone combination with grnisetron it has found to be effective as antiemetic in cases after laparoscopic cholecystectomy [94]. Also in combination with midazolam is better than either drug alone in reducing the incidence of PONV after middle ear surgery[95].

In a large prospective study using a multifactorial design, Apfel et al. evaluated three antiemetic interventions (4 mg ondansetron, 1.25 mg droperidol, 4 mg dexamethasone) and three anesthetic interventions for the prevention of PONV. Their data suggest that antiemetics with different mechanisms of action have additive rather than synergistic effects on the incidence of PONV. Each antiemetic reduced the risk of PONV by approximately 25%. When combinations of interventions were used, the benefit of each subsequent intervention was always less than that of the first intervention[91].

Multimodal Approach:

In addition to using a combination of antiemetics acting at different receptor sites, the multifactorial etiology of PONV might be better addressed by the adoption of a multimodal approach. This is especially important in patients at increased risk for PONV.

Scuderi et al, reported a multimodal approach to the management of PONV in females undergoing outpatient laparoscopy that included total intravenous anesthesia with propofol and remifentanil, avoidance of nitrous oxide and neuromuscular blockade, generous intravenous hydration (25 ml/kg), triple prophylactic antiemetics (1 mg ondansetron, 0.625 mg droperidol and 10 mg dexamethasone), and 30 mg ketorolac[96]. A multimodal approach incorporating total intravenous anesthesia with propofol, a combination of ondansetron and droperidol, and avoidance of nitrous oxide was associated with a greater complete response rate and greater patient satisfaction in the postanesthesia care unit compared with similar antiemetic prophylaxis with isoflurane/nitrous oxide-based anesthetic [93].

Other factors play role in PONV:

1- Oxygen:

The use of supplemental oxygen perioperatively has been shown to reduce PONV by 50% [97, 98] possibly by reducing gastrointestinal hypoxia [99].

Greif et al, compared 80% with 30% inspired-oxygen administration during surgery and for two hours postoperatively in patients undergoing colon resection. No prophylactic antiemetics were given. The 80% oxygen group had twice the reduction in the frequency of PONV as the 30% oxygen group[97].

2- Nitrous Oxide:

The emetogenic effect of nitrous oxide has received considerable attention in the literature with numerous studies in the 1980s and meta-analyses in the 1990s emphasizing the increased incidence of PONV with this agent [100] However, in practice, the emetogenic effects of nitrous oxide and volatile anesthetics are independent, that is, they are additive and not synergistic overlapping [91]. Bivariate analysis indicated that substituting propofol for a volatile anesthetic reduced the risk of PONV by about 19%, whereas substituting nitrogen for nitrous oxide reduced the risk by about 12% [91]. In a prospective randomized study of 2050 patients avoidance of nitrous oxide and the concomitant increase in inspired oxygen concentration decreases the incidence of complications after major surgery, but does not significantly affect the duration of hospital stay[101]. A recent meta-analysis demonstrated an overall reduction in risk of PONV of 20% by avoiding N_2O [102].

3- Volatile anesthetics:

The use of inhalational anesthetic agents was the strongest risk factor in the development of PONV. However, this emetogenic effect was primarily evident in the early postoperative period (up to two hours) and was mostly dependent on the

duration of anesthesia, particularly in procedures lasting longer than three hours. Furthermore, PONV was not dependent on the volatile agent used[23].

4- Gastric Suctioning::

Gastric suctioning may be useful in reducing PONV following procedures involving the nose, mouth, and oropharynx in which large amounts of blood (a potent emetogenic) can enter the stomach. Gastric distention resulting from vigorous positive-pressure ventilation through a facemask may also cause vomiting. Gastric distention can be reduced by suctioning before extubation[2].

In general, however, gastric suctioning has not been shown to reduce PONV; in fact, the presence of a nasogastric tube during the postoperative period may stimulate the gag reflex [103].

5- Reversal Agent:

Anticholinesterase drugs are routinely administered at the end of surgery to antagonize any residual effect of nondepolarizing neuro-muscular blocking agents. These agents may contribute to PONV, because they increase gastrointestinal motility and gastric secretions. In actual practice, these effects are usually countered by concurrent administration of an anticholinergic agent, such as glycopyrrolate.

A systematic review of the effect of omitting reversal agents on the risk for PONV found little evidence of benefit unless large doses (>2.5 mg of neostigmine methylsulfate) were used[104].

6- Hydration Status:

Postoperative outcomes such as thirst, dizziness, drowsiness, and nausea may be influenced by the surgical patient's fluid status before and after surgery. Pre-operative dehydration may occur due to the preoperative nothing-by-mouth (NPO)

orders that often go into effect many hours before surgery. Preoperative dehydration may be compounded in a patient whose scheduled surgery is delayed.

Perioperative hydration with infusions at rates of up to 20 ml/kg/hr has been shown to effectively deter postoperative nausea, as well as thirst, dizziness, and drowsiness [105]. Recently, more liberal preoperative NPO guidelines have been introduced in an effort to avoid preoperative dehydration [106].

B) Nonpharmacological treatment of PONV:

Acupuncture:

Manual electrical stimulation of the P-6 acupuncture point (Neiguan) by needle results in decrease in incidence of PONV upto 6 hours , to find p-6 acupuncture point measure the distance from your wrist crease to your elbow crease, Divide this distance by 6,the point is one sixth of the way up the arm from the wrist between the two tendons, application of pressure on P-6 point every 2 hours is reported to produce effect for 24 hours, figure-4, [30].

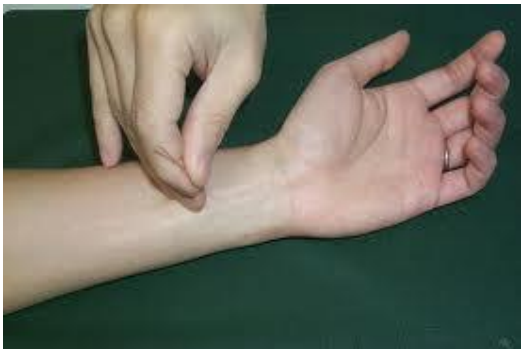

Figure-4: Acupuncture

The mechanism of action of acupuncture is still uncertain. It may be that low frequency stimulation of the skin activates A-b and A-d fibres, which may influence neurotransmission in the dorsal horn or higher centres. The endogenous opioid system is probably involved; increased concentrations of b-endorphins were reported in human cerebrospinal fluid after acupuncture in patients with chronic pain[107].

Two studies in patients undergoing ambulatory plastic surgery and laparoscopic surgery found comparable efficacy between the acupoint intervention and i.v. ondansetron, and the combination of the two interventions was more efficacious than either one alone [108,109]

Acupressure wristbands:

Acupressure is a variation of acupuncture involving constant pressure on acupuncture points without puncture of the skin, figure-5.

Figure-5: Acupressure wristbands

A British product has been marketed (Sea Bands) which comprises bands of elasticated fabric with a small round plastic button inside each, to be born on both wrists. The buttons exert constant pressure on the Neiguan (P6) acupuncture points, located on the anterior surface of the wrists three fingers breadth above the distal skin crease of the wrist joint between the tendons of palmaris longus and flexor carpi radialis.

Alkaissi and workers [110, 111] had published two studies investigating acupressure administered by a Sea-Band in women undergoing minor gynaecological surgery.The first study [110] involved only 20 patients per group and the placebo stimulation group seemed to have an antiemetic effect as well as the active stimulation group. Their second study [111] was larger and multi-centre; it involved 410 women. A complete response (no PONV) was more likely in the active group compared with those receiving no acupressure (67 vs 54%; $P<0.05$) [111].

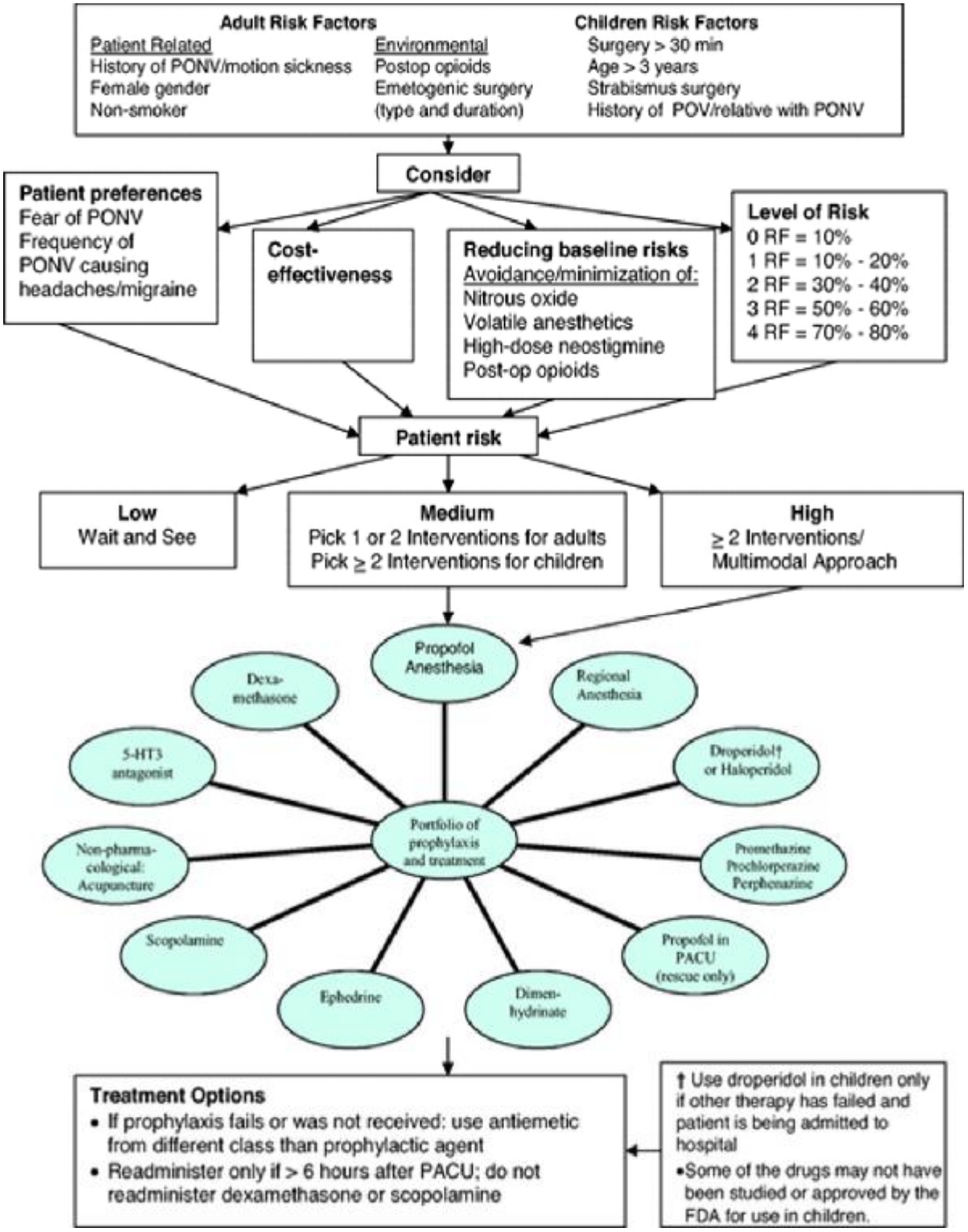

Figure- 6: Algorithm for the management of postoperative nausea and vomiting (PONV) and portfolio of antiemetics recommended by the Society for Ambulatory Anesthesia PONV Consensus Group. 5-HT3= 5-hydroxy tryptamine 3; PACU =postanesthesia care unit;POV = postoperative vomiting[(1)].

AIMS OF THE STUDY

The aims of the study were:

1- To evaluate and compare the efficacy of the combination of midazolam and dexamethasone, with efficacy midazolam and dexamethasone alone, for the prevention of intraoperative and postoperative nausea and vomiting in female patients undergoing elective cesarean section under spinal anesthesia.

2- To assess intraoperative and postoperative adverse effects of agents administered(dexamethasone, midazolam).

PATIENTS AND METHOD

1. PATIENTS:

This study included 80 female adult patients admitted to El-Jamhoria hospital in Benghazi 2010 and scheduled for elective cesarean section under spinal anesthesia, the samples were taken based on pilot study.

- Inclusion criteria:

After obtaining consent from the patients, 80 patients it was full-term pregnancy aged from 20 to 40 years with ASA physical status I or II scheduled for elective caesarean were included in the study.

- Exclusion criteria:

a. Hyperemesis gravidarum.

b. History of sensitivity to any of the drugs used in the study.

c. History of gastrointestinal diseases.

d. Fetal prematurity.

e. Patients who had received antiemetics 24 hours prior to surgery .

f. Non fasting (e.g. emergency cesarean section).

g. Partially or failed spinal block.

h. History of middle ear diseases.

i. History of motion sickness.

2- METHODS:

(I) Grouping:

The 80 patients were distributed equally using envelop technique into 4 groups:

- Group I: (control group) included 20 patients who received IV 10 ml of isotonic saline.
- Group II: dexamethasone (D) group included 20 patients who received IV dexamethasone 8mg (in 10 ml diluted) [45].
- Group III: midazolam (M) group included 20 patients who received IV midazolam 50 microgram/kg (in 10 ml dilution).
- Group IV: combination (DM) group included 20 patients who received combined IV midazolam (50 microgram/kg) and dexamethasone (8mg) in 10 ml dilution

(II) The Anti-emetics:

The studied drugs in all groups were injected immediately after clamping of the fetal umbilical cord. Rescue anti-emetic (10mg IV metoclopramide) was given for patients who experience nausea for more 5 minutes or having 2 or more episodes of vomiting or retching, or who demand for their symptoms and repeated if necessary[112].

(III) Anesthesia management:

- Patients were be premedicated and all were preloaded with 10 ml/kg of isotonic saline before the start of spinal anesthesia[113].
- Spinal anesthesia was performed in the sitting position using midline approach, and ,2.5 ml of o.5% hyperbaric bupivacaine (Astrazeneca) , was injected intrathecally at the level L3-L4 interspinous space using 25 gauge spinal needle(B.Braun Melsungen).

- Level of the block was assessed by pinprick test before surgical incision.

- Intraoperative hypotension was treated by IV fluid and IV ephedrine (6 mg titrations) [114].

(IV) Measurements:

(A) Preoperative measurements:

Patient's age (years), body weight (kilogram), height (centimeter) .

(B) Intraoperative measurements:

- Continuous ECG monitoring with heart rate, non-invasive blood pressure, respiratory rate and peripheral oxygen saturation (SpO2);(every 5 minutes).

- Any intraoperative nausea, retching, or vomiting were recorded. Nausea was defined as subjectively unpleasant sensation associated with awareness of the urge to vomit, Vomiting was defined as the forceful expulsion of gastric contents from the mouth [115].

- For the purpose of data collection, retching (the same as vomiting but without expulsion of gastric content), vomiting episode was defined as the events of vomiting that occurred in a rapid sequence (<1 min between events). If events of vomiting were separated by more than 1 min, they were considered to be separate episodes.

- Any related complication.

- Fetal observation(using apgar score).

(C) Postoperative measurements and recording:

- All patients were followed up for the first 24 hours postoperatively, and the following data were recorded:

1- Incidence of nausea and vomiting during the first 24 hours after end of the surgery. Vomiting which occurred more than 4 times within 24 hours was considered as severe vomiting [(18)].

2- Pain intensity was evaluated by the four-category verbal rating scale (VRS) (no pain (I), mild pain (II), moderate pain (III), and severe pain (IV). Postoperative pain management was standardized in all groups by giving 75 mg of diclofenac sodium intramuscularly when VRS ≥ 3[(116)].

3-Postoperative complications related to the antiemetic drugs used in the study.

4- postoperative blood pressure and heart rate were recorded every 6 hours for 24 hours postoperatively.

5-Postoperative respiratory rate were recorded 6 hourly for 24 hours postoperatively.

Statistical tests used:

Values are presented as mean ± standard deviation (SD). One way ANOVA test was used for normally distributed variables, and the Newman-Keuls post-hoc test was used for multiple comparisons to determine the significance of differences in means. Kruskal-Wallis ANOVA was used for non-normally distributed data. $P<0.05$ was considered statistically significant.

RESULTS

Demographic characteristics and surgical and anesthetic data were comparable (P >0.05) in all groups. Spinal anesthesia was successful and adequate in all groups, with a similar peak sensory block height ranged from T4 to T6.

Measurements of vital signs did not differ significantly between the groups at any time-interval.

1. Demographic data:

a. Age:

The mean age and±SD of the patients in the four studied groups were 32.9 years±(5.87) in group I, 30 years±(6.94) in group II (D), 33.2 years±(5.39) in group III (M), and 32.9 years±(4.8) in group IV (DM) with no inter-groups significant differences (P> 0.05), (Tables 1-7)

B. Weight: (Tables 1-6)

The mean weight of the patients in the four studied groups were 85.5 kg±(14.2) in group- I,79.8 kg±(10.1) in group- II(D), 79.2 kg±(10.1) in group- III (M) and 79.8 kg±(13.8) in group- IV (DM) with no inter-groups significant differences (P> 0.05), (Tables 1-7).

C. Height:

The mean height of the patients in the four studied groups were 164 cm±(8.68) in group- I, 165cm±(5.56) in group- II (D), 168cm ±(4.96)in group- III (M) and 166 cm±(7.40) in group- IV(DM) with no inter-groups significant differences (P>0.05), (Tables 1-7).

D. ASA grades:

14, 10, 16, and 13 parients were of ASA-I in groups I, D, M, and DM respectively. The corresponding numbers of patients of ASA-II were 6, 10, 4 and 7, (Tables 1-7).

Table-1. Demographic data for group-I (control) patients, including mean and standard deviation ± (SD):

Pt. NO.	**Age (years)**	**Weight (Kg)**	**Height (cm)**	**ASA**
1	20	95	181	I
2	29	104	175	II
3	24	77	155	I
4	40	75	167	I
5	34	75	170	I
6	40	120	165	II
7	31	85	179	I
8	36	95	160	I
9	39	80	155	I
10	37	67	156	II
11	32	90	160	II
12	31	77	163	I
13	25	110	165	I
14	37	100	165	II
15	40	82	163	I
16	34	77	165	I
17	30	76	153	I
18	29	78	162	I
19	29	72	164	I
20	40	75	152	II
Mean	32.9	85.5	164	--
Range	20-40	67-120	152-181	I-II
SD±	5.87	14.2	8.68	--

Table-2: Demographic data for group-II (D) patients, including mean and standard deviation ± (SD):

Pt. NO.	**Age (years)**	**Weight (Kg)**	**Height (cm)**	**ASA**
1.	27	85	177	II
2.	26	91	166	II
3.	27	85	171	II
4.	31	70	166	I
5.	31	75	165	I
6.	18	80	170	II
7.	39	87	155	II
8.	30	90	160	II
9.	40	109	165	II
10.	20	75	155	II
11.	40	76	160	I
12.	20	75	160	II
13.	32	60	156	I
14.	25	85	167	I
15.	28	75	167	I
16.	40	78	166	II
17.	40	70	166	I
18.	27	75	168	I
19.	32	75	167	I
20.	27	79	167	I
Mean	30.0	79.8	165	--
Range	18-40	60-109	155-177	I-II
SD±	6.94	10.1	5.56	--

Table-3: Demographic data for group-III (M) patients, including mean and standard deviation± (SD):

Pt. NO.	**Age (years)**	**Weight (Kg)**	**Height (cm)**	**ASA**
1.	39	80	170	I
2.	35	70	163	I
3.	25	95	172	I
4.	38	80	170	I
5.	39	70	165	I
6.	34	82	172	I
7.	36	70	166	II
8.	37	90	165	II
9.	35	80	170	I
10.	25	75	170	I
11.	22	70	155	I
12.	35	82	170	I
13.	34	100	169	II
14.	24	70	165	I
15.	40	100	163	II
16.	32	70	170	I
17.	30	80	175	I
18.	38	80	175	I
19.	32	70	169	I
20.	34	70	160	I
Mean	33.2	79.2	168	--
Range	22-40	70-100	155-175	I-II
SD±	5.39	10.1	4.96	--

Table-4: Demographic data for group-IV (DM) patients, including mean and standard deviation ± (SD):

Pt. NO.	**Age (years)**	**Weight (Kg)**	**Height (cm)**	**ASA**
1.	26	85	155	I
2.	34	70	165	I
3.	26	76	170	I
4.	34	70	172	I
5.	40	73	172	I
6.	40	75	168	I
7.	37	80	165	I
8.	34	77	168	II
9.	35	80	165	I
10.	34	80	166	I
11.	34	120	169	II
12.	32	102	162	II
13.	37	60	150	II
14.	28	80	165	I
15.	33	70	167	II
16.	40	82	168	I
17.	30	65	155	I
18.	29	100	170	II
19.	32	80	160	II
20.	23	70	185	I
Mean	32.9	79.8	166	
Range	23-40	60-120	150-185	
SD±	4.80	13.8	7.40	I-II

Table-5: Summary of age results (years):

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Mean	32.9	30.0	33.2	32.9
Range	20-40	18-40	22-40	23-40
Standard deviation (SD) ±	5.87	6.94	5.39	4.80
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

P value= 0.2691. (P<0.05) was considered statistically significant.

Table-6: Summary of weight results (kg):

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Mean	85.5	79.8	79.2	79.8
Range	67-120	60-109	70-100	60 -120
Standard deviation (SD) ±	14.2	10.1	10.1	13.8
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

P value = 0.3198. (P<0.05) was considered statistically significant.

Table-7: Summary of height results (cm):

	Group-1	**Group-D**	**Group-M**	**Group-DM**
Mean	164	165	168	166
Range	152-181	155-177	155-175	150-185
Standard deviation (SD) ±	8.68	5.56	4.96	7.40
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

P value = 0.3887 (P<0.05) was considered statistically significant.

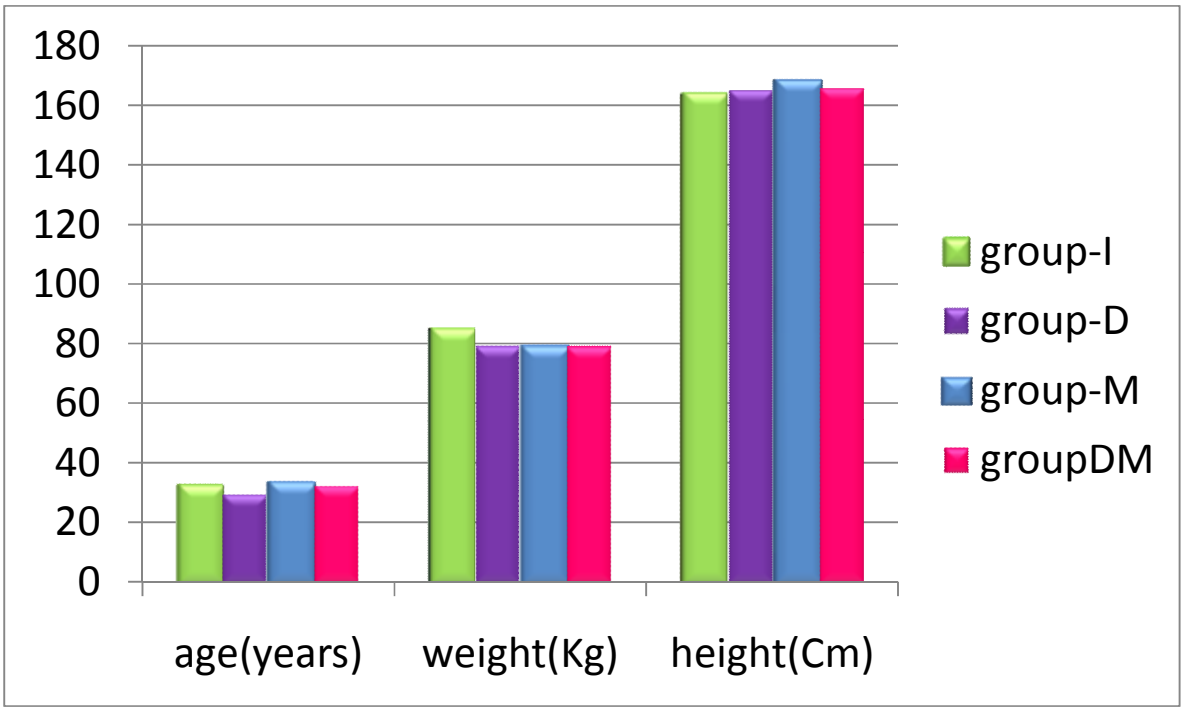

Figure 7: Demographic data of all studied groups.

2.Vital signs data:

Intra- and post-operative measurements of heart rate and, blood pressure, and SpO2 did not differ significantly between the groups at any time-interval.

a. Intraoperative heart rate(beat/min): (tables 8-12, figure-7 and 8)

Group-I (D):

The mean±SD of intra-operative heart rate at zero time, 5, 10, 15 and 20minutes were 107±(15.6), 107±(19.8), 103±(15.1), 102±(15.8) and 100 beats/min±(13.2), respectively.

Group-II (D):

The mean±SD of intra-operative heart rate at zero time, 5, 10, 15 and 20minutes were 101±(16.5), 95.6±(19.5), 101±(22.1), 96.9±(18.6) and 96.7 beats/min±(20.0), respectively.

Group-III (M):

The mean±SD of intra-operative heart rate at zero time, 5, 10, 15 and 20minutes were 101±(17.8),104±(16.7), 105±(16.4), 105±(10.7) and 104 beats/min±(13.3), respectively.

Group-IV (DM):

The mean±SD of intra-operative heart rate at zero time, 5, 10, 15 and 20minutes were 96.8±(16.4) ,98.7±(21.5), 105±(17.5), 106±(14.7) and 105 beats/min±(18.0), respectively.

Table-8: Intraoperative Heart rate(beat/min) data for group-I patients, including mean and standard deviation ± (SD):

Pt. No	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1	120	125	130	130	130
2	108	84	89	89	94
3	92	149	122	115	104
4	125	75	101	84	93
5	99	104	115	108	117
6	125	110	87	117	100
7	122	127	118	124	115
8	102	118	115	101	98
9	116	120	120	122	115
10	115	99	106	95	90
11	100	85	81	80	90
12	95	118	80	92	90
13	110	104	100	95	95
14	92	78	82	78	77
15	113	128	90	101	91
16	85	80	95	110	95
17	89	120	102	105	95
18	75	93	103	76	93
19	134	106	120	115	123
20	117	115	100	102	100
Mean	107	107	103	102	100
Range	75-134	75-149	80-130	76-130	77-130
SD±	15.6	19.8	15.1	15.8	13.2

Table-9: Intraoperative Heart rate(beat/min) data for group-II (D) patients, including mean and standard deviation± (SD):

Pt. NO	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	100	81	82	78	87
2.	99	87	117	119	129
3.	100	81	82	78	87
4.	90	120	124	122	125
5.	88	93	99	94	89
6.	70	80	68	69	87
7.	105	68	70	72	75
8.	94	82	76	72	75
9.	85	75	87	106	66
10.	90	72	104	82	72
11.	85	105	115	120	121
12.	120	101	96	91	101
13.	135	106	89	92	79
14.	112	111	118	104	108
15.	98	94	93	94	91
16.	119	114	121	120	133
17.	89	71	82	90	90
18.	117	115	136	93	96
19.	130	135	127	124	114
20.	100	120	140	117	109
Mean	101	95.6	101	96.9	96.7
Range	70-135	68-135	68-140	69-124	66-133
SD±	16.5	19.5	22.1	18.6	20.0
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-10: Intraoperative Heart rate(beat/min) data for group-III (M) patients, including mean and standard deviation ± (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	109	95	138	112	138
2.	130	100	83	90	97
3.	123	130	103	97	95
4.	112	104	114	110	108
5.	110	112	97	94	94
6.	112	120	109	111	109
7.	103	90	100	102	92
8.	108	100	129	123	115
9.	100	116	132	120	119
10.	91	111	102	113	115
11.	85	87	101	101	100
12.	58	109	102	92	88
13.	83	120	79	108	110
14.	120	125	85	111	110
15.	100	91	127	103	92
16.	116	121	118	113	119
17.	80	77	91	111	107
18.	87	113	100	107	103
19.	110	77	100	86	85
20.	80	76	97	87	88
Mean	101	104	105	105	104
Range	58-130	76-130	79-138	86-123	85-138
SD±	17.8	16.7	16.4	10.7	13.3
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-11: Intraoperative Heart rate(beat/min) data for group-IV (DM) patients, including mean and standard deviation± (SD):

Pt NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	90	114	155	132	107
2.	93	71	93	87	80
3.	90	95	99	98	96
4.	90	116	110	102	110
5.	100	110	115	107	101
6.	125	103	110	111	108
7.	72	86	89	89	87
8.	90	70	94	80	74
9.	93	74	88	103	102
10.	136	140	117	117	140
11.	110	115	91	120	122
12.	99	107	103	105	115
13.	78	70	78	99	81
14.	112	133	125	120	130
15.	88	100	103	102	106
16.	88	106	99	116	109
17.	98	76	102	119	121
18.	120	123	107	84	91
19.	84	80	130	130	126
20.	79	84	93	96	86
Mean	96.8	98.7	105	106	105
Range	72-136	70-140	78-155	80-132	74-140
SD±	16.4	21.5	17.5	14.7	18.0
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

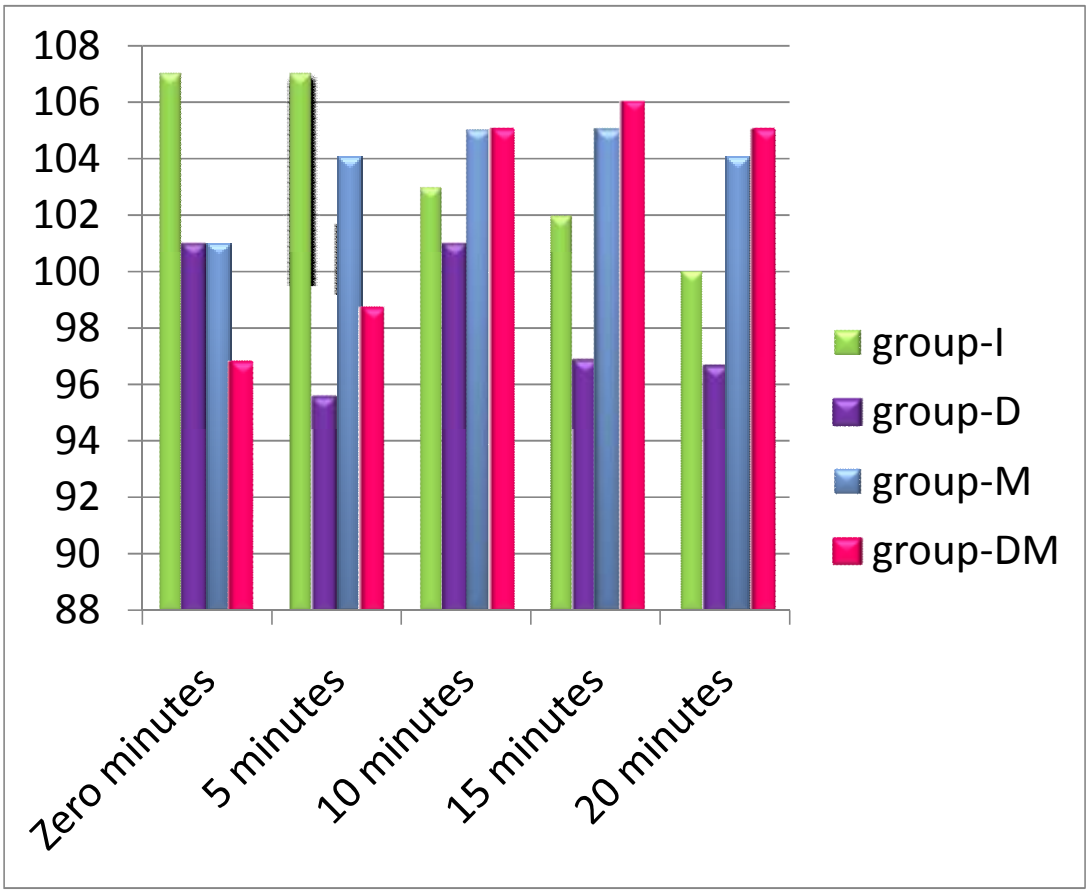

Figure 8: Intraoperative Heart rate(beat/min) data for all studied groups.

Table-12: Summary of mean ± (SD) of Intraoperative heart rate(beat/min) in all studied groups:

	Zero minutes	**5 minutes**	**10 minutes**	**15 minutes**	**20 minutes**
Group-I	107± (15.6)	107± (19.8)	103± (15.1)	102± (15.8)	100± (13.2)
Group-D	101± (16.5)	95.6± (19.5)	101± (22.1)	96.9± (18.6)	96.7± (20.0)
Group-M	101± (17.8)	104± (16.7)	105± (16.4)	105± (10.7)	104± (13.3)
Group-DM	96.8± (16.4)	98.7± (21.5)	105± (17.5)	106± (14.7)	105± (18.0)
Inter-groups *P* value	0.3118	0.2620	0.8761	0.2594	0.3839

(P<0.05) was considered statistically significant.

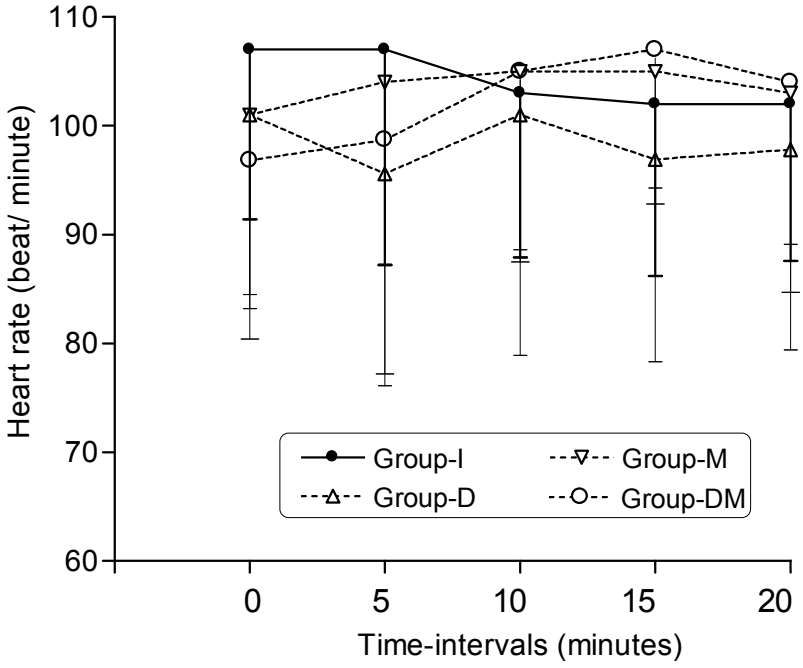

Figure-9: Mean of intraoperative heart rate(beat/min) in all studied groups. Zero interval is the time just before induction of anesthesia. No significant inter-group differences were detected at any interval. Vertical bars are the standard deviation.

b- Respiratory rate data(breath\min) including mean and ±SD:(tables 13-17)

Table 13:Intraoperative respiratory rate (breath\min)for group I including Mean and± SD:

Pt NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	14	15	14	15	14
2.	14	14	14	15	16
3.	14	14	14	15	13
4.	12	16	16	16	14
5.	15	18	15	14	15
6.	15	13	15	15	14
7.	17	15	13	16	17
8.	14	14	14	17	16
9.	16	15	16	16	14
10.	14	15	14	15	13
11.	16	14	12	16	16
12.	14	14	14	17	15
13.	16	18	16	17	16
14.	15	16	15	16	14
15.	16	16	17	16	16
16.	15	16	15	15	17
17.	14	16	17	16	15
18.	16	14	14	15	14
19.	15	15	16	16	16
20.	16	15	16	16	15
Mean	14.9	15.15	14.85	15.7	15
Range	12-17	13-18	12-17	14-17	13-17
±SD	1.16	1.30	1.31	0.80	1.2

Table14: intraoprative respiratory rate (breath\min) for group D including Mean and± SD:t

Pt NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	15	12	14	16	15
2.	12	13	14	13	14
3.	14	15	16	15	13
4.	14	16	16	18	16
5.	16	18	17	15	16
6.	14	12	13	14	14
7.	15	18	15	16	17
8.	14	16	14	18	15
9.	14	16	16	13	13
10.	17	16	14	15	13
11.	15	12	13	14	15
12.	15	13	14	15	14
13.	16	16	17	18	13
14.	15	16	15	16	15
15.	17	16	15	16	14
16.	16	17	16	15	14
17.	15	15	16	17	16
18.	15	14	14	16	15
19.	16	17	16	15	14
20.	13	14	16	14	15
Mean	14.9	15.1	15.05	15.45	14.55
Range	12-17	12-18	13-17	13-18	13-17
±SD	1.25	2.0	1.2	1.5	1.1

Table 15: Intraoperative respiratory rate (breath\min) for group M including Mean and± SD:

Pt NO.	Zero minutes	5 minutes	10minutes	15 minutes	20 minutes
1.	15	15	15	17	15
2.	13	15	14	16	16
3.	13	14	16	15	15
4.	14	17	15	17	15
5.	16	18	17	14	16
6.	14	16	13	16	14
7.	15	17	16	16	16
8.	13	15	14	17	16
9.	16	16	14	15	17
10.	16	16	14	15	13
11.	15	16	15	16	15
12.	15	17	14	14	15
13.	12	14	16	15	13
14.	17	16	13	15	17
15.	17	16	18	17	15
16.	14	15	14	15	15
17.	13	16	15	16	14
18.	16	15	16	17	16
19.	18	15	16	16	15
20.	5	14	16	15	14
Mean	14.85	15.65	15.05	15.7	15.1
Range	12-18	14-18	13-18	14-17	13-17
±SD	1.65	1.1	1.3	1.0	1.1

Table 16 : Intraoperative respiratory rate (breath\min) for group DM including Mean and ±SD:

Pt NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	14	15	14	16	15
2.	15	14	13	13	16
3.	15	14	14	15	13
4.	12	16	16	17	15
5.	14	16	15	14	12
6.	16	14	15	14	14
7.	17	15	13	16	15
8.	14	16	14	18	14
9.	14	15	16	17	16
10.	15	15	16	16	15
11.	15	15	14	16	16
12.	16	15	14	15	17
13.	16	16	16	18	15
14.	14	14	14	16	15
15.	17	16	15	16	14
16.	16	14	16	16	15
17.	15	14	16	17	14
18.	14	16	15	14	15
19.	15	15	16	16	16
20.	14	15	16	16	14
Mean	14.9	15	14.9	15.8	14.8
Range	12-17	14-16	13-16	13-18	12-17
±SD	1.2	0.8	1.0	1.3	1.1

Table17-. Summary of mean ± (SD)of Intraoperative respiratory rate(breath\min) in all studied groups.

	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
Group-1	**14.9**±(1.16)	**15.15**±(1.30)	**14.85**±(1.31)	**15.7**±(0.8)	**15**±(1.2)
Group-D	**14.9**±(1.25)	**15.1**±(2.0)	**15.05**±(1.2)	**15.45**±(1.5)	±(1.5)**14.55**
Group-M	**14.85**±(1.65)	**15.65**±(1.1)	**15.05**±(1.3)	**15.7**±(1.0)	±(1.1)**15.1**
Group-4	**14.9**±(1.2)	**15**±(0.8)	**14.9**±(1.0)	**15.8**±(1.3)	±(1.1)**14.8**
Inter-group P value	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

(P<0.05) was considered statistically significant.

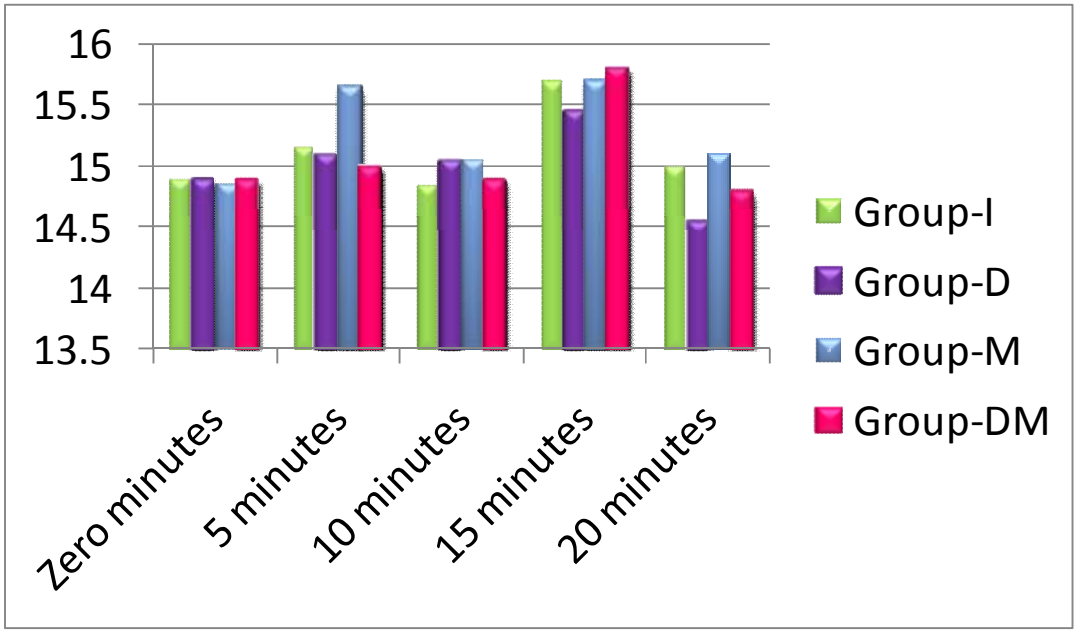

Figure 10 : Mean of intraoperative respiratory rate(breath/min) in all studied groups.

C. Peripheral oxygen saturation (SpO2) data: (tables 18-22)

Group-I:

The mean of (SpO2) at zero time,5, 10, 15 and 20 minutes were 98.6% , 98.4 %, 98.8%, 99.0% and 99.0%, respectively**.**

Group-II (D):

The mean of (SpO2) at zero time,5, 10, 15 and 20 minutes were 98.8 %, 99.1% , 98.9 % , 98.5% and 98.7%, respectively.

Group-III (M):

The mean of (SpO2) at zero time,5, 10, 15 and 20 minutes were 99.0%, 99.0 %, 98.4 %, 97.9 % and 97.9 %, respectively.

Group-IV (DM):

The mean of (SpO2) at zero time,5, 10, 15 and 20 minutes were 99.0 %, 99.1 %, 98.9 %, 98.9 % and 98.7%, respectively

Table-18: The SpO2(%) data for group-I (Control) patients, including mean and standard deviation ± (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
	97	99	100	99	99
2.	98	97	97	95	99
3.	99	98	100	99	100
4.	99	99	100	100	100
5.	99	97	98	99	100
6.	99	99	99	99	97
7.	100	99	98	98	99
8.	98	98	99	97	98
9.	100	99	100	100	100
10.	99	99	100	100	99
11.	99	98	99	99	99
12.	97	96	98	97	98
13.	99	99	97	97	98
14.	98	97	98	97	96
15.	98	99	96	98	99
16.	99	100	100	100	100
17.	98	100	99	100	100
18.	99	100	99	100	99
19.	97	99	100	99	99
20.	99	96	99	99	100
Mean	98.6	98.4	98.8	99.0	99.0
Range	97-100	96-100	96-100	96-100	96-100
SD±	0.887	1.23	1.20	1.10	1.10

Table-19: The SPO2(%) data for group-II (D) patients, including mean andstandard deviation± (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	98	99	99	99	99
2.	99	99	99	98	98
3.	98	99	99	99	99
4.	99	97	97	96	97
5.	99	100	99	98	98
6.	100	100	98	99	99
7.	99	100	99	100	100
8.	100	100	99	98	99
9.	99	99	99	96	99
10.	99	98	98	98	99
11.	99	99	100	100	99
12.	94	99	100	100	100
13.	100	99	100	100	100
14.	99	99	99	99	97
15.	100	100	100	100	100
16.	99	99	99	99	99
17.	99	98	97	97	96
18.	98	99	99	97	98
19.	99	100	98	98	99
20.	99	99	99	98	99
Mean	98.8	99.1	98.9	98.5	98.7
Range	94-100	97-100	97-100	96-100	96-100
SD±	1.28	0.788	0.875	1.28	1.08
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-20: The SPO2(%) data for group-III (M) patients, including mean andstandard deviation± (SD):

Pt. NO	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	99	99	98	97	97
2.	99	99	99	99	99
3.	99	99	96	97	98
4.	100	99	99	99	98
5.	100	99	97	97	99
6.	100	100	100	100	100
7.	99	97	98	97	99
8.	97	100	100	100	100
9.	99	99	98	95	95
10.	99	99	97	96	96
11.	98	98	98	95	95
12.	99	99	99	99	99
13.	99	100	99	97	99
14.	100	100	100	100	98
15.	99	99	99	96	96
16.	97	98	97	98	97
17.	99	99	100	98	99
18.	99	99	100	98	98
19.	98	98	94	100	96
20.	100	100	100	100	100
Mean	99.0	99.0	98.4	97.9	97.9
Range	97-100	97-100	94-100	95-100	95-100
SD±	0.887	0.795	1.60	1.68	1.62
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-21:. The SPO2(%) data for group-IV (DM) patients, including mean andstandard deviation ± (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	99	99	98	99	100
2.	99	98	95	97	100
3.	100	100	100	100	100
4.	100	100	99	99	99
5.	100	100	100	100	100
6.	100	100	100	100	100
7.	100	98	96	98	97
8.	100	100	99	98	97
9.	98	98	97	100	96
10.	95	96	97	96	96
11.	98	99	100	100	96
12.	100	99	99	96	99
13.	99	99	100	99	99
14.	97	99	99	99	99
15.	100	100	99	98	99
16.	99	100	100	100	100
17.	100	99	100	100	100
18.	100	99	100	99	97
19.	99	99	99	99	99
20.	100	100	100	100	100
Mean	99.2	99.1	98.9	98.9	98.7
Range	95-100	96-100	95-100	96-100	96-100
SD±	1.31	1.02	1.50	1.31	1.53
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-22: Summary of Mean ± (SD) of peripheral O2(%) saturation in all studied groups.

	Zero minutes	**5 minutes**	**10 minutes**	**15 minutes**	**20 minutes**
Group-I	98.6± (0.887)	98.4± (1.23)	98.8± (1.20)	99.0± (1.10)	99.0± (1.10)
Group-D	98.8± (1.28)	99.1± (0.788)	98.9± (0.87)	98.5± (1.28)	98.7± (1.08)
Group-M	99.0± (0.887)	99.0± (0.795)	98.4± (1.60)	97.9± (1.68)	97.9± (1.62)
Group-DM	99.2± (1.31)	99.1± (1.02)	98.9± (1.50)	98.9± (1.31)	98.7± (1.53)
Inter-group P value	0.3807	0.0763	0.6547	0.0688	0.0911

(P<0.05) was considered statistically significant.

d. Intraoperative systolic blood pressure (BPmmHg) data: (tables 23-27) **Group-I:**

The mean and±SD of systolic BP at zero time,5, 10, 15 and 20 minutes were 138±(16), 120±(25.9), 120±(24.2) ,127 ±(23.5) and 124 mmHg±(19.5), respectively.

Group-II (D):

The mean and±SD of systolic BP at zero time,5, 10, 15 and 20 minutes were 141±(20.1), 132±(23.3), 128±(24.7), 123±(16.1)and 123 mmHg±(18.0), respectively.

Group-III (M): The mean and±SD of systolic BP at zero time, 5, 10, 15 and 20 minutes were 130±(10.8),122 ±(23.9), 117±(16.3), 117±(14.8) and 113 mmHg±(12.7), respectively.

Group-IV (DM): The mean and±SD of systolic BP at zero time, 5, 10, 15 and 20 minutes were 131±(15.8), 118±(13.5), 115±(13.7), 118±(16.7) and 115 mmHg±(13.6), respectively.

Table-23: Intraoperative Systolic BP(mmHg) data for group-I patients, including mean and standard deviation± (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	130	102	90	130	130
2	130	178	152	174	177
3	134	84	133	131	128
4	136	100	118	119	110
5	135	155	142	145	141
6	110	105	90	110	110
7	128	109	89	95	104
8	160	128	127	130	116
9	130	99	107	99	102
10	162	155	143	133	130
11	168	155	174	176	130
12	150	108	75	111	112
13	142	110	112	122	127
14	137	127	127	119	104
15	144	123	115	99	114
16	130	110	105	115	120
17	144	147	129	147	130
18	120	92	121	100	105
19	163	92	116	125	120
20	115	130	144	158	164
Mean	138	120	120	127	124
Range	110-168	84-178	75-174	95-176	102-177
SD±	16.0	25.9	24.2	23.5	19.5

Table-24:. Intraoperative Systolic BP(mmHg) data for group-II (D) patients, including mean and standard deviation (SD):

P t. NO	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	129	128	133	119	116
2.	196	128	133	111	111
3.	129	128	133	119	116
4.	150	124	137	137	130
5.	175	170	147	152	130
6.	120	120	120	131	130
7.	130	114	90	117	128
8.	123	115	110	108	113
9.	130	132	113	104	108
10.	159	100	129	113	98
11.	162	147	140	139	136
12.	137	151	158	139	162
13.	130	101	110	108	106
14.	130	148	159	104	114
15.	140	152	144	163	168
16.	130	123	186	129	101
17.	126	186	114	110	118
18.	158	148	114	128	133
19.	136	93	100	119	120
20.	120	126	85	119	113
Mean	141	132	128	123	123
Range	120-196	93-186	85-186	104-150	98-168
SD±	20.1	23.3	24.7	16.1	18.0
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-25: Intraoperative Systolic BP(mmHg) data for group-III (M) patients, including mean and standard deviation (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	134	102	117	129	109
2.	128	110	121	118	106
3.	122	88	114	107	105
4.	112	109	105	108	108
5.	129	90	92	103	105
6.	138	129	118	113	111
7.	145	122	118	120	119
8.	139	130	125	119	118
9.	135	111	108	117	105
10.	123	151	111	139	123
11.	118	119	107	95	113
12.	143	108	110	118	109
13.	139	140	148	150	118
14.	138	147	89	111	107
15.	140	157	137	140	156
16.	129	106	130	133	126
17.	111	86	113	103	92
18.	145	176	155	104	113
19.	116	125	107	102	108
20.	124	130	111	105	105
Mean	130	122	117	117	113
Range	111-145	86-176	89-155	95-150	92-156
SD±	10.8	23.9	16.3	14.8	12.7
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-26: Intraoperative Systolic BP(mmHg) data for group-IV (DM) patients, including mean and standard deviation ± (SD):

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	133	115	131	140	156
2.	140	110	91	105	102
3.	120	139	117	116	120
4.	141	118	120	95	95
5.	140	103	124	96	100
6.	120	102	126	126	128
7.	124	111	110	119	107
8.	133	114	99	99	102
9.	140	101	93	117	113
10.	109	97	112	147	123
11.	173	114	115	146	110
12.	135	118	132	133	124
13.	126	135	129	107	113
14.	112	132	127	130	127
15.	118	120	115	122	119
16.	153	145	126	115	119
17.	115	116	130	134	121
18.	145	135	101	113	111
19.	114	107	94	106	111
20.	123	120	103	93	101
Mean	131	118	115	118	115
Range	109-173	97-145	91-132	93-147	95-156
SD±	15.8	13.5	13.7	16.7	13.6
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-27: Summary of mean ± (SD) of Intraoperative systolic blood pressure(mmHg) in all studied groups.

	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
Group-1	138 ± (16)	120 ± (25.9)	120 ± (24.2)	127 ± (23.5)	124 ± (19.5)
Group-D	141 ± (20.1)	132 ± (23.3)	128 ± (24.7)	123 ± (16.1)	123 ± (18.0)
Group-M	130 ± (10.8)	122 ± (23.9)	117 ± (16.3)	117 ± (14.8)	113 ± (12.7)
Group-DM	131 ± (15.8)	118 ± (13.5)	115 ± (13.7)	118 ± (16.7)	115 ± (13.6)
Inter-group P value	0.1049	0.2140	0.1999	0.2527	0.0930

($P<0.05$) was considered statistically significant.

e-Intraoperative diastolic blood pressure (BP) (mmHg): (tables 28-32)

Group-I:

The mean and ±SD of diastolic BP at zero time,5, 10, 15 and 20 minutes were 84.3±(12.0), 65.3±(12.1), 63.3 ±(10.4), 61.4±(10.5) and 62.7 mmHg±(11.9), respectively.

Group-II (D):

The mean and ±SD of diastolic BP at zero time, 5, 10, 15 and 20 minutes were 77.8±(11.7),68.8 ±(13.5), 61.6±(13.1), 62.0±(10.6) and 59.3 mmHg±(11.1), respectively.

Group-III (M): The mean and ±SD of diastolic BP at zero time, 5, 10, 15 and 20 minutes were 79.6±(13.3),67.5 ±(13.1) , 60.7±(10.8), 59.9 ±(11.6) and 59.3 mmHg±(11.3), respectively.

Group-IV (DM): The mean and ±SD of diastolic BP at zero time, 5, 10, 15 and 20 minutes were 73.6±(13.8), 63.9±(12.9), 61.8±(14.8), 59.6±(11.9) and 58.4 mmHg±(11.0), respectively.

Table-28: Intraoperative Diastolic BP(mmHg) data for group-I patients, including mean and standard deviation± (SD)

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	78	68	50	70	69
2.	60	82	63	72	71
3.	97	54	79	61	55
4.	81	50	52	47	60
5.	95	66	54	55	63
6.	60	50	50	40	40
7.	85	66	65	53	58
8.	83	82	81	67	53
9.	83	67	67	64	65
10.	104	85	73	69	88
11.	85	68	68	83	88
12.	75	49	48	54	53
13.	93	56	55	62	64
14.	78	71	72	62	45
15.	101	59	57	49	61
16.	70	60	55	65	63
17.	88	78	73	78	70
18.	92	72	78	55	55
19.	94	45	65	57	61
20.	84	78	60	65	72
Mean	84.3	65.3	63.3	61.4	62.7
Range	60-104	45-85	48-81	40-83	40-88
SD±	12.0	12.1	10.4	10.5	11.9

Table-29:. Intraoperative Diastolic BP(mmHg) data for group-II (D) patients, including mean and standard deviation± (SD).

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	52	70	65	70	55
2.	100	64	67	48	40
3.	52	70	65	70	55
4.	80	60	73	71	78
5.	82	75	56	63	60
6.	70	70	54	55	60
7.	77	52	43	50	60
8.	81	54	58	52	75
9.	70	75	55	48	57
10.	90	63	44	64	44
11.	67	54	55	53	43
12.	92	83	65	69	61
13.	82	58	57	60	56
14.	75	76	93	57	56
15.	85	67	89	86	81
16.	79	77	73	68	56
17.	76	42	45	53	56
18.	85	98	60	81	77
19.	80	79	60	65	60
20.	80	89	55	57	55
Mean	77.8	68.8	61.6	62.0	59.3
Range	52-100	42-98	43-93	48-86	40-81
SD±	11.7	13.5	13.1	10.6	11.1
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-30: Intraoperative Diastolic BP(mmHg) data for group-III (M) patients, including mean and standard deviation± (SD).

Pt . NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	85	51	58	68	61
2.	91	81	74	62	60
3.	63	56	45	44	50
4.	82	59	53	51	62
5.	78	50	43	53	50
6.	87	73	60	70	75
7.	64	66	67	67	64
8.	81	79	74	67	73
9.	109	60	58	70	57
10.	80	71	67	64	55
11.	82	60	49	40	45
12.	87	65	70	70	59
13.	99	92	69	71	70
14.	85	86	65	75	63
15.	85	86	76	61	79
16.	75	66	67	63	65
17.	54	42	41	35	33
18.	79	73	69	51	46
19.	60	69	57	47	51
20.	65	64	51	68	67
Mean	79.6	67.5	60.7	59.9	59.3
Range	54-109	42-92	41-76	35-75	33-79
SD±	13.3	13.1	10.8	11.6	11.3
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-31: Intraoperative Diastolic BP(mmHg) data for group-IV (DM) patients, including mean and standard deviation ± (SD).

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	75	52	56	61	79
2.	66	62	39	53	56
3.	79	84	91	68	65
4.	65	45	53	34	34
5.	100	70	76	54	53
6.	50	51	45	47	45
7.	57	48	61	60	53
8.	82	68	45	47	53
9.	99	53	48	49	59
10.	68	49	47	83	58
11.	88	66	75	71	56
12.	72	67	66	64	55
13.	91	98	90	80	81
14.	66	63	62	64	57
15.	62	62	66	62	59
16.	77	69	62	55	59
17.	68	68	81	72	73
18.	84	78	53	63	50
19.	58	60	55	56	69
20.	64	64	65	48	53
Mean	73.6	63.9	61.8	59.6	58.4
Range	50-100	45-98	39-91	34-83	34-81
SD±	13.8	12.9	14.8	11.9	11.0
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-32:. Summary of mean ± (SD) of Intraoperative diastolic BP(mmHg) in all studied groups.

	Zero minutes	**5 minutes**	**10 minutes**	**15 minutes**	**20 minutes**
Group-1	84.3 ± (12.0)	65.3 ± (12.1)	63.3 ± (10.4)	61.4 ± (10.5)	62.7 ± (11.9)
Group-D	77.8 ± (11.7)	68.8 ± (13.5)	61.6 ± (13.1)	62.0 ± (10.6)	59.3 ± (11.1)
Group-M	79.6 ± (13.3)	67.5 ± (13.1)	60.7 ± (10.8)	59.9 ± (11.6)	59.3 ± (11.3)
Group-DM	73.6 ± (13.8)	63.9 ± (12.9)	61.8 ± (14.8)	59.6 ± (11.9)	58.4 ± (11.0)
Inter-group P value	0.0708	0.6278	0.9295	0.8787	0.6334

($P<0.05$) was considered statistically significant.

f. Intraoperative mean blood pressurs (MBP) (mmHg) data: (tables 33-37, figure-11 and 12)

Group-I:

The mean and ±SD of MBP at zero time, 5, 10, 15 and 20 minutes were 105±(14.4), 87.7±(17.8),82.5 ±(20.3), 81.2±(15.3) and 83.6 mmHg±(15.2), respectively.

Group-II (D):

The mean and ±SD of MBP at zero time, 5, 10, 15 and 20 minutes were 100±(13.9), 92.1±(14.3),82.3 ±(13.8), 81.9±(15.1) and 79.5 mmHg±(12.2), respectively.

Group-III (M):

The mean and ±SD of MBP at zero time, 5, 10, 15 and 20 minutes were 96.5±(12.8), 86.1±(14.1),80.5 ±(12.3),79.5 ±(14.4) and 77.7 mmHg±(10.3), respectively.

Group-III (DM): The mean and ±SD of MBP at zero time, 5, 10, 15 and 20 minutes were 93.7±(13.1), 82.7±(14.4), 80.2 ±(13.8), 77.3±(12.4) and 77.2 mmHg±(13.3), respectively.

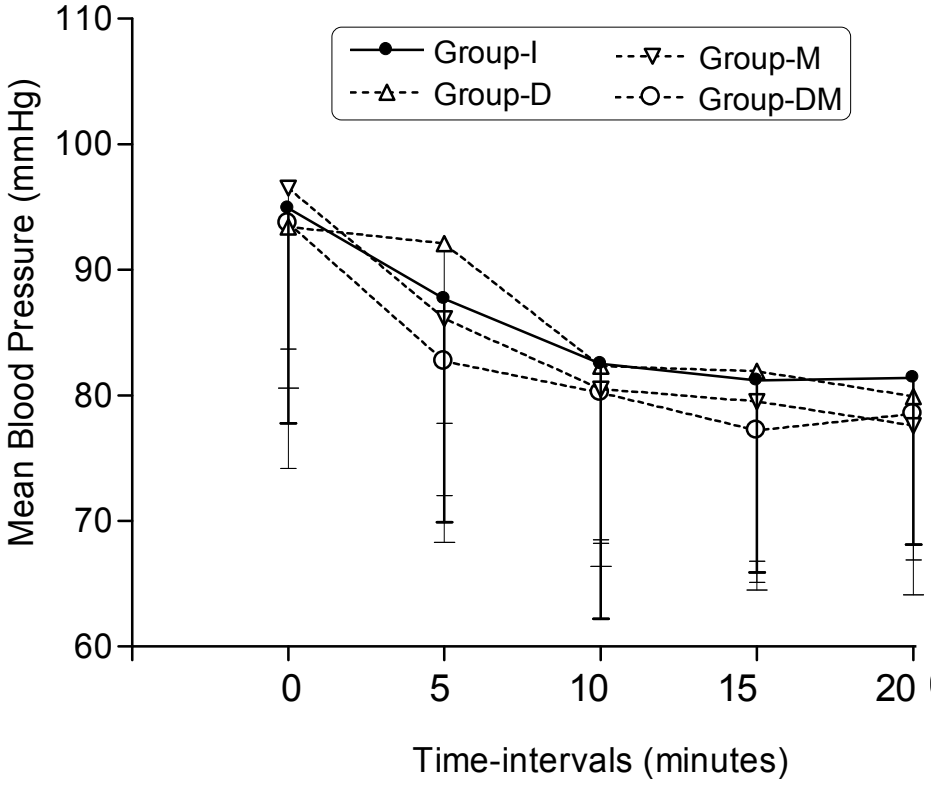

Figure-11: Mean of intraoperative mean arterial blood pressure(mmHg) in all studied groups. Zero interval is the time just before induction of anesthesia. No significant inter-group differences were detected at any interval. Vertical bars are the standard deviation.

Table-33: Intraoperative mean blood pressure(mmHg) data for group-I patients, including mean and standard deviation ± (SD).

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	83	81	51	91	89
2.	83	126	119	114	122
3.	116	95	118	84	79
4.	96	60	65	56	71
5.	116	90	72	75	84
6.	76	67	60	63	63
7.	98	92	75	69	77
8.	115	111	98	83	69
9.	98	83	83	76	75
10.	120	111	60	94	105
11.	128	100	114	114	105
12.	120	62	56	69	77
13.	120	74	75	79	86
14.	101	100	100	76	64
15.	110	93	73	63	72
16.	90	77	72	82	82
17.	109	97	92	92	90
18.	100	77	91	71	71
19.	114	63	83	82	92
20.	106	95	92	91	98
Mean	105	87.7	82.5	81.2	83.6
Range	76-128	60-126	51-119	56-114	63-122
SD±	14.4	17.8	20.3	15.3	15.2

Table-34: Intraoperative mean blood pressure(mmHg) data for group-II (D) patients, including mean and standard deviation ± (SD).

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	75	91	98	92	78
2.	119	79	91	58	65
3.	75	91	98	92	78
4.	100	100	90	84	83
5.	126	110	77	119	83
6.	90	90	74	79	83
7.	103	91	69	77	90
8.	96	85	80	71	93
9.	90	93	76	69	77
10.	113	78	63	77	56
11.	122	90	92	84	77
12.	114	97	84	92	91
13.	92	70	64	70	63
14.	93	115	111	57	71
15.	103	99	101	108	109
16.	95	100	81	90	78
17.	94	56	61	71	71
18.	109	112	68	90	94
19.	98	89	75	83	80
20.	93	106	78	74	69
Mean	100	92.1	82.3	81.9	79.5
Range	75-126	56-115	61-111	57-119	56-109
SD±	13.9	14.3	13.8	15.1	12.2
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-35: Intraoperative mean blood pressure(mmHg) data for group-III (M) patients, including mean and standard deviation± (SD).

Pt NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	95	83	71	91	73
2.	99	92	82	102	86
3.	92	72	70	70	65
4.	95	72	68	64	76
5.	92	64	71	64	65
6.	97	101	69	80	88
7.	70	76	78	86	78
8.	107	96	91	84	92
9.	122	79	70	96	72
10.	86	88	92	85	73
11.	95	76	67	58	73
12.	99	72	88	89	86
13.	110	98	106	98	89
14.	114	100	98	77	78
15.	113	97	87	84	90
16.	97	98	97	96	97
17.	75	58	66	50	59
18.	99	107	88	81	73
19.	92	94	82	67	74
20.	81	99	68	68	67
Mean	96.5	86.1	80.5	79.5	77.7
Range	70-122	58-107	66-106	50-102	59-97
SD±	12.8	14.1	12.3	14.4	10.3
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-36: Intraoperative mean blood pressure(mmHg) data for group-IV (DM) patients, including mean and standard deviation ± (SD).

Pt. NO.	Zero minutes	5 minutes	10 minutes	15 minutes	20 minutes
1.	92	75	82	84	90
2.	101	82	56	57	74
3.	98	111	107	85	106
4.	90	64	69	54	54
5.	114	83	93	69	70
6.	75	73	86	83	69
7.	81	71	71	81	68
8.	104	87	61	65	73
9.	119	73	66	74	66
10.	86	60	67	102	76
11.	116	84	91	93	71
12.	91	76	99	83	77
13.	103	120	100	87	110
14.	80	86	83	85	81
15.	79	73	80	74	80
16.	91	96	78	73	80
17.	83	91	92	88	86
18.	104	90	75	79	66
19.	84	79	70	71	79
20.	83	80	78	59	67
Mean	93.7	82.7	80.2	77.3	77.2
Range	75-119	60-120	56-107	54-102	54-110
SD±	13.1	14.4	13.8	12.4	13.3
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

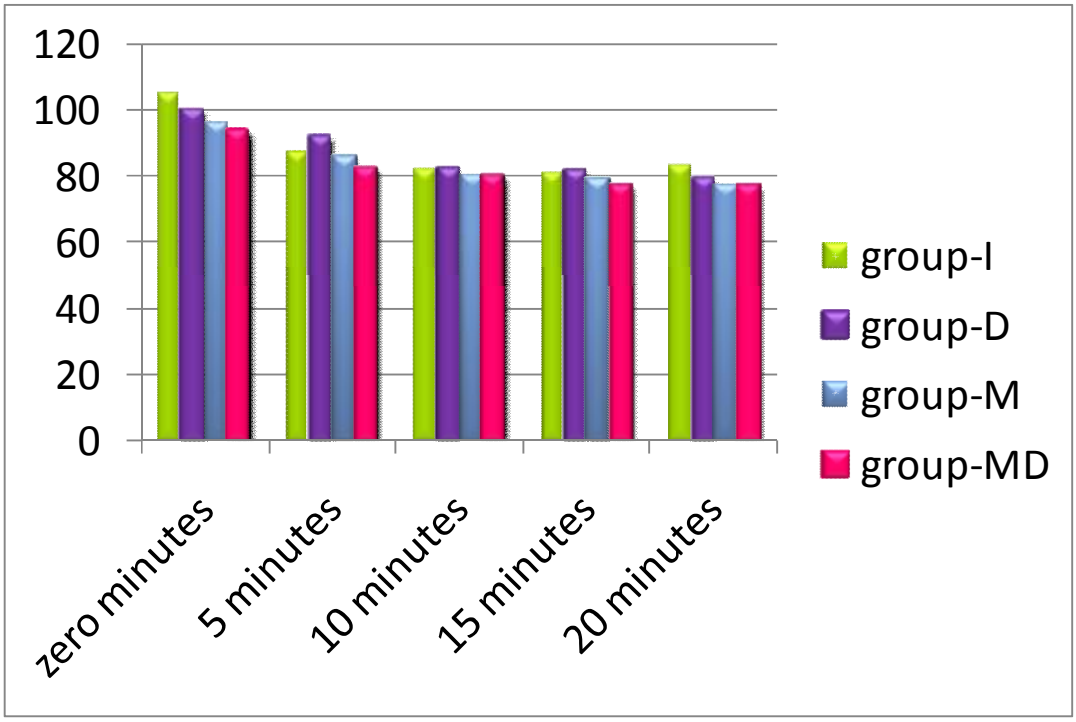

Figure 12: Intraoperative mean BP(mmHg) data in all studied groups.

Table-37: Summary of mean ± (SD)of Intraoperative mean blood pressure(mmHg) in all studied groups.

	Zero minutes	**5 minutes**	**10 minutes**	**15 minutes**	**20 minutes**
Group-1	105 ± (14.4)	87.7 ± (17.8)	82.5 ± (20.3)	81.2 ± (15.3)	83.6 ± (15.2)
Group-D	100 ± (13.9)	92.1 ± (14.3)	82.3 ± (13.8)	81.9 ± (15.1)	79.5 ± (12.2)
Group-M	96.5 ± (12.8)	86.1 ± (14.1)	80.5 ± (12.3)	79.5 ± (14.4)	77.7 ± (10.3)
Group-DM	93.7 ± (13.1)	82.7 ± (14.4)	80.2 ± (13.8)	77.3 ± (12.4)	77.2 ± (13.3)
Inter-group P value	0.0613	0.2756	0.9502	0.7519	0.3931

($P<0.05$) was considered statistically significant.

3. Duration of surgery(minutes) : (table-38, figure 12)

The mean of duration of surgery for I, D, M, and DM groups were 40.1, 39.3, 41.0 and 40.7 minutes, respectively, table-38.

4. Level of spinal block and duration of anesthesia(minutes): (table-39 and 40)

Level of spinal block in the four studied groups was ranged from T6 to T10. The mean duration of spinal anesthesia were 247 minutes in group-I, 253 minutes in group-D, 237 minutes in group-M and 238 minutes in group-DM, table-39 and 40.

Table-38: Duration of surgery(minutes) in all studied groups, including mean and standard deviation ± (SD):

Pt. NO	Group-I	Group-D	Group-M	Group-MD
1.	43.0	61.0	39.0	35.0
2.	28.0	49.0	33.0	55.0
3.	33.0	55.0	54.0	35.0
4.	27.0	44.0	46.0	52.0
5.	58.0	27.0	38.0	29.0
6.	36.0	36.0	64.0	43.0
7.	39.0	54.0	44.0	34.0
8.	46.0	26.0	57.0	64.0
9.	56.0	35.0	25.0	51.0
10.	49.0	22.0	41.0	32.0
11.	38.0	44.0	24.0	21.0
12.	39.0	43.0	34.0	60.0
13.	24.0	42.0	25.0	49.0
14.	49.0	30.0	43.0	30.0
15.	40.0	31.0	48.0	35.0
16.	38.0	26.0	40.0	26.0
17.	29.0	33.0	36.0	48.0
18.	41.0	30.0	51.0	20.0
19.	33.0	40.0	46.0	39.0
20.	55.0	57.0	31.0	55.0
Mean	40.1	39.3	41.0	40.7
Range	24-58	22-61	24-64	20-64
SD±	9.81	11.5	10.8	13.0
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

$P = 0.9666$ ($P<0.05$) was considered statistically significant.

Table-39: Level of spinal block in all studied groups, including mean and standard deviation ± (SD):

Pt. NO	Group-I	Group-D	Group-M	Group-MD
1.	T8	T 6	T8	T8
2.	T9	T8	T9	T 7
3.	T 7-T 8	T 7-T8	T7	T9
4.	T8	T6-T7	T7	T 7
5.	T8-T9	T9	T8	T6
6.	T9	T 7-T8	T9	T8
7.	T10	T8-T9	T7	T9
8.	T7	T 7-T8	T6	T 7
9.	T8	T6-T 7	T7	T 7
10.	T9	T8	T8	T10
11.	T8	T9	T10	T8
12.	T 7-T8	T 7	T7	T8
13.	T8	T 8-T9	T9	T 7
14.	T9	T8	T8	T6
15.	T8	T 7	T7	T9
16.	T8	T9	T8	T9
17.	T7	T8	T7	T6
18.	T9	T10	T6	T8
19.	T9	T8-T9	T7	T 7
20.	T8-T9	T9	T8	T9
Mean	--	--	--	--
Range	T7-T10	T6-T10	T6-T10	T6-T10
SD±	--	--	--	--
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

$P = 0.213$. ($P<0.05$) was considered statistically significant.

Table-40: Duration of anesthesia(minutes) in all studied groups, including mean and standard deviation± (SD):

Pt. NO	Group-I	Group-D	Group-M	Group-MD
1.	240	240	245	240
2.	245	265	220	275
3.	260	260	245	220
4.	245	270	210	260
5.	200	275	255	255
6.	248	260	240	230
7.	255	267	230	220
8.	270	270	225	195
9.	266	265	255	210
10.	250	200	244	200
11.	255	270	260	270
12.	260	245	200	200
13.	250	255	235	230
14.	200	240	198	230
15.	240	260	220	260
16.	205	250	230	220
17.	260	248	265	275
18.	257	205	255	265
19.	264	266	270	255
20.	272	255	240	245
Mean	247	253	237	238
Range	200-272	200-275	198-270	195-275
SD±	21.6	20.1	20.5	26.4
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

$P = 0.0753$. ($P<0.05$) was considered statistically significant.

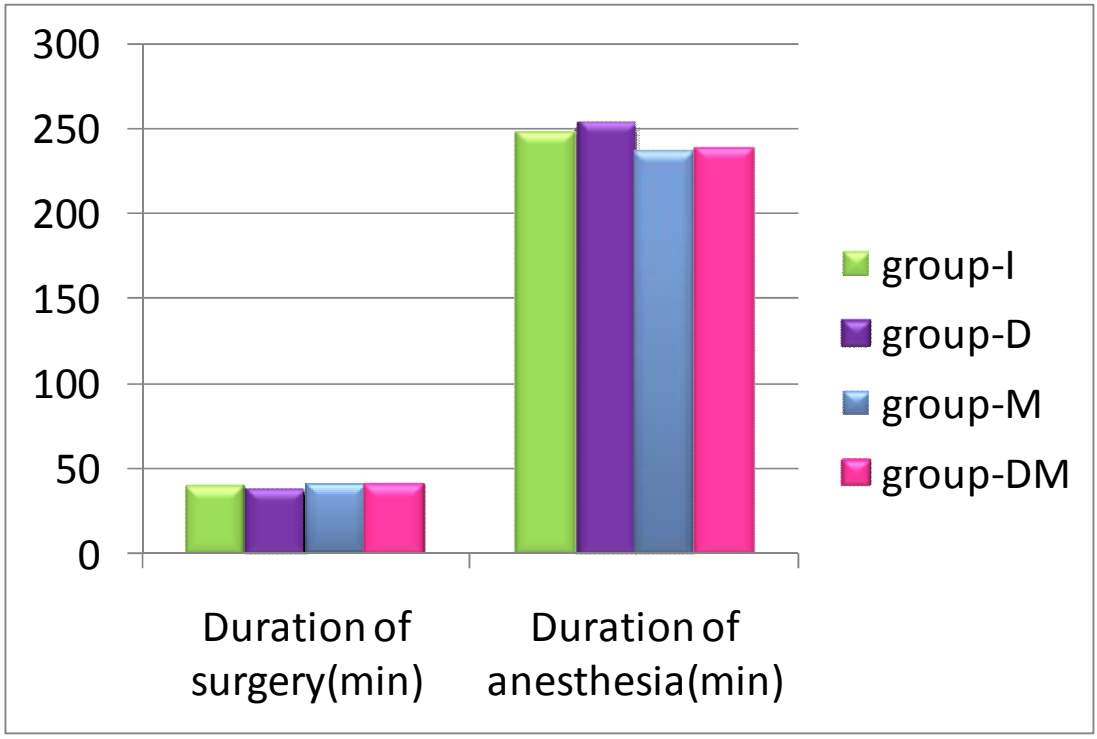

Figure 13: Duration of surgery and Duration of anesthesia(minutes) of all groups.

5- fetal apgar score : apgar score was done at 1 minute and after 5 minutes of delivery , all babies were within the normal range (7-10).

6. Postoperative pain intensity data: (tables 41-45)

Postoperative pain intensity was evaluated by the four-category verbal rating scale-VRS (no pain (I), mild pain (II), moderate pain (III), and severe pain (IV)) at 4 different intervals: 6^{th} hour (T0), 12^{th} hour (T1), 18^{th} hour (T2), and 24^{th} hour (T3). Postoperative pain management was standardized in all groups by giving 75 mg of diclofenac sodium intramuscularly when VRS $\geq$ 3.

Group-I:

The means of VRS after 6 hours, 12 hours, 18 hours, 24 hours were 1.20, 1.60, 1.65 and 1.30, respectively.

Group-II (D):

The means of VRS after 6 hours, 12 hours, 18 hours, 24 hours were 1.10, 1.40, 1.55 and 1.15, respectively.

Group-III (M):

The means of VRS after 6 hours, 12 hours, 18 hours, 24 hours were 1.15 , 1.50 , 1.75 and 1.20, respectively.

Group-IV (DM):

The means of VRS after 6 hours, 12 hours, 18 hours, 24 hours were 1.05, 1.70 , 1.70 and 1.15, respectively.

7.Rescue IM diclofenac given postoperatively: (tables 41-45)

The mean of doses of IM diclofenac given postoperatively were 90.0, 71.3, 86.3 and 67.5 in groups I, D, M, and DM, respectively.

Table-41: Pain intensity at different intervals, and IM voltaren given postoperatively for group-I patients, including the mean and standard deviation ± (SD).

Pt. NO.	6 hrs T(0)	12 hrs T(1)	18 hrs T(2)	24 hrs T(3)	IM diclofenac sodium (mg)
1.	1.0	2	3.0	2.0	75
2.	1.0	2	2.0	1.0	75
3.	1.0	1	1.0	2.0	75
4.	2.0	1	1.0	1.0	75
5.	1.0	2	2.0	2.0	150
6.	1.0	3	3.0	1.0	75
7.	1.0	1	1.0	1.0	75
8.	2.0	1	2.0	1.0	75
9.	1.0	2	1.0	1.0	150
10.	1.0	1	1.0	1.0	75
11.	1.0	1	3.0	3.0	75.0
12.	1.0	1	1.0	1.0	75.0
13.	1.0	1	1.0	1.0	150
14.	2.0	2	1.0	1.0	75.0
15.	1.0	1	2.0	1.0	75.0
16.	1.0	2	2.0	1.0	75.0
17.	2.0	3	2.0	1.0	150
18.	1.0	2	2.0	2.0	75.0
19.	1.0	1	1.0	1.0	75.0
20.	1.0	2	1.0	1.0	75.0
Mean	1.20	1.60	1.65	1.30	90.0
Range	1-2	1-3	1-3	1-3	75-150
SD±	0.410	0.681	0.745	0.571	30.8

Table-42: Pain intensity at different intervals, and IM voltaren given postoperatively for group-II (D) patients, including the mean and standard deviation ± (SD).

Pt. NO.	6 hrs T(0)	12 hrs T(1)	18 hrs T(2)	24 hrs T(3)	IM diclofenac sodium (mg)
1.	1.0	1	2	1.0	75.0
2.	1.0	1	2	1.0	75.0
3.	1.0	2	1	2.0	75.0
4.	2.0	1	1	1.0	75.0
5.	1.0	1	1	1.0	0.0
6.	1.0	1	2	2.0	75.0
7.	1.0	1	1	1.0	0.0
8.	1.0	3	2	1.0	75.0
9.	1.0	1	2	1.0	150
10.	2.0	2	1	1.0	75.0
11.	1.0	2	1	1.0	75.0
12.	1.0	1	2	1.0	75.0
13.	1.0	1	2	1.0	75.0
14.	1.0	3	2	1.0	75.0
15.	1.0	1	1	1.0	150
16.	1.0	1	2	1.0	75.0
17.	1.0	2	1	1.0	75.0
18.	1.0	1	2	1.0	75.0
19.	1.0	1	2	1.0	75.0
20.	1.0	1	1	1.0	0.0
Mean	1.10	1.40	1.55	1.15	71.3
Range	1-2	1-3	1-2	1-2	0-150
SD±	0.308	0.681	0.51	0.366	38.3
P value between group-I and II	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-43: Pain intensity at different intervals, and IM voltaren given postoperatively for group-III (M) patients, including the mean and standard deviation± (SD).

Pt .NO.	6 hrs T(0)	12 hrs T(1)	18 hrs T(2)	24 hrs T(3)	IM diclofenac sodium (mg)
1.	1.0	1	2	1.0	75.0
2.	1.0	2	1	2.0	75.0
3.	1.0	1	2	1.0	75.0
4.	1.0	2	1	1.0	75.0
5.	1.0	2	2	1.0	75.0
6.	1.0	1	2	2.0	75.0
7.	1.0	2	1	1.0	75.0
8.	2.0	1	2	1.0	150.0
9.	1.0	1	1	1.0	75.0
10.	1.0	1	2	1.0	75.0
11.	2.0	3	3	2.0	75.0
12.	1.0	1	2	1.0	75.0
13.	1.0	2	2	1.0	75.0
14.	2.0	3	2	1.0	150.0
15.	1.0	2	2	1.0	75.0
16.	1.0	1	2	2.0	75.0
17.	1.0	1	2	1.0	75.0
18.	1.0	1	2	1.0	75.0
19.	1.0	1	1	1.0	150.0
20.	1.0	1	1	1.0	75.0
Mean	1.15	1.50	1.75	1.20	86.3
Range	1-2	1-3	1-3	1-2	75-150
SD±	0.366	0.688	0.550	0.410	27.5
P value between group-I and III	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-44: Pain intensity at different intervals, and IM voltaren given postoperatively for group-IV (DM) patients, including the mean and standard deviation ± (SD).

Pt. NO.	6 hrs T(0)	12 hrs T(1)	18 hrs T(2)	24 hrs T(3)	IM diclofenac sodium (mg)
1.	1.0	1	2	3.0	75.0
2.	1.0	1	2	1.0	75.0
3.	1.0	1	1	1.0	75.0
4.	1.0	2	2	1.0	0.0
5.	1.0	1	2	1.0	0.0
6.	1.0	1	2	1.0	75.0
7.	1.0	3	2	1.0	75.0
8.	1.0	1	2	1.0	75.0
9.	1.0	1	2	1.0	75.0
10.	2.0	2	1	1.0	150
11.	1.0	2	1	1.0	75.0
12.	1.0	1	2	1.0	75.0
13	1.0	1	1	1.0	0.0
14.	1.0	3	2	1.0	75.0
15.	1.0	2	2	2.0	75.0
16.	1.0	3	2	1.0	75.0
17.	1.0	2	1	1.0	75.0
18.	1.0	3	2	1.0	75.0
19.	1.0	2	1	1.0	75.0
20.	1.0	1	2	1.0	75.0
Mean	1.05	1.70	1.70	1.15	67.5
Range	1-2	1-3	1-2	1-3	0-150
SD±	0.224	0.801	0.470	0.489	33.5
P value between group-I and IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table-45: Summary of means of VRS in all studied groups:

	Group-I	Group-D	Group-M	Group-DM	*P*-value
T(0) interval	1.2 (±0.41)	1.1 (±0.308)	1.15 (±0.366)	1.05 (±0.224)	0.5285
T(1) interval	1.6 (±0.681)	1.4 (±0.681)	1.5 (±0.688)	1.7 (±0.801)	0.5836
T(2) interval	1.65 (±0.745)	1.55 (±0.51)	1.75 (±0.55)	1.7 (±0.47)	0.7282
T(3) interval	1.3 (±0.571)	1.15 (±0.366)	1.2 (±0.41)	1.15 (±0.489)	0.2885

P= 0.5924. ($P<0.05$) was considered statistically significant.

8- postoperative heart rate data(beat / min):as shown in tables (45-49)

Table 45: Postoperative Heart rate(beat/min) data for group-I patients, including mean and standard deviation± (SD):

Pt. No	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1	102.0	65.0	66.0	62.0
2	80.0	84.0	90.0	85.0
3	77.0	62.0	72.0	90.0
4	100.0	90.0	88.0	88.0
5	73.0	92.0	85.0	90.0
6	63.0	110.0	100.0	115.0
7	111.0	115.0	92.0	85.0
8	102.0	64.0	62.0	80.0
9	64.0	100.0	95.0	80.0
10	95.0	99.0	77.0	75.0
11	80.0	90.0	85.0	95.0
12	95.0	100.0	80.0	90.0
13	95.0	77.0	88.0	95.0
14	75.0	85.0	63.0	78.0
15	88.0	95.0	90.0	85.0
16	85.0	80.0	94.0	90.0
17	66.0	78.0	77.0	66.0
18	75.0	80.0	80.0	85.0
19	67.0	80.0	90.0	64.0
20	100.0	85.0	85.0	75.0
Mean	84.7	86.6	83.0	83.7
±SD	14.7	14.3	10.7	12.1
Range	63-111	62-115	62-100	62-115

Tables 46: Postoperative Heart rate(beat/min) data for group-II (D) patients, including mean and standard deviation± (SD):

Pt. NO	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	75.0	80.0	82.0	78.0
2.	72.0	100.0	94.0	95.0
3.	95.0	90.0	85.0	80.0
4.	111.0	120.0	100.0	95.0
5.	85.0	90.0	75.0	80.0
6.	70.0	80.0	68.0	69.0
7.	80.0	75.0	70.0	68.0
8.	94.0	82.0	76.0	72.0
9.	80.0	70.0	75.0	80.0
10.	90.0	72.0	90.0	82.0
11.	115.0	110.0	90.0	75.0
12.	90.0	85.0	80.0	75.0
13.	66.0	110.0	90.0	90.0
14.	88.0	85.0	80.0	70.0
15.	98.0	90.0	80.0	80.0
16.	76.0	95.0	90.0	95.0
17.	85.0	75.0	85.0	90.0
18.	90.0	75.0	85.0	80.0
19.	82.0	94.0	90.0	80.0
20.	63.0	100.0	90.0	95.0
Mean	85.3	88.9	83.8	81.5
SD±	13.5	13.8	8.28	9.02
Range	63-111	70-120	68-100	68-95
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table 47: Postoperative Heart rate(beat/min) data for group-III (M) patients, including mean and standard deviation± (SD):

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	75.0	80.0	82.0	78.0
2.	72.0	100.0	94.0	95.0
3.	95.0	90.0	85.0	80.0
4.	111.0	120.0	100.0	95.0
5.	85.0	90.0	75.0	80.0
6.	70.0	80.0	68.0	69.0
7.	80.0	75.0	70.0	68.0
8.	94.0	82.0	76.0	72.0
9.	80.0	70.0	75.0	80.0
10.	90.0	72.0	90.0	82.0
11.	115.0	110.0	90.0	75.0
12.	90.0	85.0	80.0	75.0
13.	66.0	110.0	90.0	90.0
14.	88.0	85.0	80.0	70.0
15.	98.0	90.0	80.0	80.0
16.	76.0	95.0	90.0	95.0
17.	85.0	75.0	85.0	90.0
18.	90.0	75.0	85.0	80.0
19.	82.0	94.0	90.0	80.0
20.	63.0	100.0	90.0	95.0
Mean	93.3	86.3	88.65	84.4
SD±	9.5	10.6	7.9	7.4
Range	80-115	70-112	75-105	70-100
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table 48: Postoperative Heart rate(beat/min) data for group-IV (DM) patients, including mean and standard deviation± (SD):

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	88.0	75.0	74.0	80.0
2.	88.0	80.0	78.0	84.0
3.	111.0	80.0	80.0	85.0
4.	88.0	90.0	89.0	75.0
5.	80.0	90.0	82.0	88.0
6.	100.0	90.0	100.0	90.0
7.	92.0	70.0	78.0	68.0
8.	88.0	90.0	92.0	88.0
9.	85.0	94.0	92.0	88.0
10.	102.0	100.0	95.0	75.0
11.	74.0	88.0	88.0	74.0
12.	77.0	100.0	75.0	92.0
13.	83.0	80.0	79.0	77.0
14.	105.0	100.0	90.0	82.0
15.	80.0	84.0	92.0	77.0
16.	72.0	86.0	92.0	76.0
17.	80.0	77.0	68.0	70.0
18.	61.0	78.0	84.0	80.0
19.	92.0	88.0	90.0	95.0
20.	80.0	76.0	70.0	72.0
Mean	88.35	85.8	84.4	80.8
SD±	8.1	8.7	8.9	7.7
Range	72-105	70-100	68-100	68-95
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table49: Summary of mean ± (SD) of postoperative heart rate(beat/min) in all studied groups:

	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
Group-I	84.7±(14.7)	86.6±(14.3)	83.0±(10.7)	83.7±(12.1)
Group-D	85.3±(13.5)	±(13.8)88.9	83.8±(8.28)	81.5±(9.02)
Group-M	±(9.5)93.3	±(10.6)86.3	±(7.9)88.65	±(7.4)84.4
Group-DM	±(8.1)88.35	±(8.7)85.8	±(8.9)84.4	±(7.7)80.8
Inter-groups *P* value	0.7998	0.8544	0.8826	0.5601

(P<0.05) was considered statistically significant.

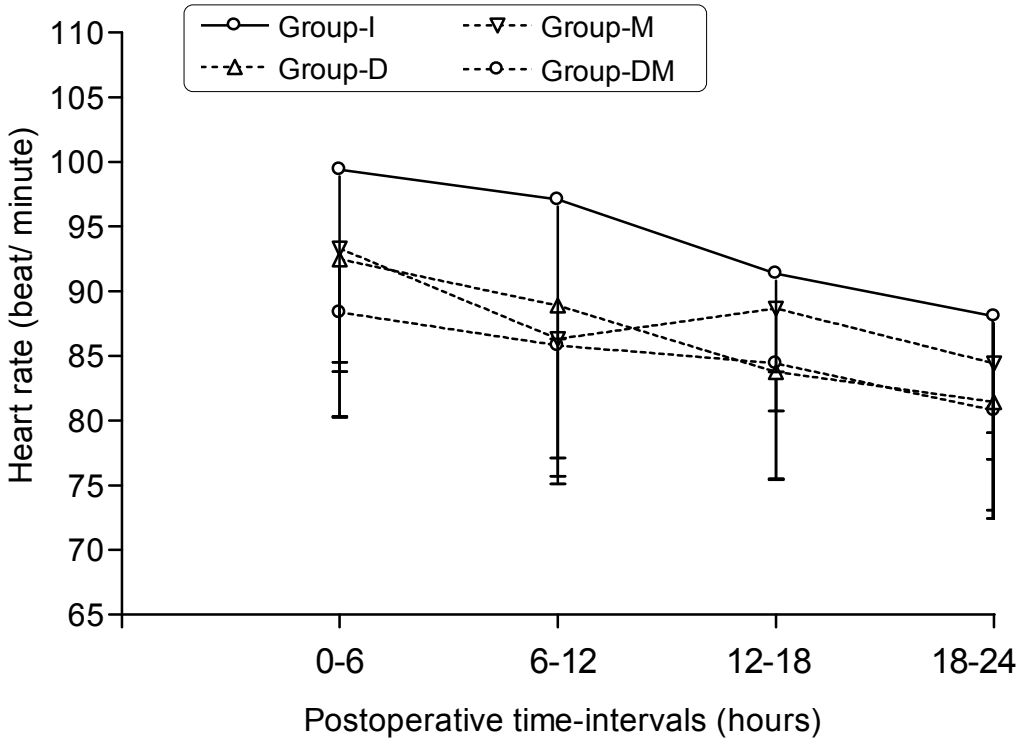

Figure 14 : Mean of postoperative heart rate in all studied groups. No significant inter-group differences were detected at any interval. Vertical bars are the standard deviation.

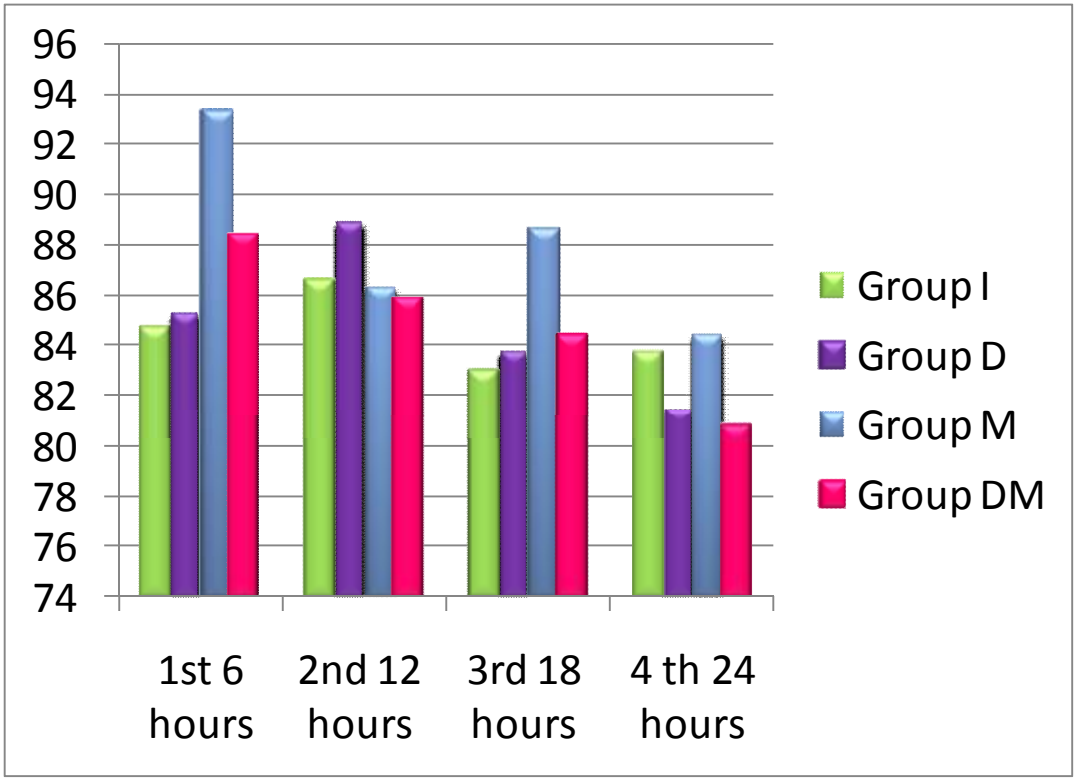

Figure 15: Mean of postoperative heart(beat/min) rate in all studied groups.

9- Postoperative Mean and ±SD data of Mean BP(mmHg) data:

Table 50: Postoperative Mean BP(mmHg)data for group I-including mean and SD:-

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	88	90	93	91
2.	83	95	90	88
3.	88	84	90	84
4.	70	84	80	76
5.	80	74	88	84
6.	82	87	60	63
7.	66	68	70	72
8.	65	66	62	70
9.	76	82	68	73
10.	70	72	69	78
11.	80	85	72	80
12.	62	66	88	80
13.	71	75	70	80
14.	82	88	88	90
15.	68	74	71	78
16.	62	64	88	80
17.	63	70	80	75
18.	73	78	77	81
19.	70	72	74	76
20.	74	75	76	84
Mean	73.65	77.45	77.7	79.15
Range	62-88	64-95	60-93	63-91
SD±	8.3	9.0	10.0	6.8

Table 51: Postoperative Mean BP(mmHg)data for group D-including mean and ±SD:-

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	78	80	82	84
2.	69	70	67	68
3.	68	68	70	72
4.	82	85	80	83
5.	72	75	69	73
6.	83	88	82	85
7.	76	78	74	78
8.	72	75	70	74
9.	84	88	83	86
10.	73	76	70	72
11.	77	80	72	80
12.	76	80	73	78
13.	70	71	66	70
14.	72	75	70	72
15.	82	84	80	82
16.	76	78	77	79
17.	70	70	72	73
18.	88	74	80	88
19.	89	75	83	80
20.	93	78	93	88
Mean	77.5	77.4	75.95	78.25
Range	68-93	68-88	66-93	68-88
SD±	7.2	5.7	7.0	6.2
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table 52: Postoperative Mean BP(mmHg)data for group M-including mean and± SD:-

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	77	78	80	82
2.	75	79	77	80
3.	73	76	74	76
4.	78	79	80	83
5.	67	68	70	73
6.	65	68	64	66
7.	69	70	70	73
8.	75	78	76	78
9.	73	75	74	76
10.	69	72	70	72
11.	83	85	82	84
12.	78	80	80	83
13.	76	78	77	80
14.	73	78	72	75
15.	93	88	93	90
16.	84	82	93	78
17.	70	68	80	74
18.	72	80	68	70
19.	80	72	74	88
20.	78	80	68	74
Mean	77.4	76.7	76.1	77.75
Range	65-93	68-88	64-93	66-90
SD±	6.5	5.6	7.5	6.0
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table 53: Postoperative Mean BP(mmHg)data for group DM-including mean and ±SD:-

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	71	75	70	80
2.	82	88	74	82
3.	68	74	71	78
4.	62	64	65	69
5.	63	70	68	75
6.	73	78	77	81
7.	70	72	74	76
8.	74	75	76	84
9.	64	66	62	68
10.	72	80	67	74
11.	83	85	82	84
12.	78	80	80	83
13.	76	78	77	80
14.	70	82	88	79
15.	93	80	88	90
16.	84	82	93	78
17.	80	68	74	74
18.	72	70	68	70
19.	84	73	74	88
20.	93	84	73	74
Mean	75.6	76.2	75.05	78.35
Range	62-93	64-88	62-93	68-90
SD±	9.0	6.6	8.0	6.0
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05

Table54:Summary of mean ± (SD)of Postoperative of mean blood(mmHg) pressure in all studied groups:

	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
Group-I	73.65±(8.3)	77.45±(9.0)	77.7±(10.0)	79.15±(6.8)
Group-D	77.5±(7.2)	77.4±(5.7)	75.95±(7.0)	78.25±(6.2)
Group-M	75.4±(6.5)	76.7±(5.6)	76.1±(7.5)	77.75±(6.0)
Group-DM	75.6±(9.0)	76.2±(6.6)	75.05±(8.0)	78.35±(6.0)
Inter-groups *P* value	0.4910	0.9123	0.7826	0.9161

(*P*<0.05) was considered statistically significant.

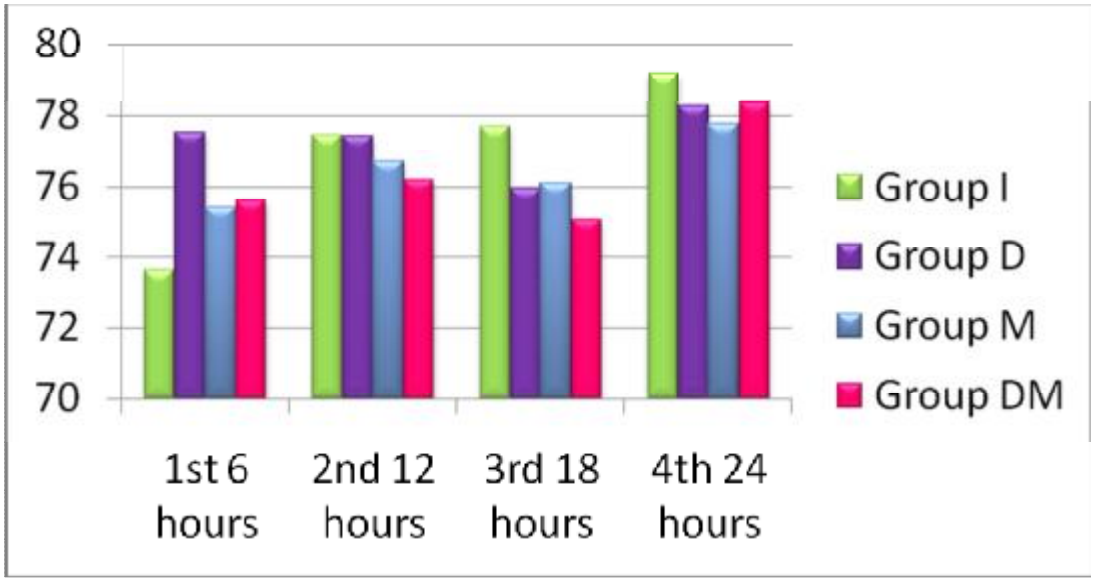

Figure 16: Mean of postoperative mean arterial blood pressure(mmHg) in all studied groups.

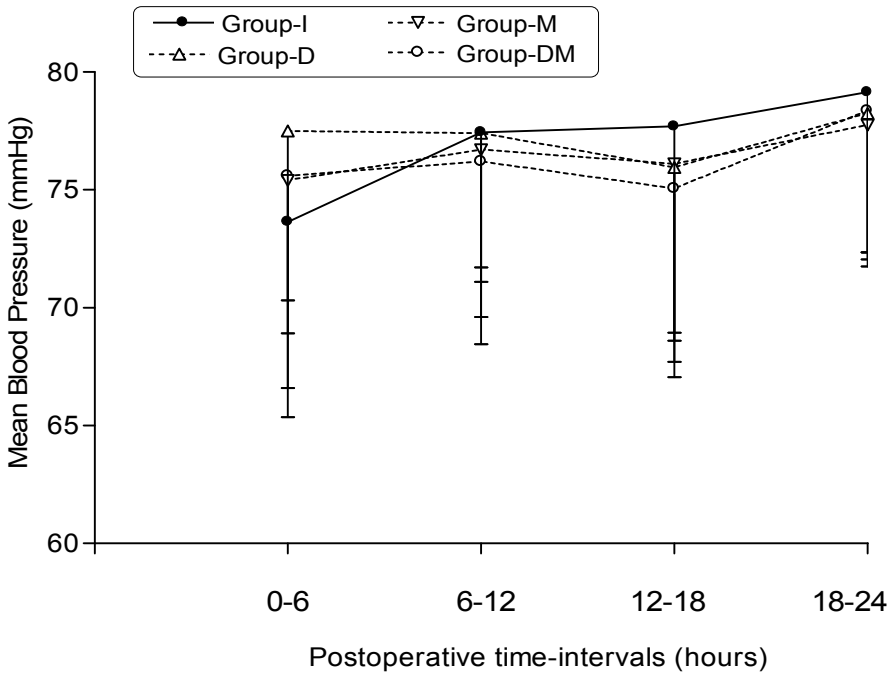

Figure 17: Mean of postoperative mean arterial blood pressure in all studied groups. No significant inter-group differences were detected at any interval. Vertical bars are the standard deviation.

10- postoperative respiratory rate data including mean and ±SD:(tables 55-58)

Table 55: Postoperative data for respiratory rate(breath/min) for group I including mean and ±SD:

Pt NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	14	15	14	16
2.	14	14	14	13
3.	14	14	14	15
4.	12	16	16	17
5.	15	18	15	15
6.	15	13	15	14
7.	17	15	13	16
8.	14	14	14	18
9.	16	15	16	15
10.	14	15	14	16
11.	16	14	12	14
12.	14	14	14	15
13.	16	15	16	18
14.	16	14	13	17
15.	15	17	15	16
16.	16	14	16	15
17.	14	14	14	18
18.	15	15	15	14
19.	16	16	16	17
20.	15	14	15	16
Mean	14.9	14.8	14.55	15.75
Range	12-17	13-18	12-16	13-16
SD ±	1.1653	1.196	1.146	1.446

(P<0.05) was considered statistically significant.

Table 56: Postoperative data for respiratory rate(breath/min) for group D including mean and ±SD:

Pt NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	14	13	15	16
2.	12	13	14	13
3.	14	14	16	15
4.	15	17	16	17
5.	16	18	17	15
6.	15	13	15	14
7.	15	18	15	16
8.	14	14	14	18
9.	14	16	16	13
10.	16	15	14	16
11.	15	16	12	15
12.	16	13	14	15
13.	15	17	16	18
14.	17	15	16	17
15.	16	17	17	16
16.	15	14	17	15
17.	14	16	14	17
18.	14	16	15	16
19.	17	16	15	15
20.	14	16	15	17
Mean	14.9	15.35	15.15	15.7
Range	12-17	13-18	12-17	13-18
SD ±	1.21	1.663	1.268	1.418
P values between group-I & II	P > 0.05	P > 0.05	P > 0.05	P > 0.05

(P<0.05) was considered statistically significant.

Table 57: Postoperative data for respiratory rate(breath/min) for group M including mean and ±SD:

Pt NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	13	15	15	16
2.	17	16	14	17
3.	15	16	16	15
4.	15	17	16	17
5.	17	18	17	15
6.	15	16	15	14
7.	17	18	15	16
8.	17	14	14	18
9.	16	18	16	13
10.	16	17	14	16
11.	16	17	15	15
12.	15	16	17	15
13.	16	17	16	18
14.	17	18	16	17
15.	16	17	17	16
16.	15	14	14	15
17.	14	15	14	17
18.	16	16	15	16
19.	17	16	16	15
20.	16	15	15	17
Mean	15.8	16.3	15.35	15.9
Range	13-17	14-18	14-17	13-18
SD ±	1.105	1.261	1.04	1.294
P values between group-I & III	P > 0.05	P > 0.05	P > 0.05	P > 0.05

($P<0.05$) was considered statistically significant.

Table 58: Postoperative data for respiratory rate(breath/min) for group DM including mean and ±SD:

Pt NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	13	15	15	16
2.	17	16	14	17
3.	15	16	16	15
4.	15	17	16	15
5.	17	18	17	15
6.	15	16	15	14
7.	16	14	14	16
8.	15	15	14	13
9.	16	15	16	13
10.	16	17	14	16
11.	16	17	15	15
12.	15	16	14	15
13.	16	15	16	18
14.	16	14	15	17
15.	14	15	14	16
16.	14	14	15	15
17.	15	14	14	16
18.	15	15	15	16
19.	15	16	15	14
20.	14	15	15	16
Mean	15.25	15.5	14.95	15.4
Range	13-17	14-18	14-17	13-18
SD ±	1.0195	1.147	0.887	1.273
P values between group-I & IV	P > 0.05	P > 0.05	P > 0.05	P > 0.05

($P<0.05$) was considered statistically significant.

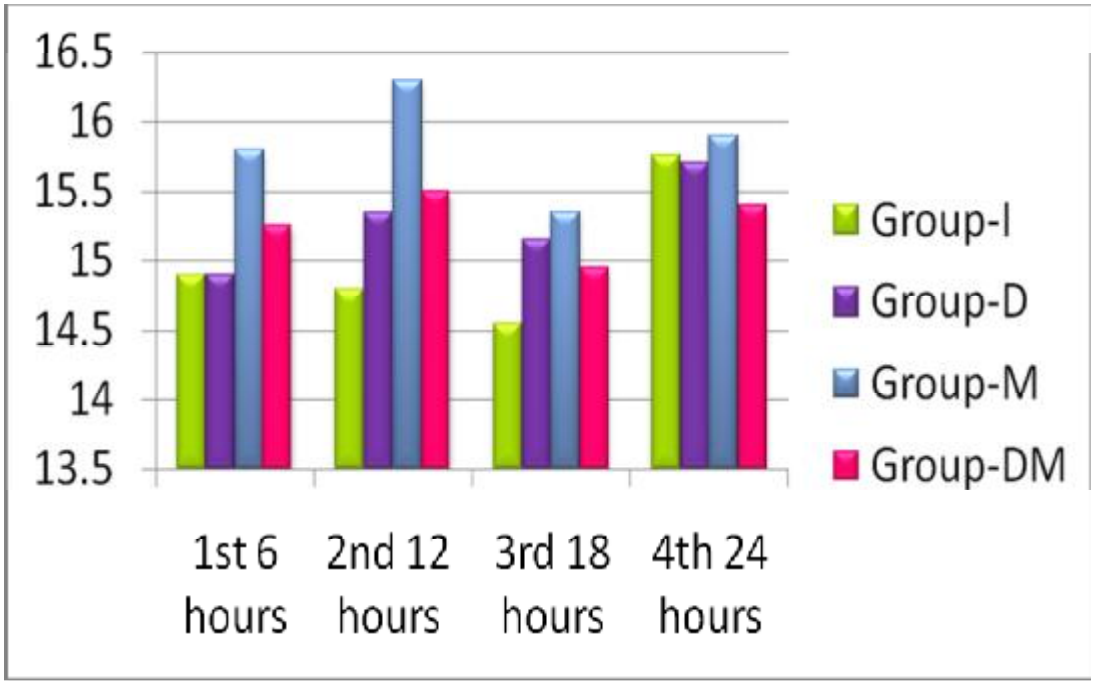

Figure 18: Mean of postoperative respiratory (cycle\min) rate pressure in all studied groups.

11. Intra- and post-operative emesis: (tables 59-72)

The overall incidence of intra-operative emetic episodes (nausea, retching and vomiting) was significantly different (P <0.0001) from the placebo group-I, and was 23, 7, 6 and 4 in the I, D, M and DM groups respectively. The corresponding postoperative overall incidence was 29, 11, 8, and 3, respectively (P<0.0001), tables-59-71. However, there were no significant statistical differences between the treated groups D, M and DM when compared to each other, neither intra- or postoperatively, (tables 59-72).

Intra-operative emetic episodes were experienced by 15 (75%), 7 (35%), 5 (25%) and 4 (20%) patients in the I, D, M and DM groups, respectively (P =0.0001). The respective postoperative values were 16 (80%), 10 (50%), 7 (35%) and 3 (15%) patients of the corresponding groups (P =0.0001). Statistically significant inter-treated group differences were obtained only between group D and DM postoperatively (p<0.05), (tables 59-72).

Intraoperatively, rescue metoclopramide was given to 5 patients in group-I and to 2 patients in group-D (summation of P value = 0.0132); unlike groups M and MD ($\boldsymbol{P}$ < 0.05), group D did not differ significantly from the control group-I. Postoperatively metoclopramide was needed only for 3 patients in group-I (summation of P value = 0.0232) with non-significant inter-treated group differences, (tables 59-72).

No complications related to the studied drugs were observed in any group.

Table-59: Intra-operative incidence of nausea, retching & vomiting data for group-I.

Pt. NO.	Type of incidence	Time of incidence (minutes from induction)	Drug Delivered
1.	No	/	/
2.	Nausea+Retching	15 min + 25 min	metoclopramide 10mg IV
3.	vomiting	5 minutes	NO
4.	Nausea	8 minutes	NO
5.	Vomiting	15 minutes	NO
6.	Nausea	35 minutes	NO
7.	Nausea+Vomiting	5 minutes+9 minutes	metoclopramide 10mg IV
8.	Nausea	25 minutes	NO
9.	Nausea+Vomiting	6 minutes+ 9 minutes	metoclopramide 10mg IV
10.	Retching	9 minutes	NO
11.	Nausea	5 minutes	NO
12.	Retching	10 minutes	metoclopramide 10mg IV
13.	NO	/	/
14.	Nausea	18 minutes	NO
15.	NO	/	/
16.	Nausea+Vomiting	10 minutes+19 minutes	metoclopramide 10mg IV
17.	Retching+Nausea	25 minutes+29 minutes	NO
18.	NO	/	/
19.	Nausea+Vomiting + Nausea	15 minutes +18 minutes + 45 minutes	metoclopramide 10mg IV
20.	NO	/	/

Table-60: Intra-operative incidence of nausea, retching & vomiting data for group-II (D).

Pt. NO.	Type of incidence	Time of incidence(minutes from induction)	Drug delivered
1.	NO	NO	NO
2.	Nausea	17 minutes	NO
3.	NO	NO	NO
4.	NO	NO	NO
5.	Vomiting	10 minutes	metoclopramide 10mg IV
6.	Nausea	20 minutes	NO
7.	Nausea	11 minutes	NO
8.	NO	NO	NO
9.	NO	NO	NO
10.	NO	NO	NO
11.	NO	NO	NO
12.	NO	NO	NO
13.	NO	NO	NO
14.	Nausea	2 minutes	metoclopramide 10mg IV
15.	NO	NO	NO
16.	NO	NO	NO
17.	Nausea	12 minutes	NO
18.	NO	NO	NO
19.	Nausea	NO	NO
20.	NO	NO	NO

Table-61: Intra-operative incidence of nausea, retching & vomiting data for group-III (M).

Pt NO.	Type of incidence	Time of incidence(minutes from induction)	Drug delivered
1.	NO	NO	NO
2.	Nausea	3 minutes	NO
3.	NO	NO	NO
4.	NO	NO	NO
5.	NO	NO	NO
6.	NO	NO	NO
7.	NO	NO	NO
8.	NO	NO	NO
9.	NO	NO	NO
10.	Nausea	15 minutes	NO
11.	NO	NO	NO
12.	Retching	50 minutes	NO
13.	NO	NO	NO
14.	NO	NO	NO
15.	Nausea + Vomiting	10 minutes + 13 minutes	NO
16.	NO	NO	NO
17.	NO	NO	NO
18.	NO	NO	NO
19.	NO	NO	NO
20.	Nausea	10 minutes	NO

Table-62: Intra-operative incidence of nausea, retching & vomiting for group-IV (DM).

Pt NO.	Type of incidence	Time of incidence(minutes from induction)	Drug delivered
1.	NO	NO	NO
2.	NO	NO	NO
3.	NO	NO	NO
4.	NO	NO	NO
5.	Nausea	15 Minutes	NO
6.	NO	NO	NO
7.	NO	NO	NO
8.	NO	NO	NO
9.	NO	NO	NO
10.	NO	NO	NO
11.	NO	NO	NO
12.	NO	NO	NO
13.	Nausea	10 Minutes	NO
14.	NO	NO	NO
15.	NO	NO	NO
16.	Retching	20 minutes	NO
17.	NO	NO	NO
18	NO	NO	NO
19.	NO	NO	NO
20.	Nausea	10 minutes	NO

Table-63: Types and incidence of intra-operative emetic episodes in each of the studied groups.

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Nausea	13 episodes (12 pts) (60% of pts)	6 episodes (6 pts) (30%)	4 episodes (4 pts) (20%)	3 episodes (3 pts) (15%)
Retching	4 episodes (4) (20%)	0 episode (0) (0%)	1 episode (1) (5%)	1 episode (1) (5%)
Vomiting	6 episode (6) (30%)	1 episode (1) (5%)	1 episode (1) (5%)	0 episode (0) (0%)
Total	23 episodes in 15 pts (75%)	7 episodes in 7pts (35%)	6 episodes in 5pts (25%)	4 episodes in 4pts (20%)

Values are expressed as total numbers of episodes (and percentage of patients).

Table-64: Summation of intra-operative emetic episodes in all studied groups

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Mean	1.10	0.400	0.300	0.200
Range	0-3	0-2	0-2	0-1
SD±	0.788	0.598	0.571	0.410
P value between group-I and other groups	--	P < 0.001	P < 0.001	P < 0.001

NB. No significant differences between D vs M or DM, M vs DM. (*P<0.0001)*

Table-65: Intra-operative IV metoclopramide requirements (mg) in all studied groups:

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Mean	2.50	1.00	0.000	0.000
Range	0-10	0-10	0.000	0.000
SD±	4.44	3.08	0.000	0.000
P value between group-I and other groups	**--**	P > 0.05	P < 0.05*	P < 0.05*

NB. No significant differences between D vs M or DM, M vs DM. *P*= 0.0132

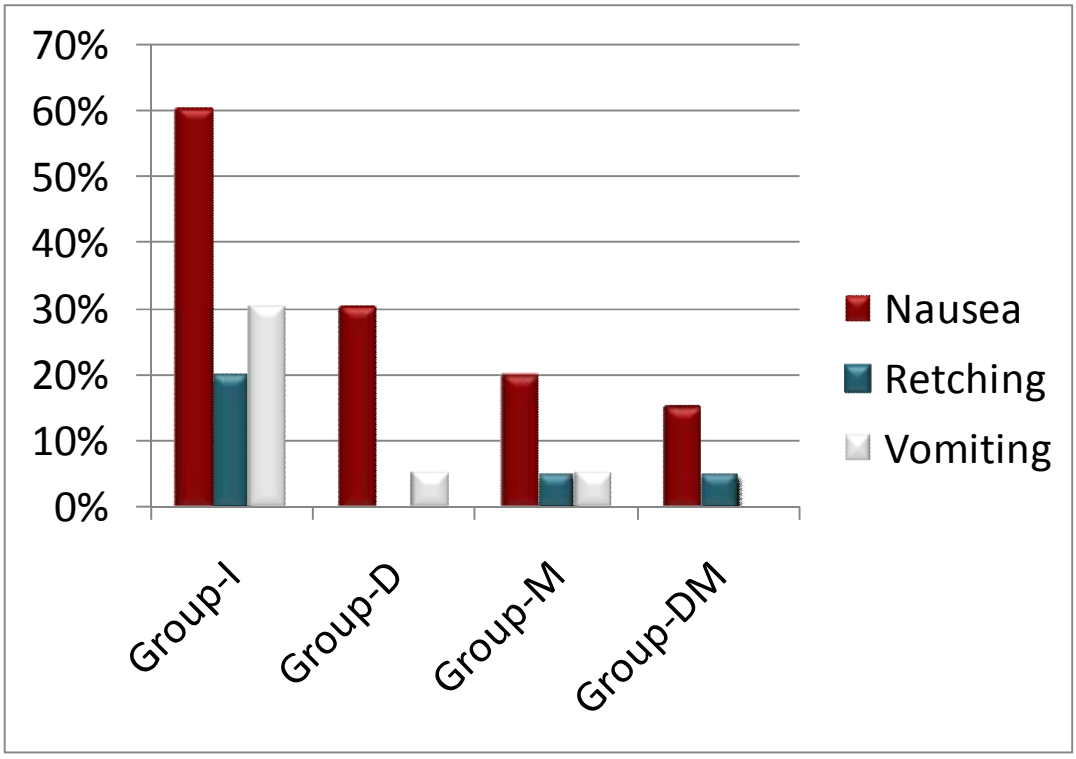

Figure 19: Intraoperative emetic episodes in all studied groups.

Note : Group D retching is 0% (0 episode).

Group DM vomiting is 0% (0 episoide).

Table-66: Postoperative assessment of nausea, retching and vomiting of group-I.

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours	Drug delivered
1.	Vomiting	Retching	No	No	NO
2.	No	No	No	No	NO
3.	Nausea	No	No	Vomiting	NO
4.	Nausea	No	No	No	NO
5.	No	Vomiting	Retching	No	NO
6.	Vomiting	No	No	No	NO
7.	No	Nausea	Nausea	No	metoclopramide 10mg IV
8.	Nausea	No	No	No	NO
9.	No	No	Nausea	Nausea	metoclopramide 10mg IV
10.	Retching	No	No	No	NO
11.	Nausea	Nausea	No	No	NO
12.	Vomiting	No	Nausea	No	NO
13.	No	Nausea	No	Nausea	NO
14.	Retching	Nausea	No	No	NO
15.	No	No	No	No	NO
16.	Nausea	Nausea	Vomiting	No	metoclopramide 10mg IV
17.	No	No	No	No	NO
18.	Vomiting	No	Nausea	No	NO
19.	No	No	No	No	NO
20.	Nausea	No	Vomiting	No	NO

Table-67: Post operative assessment of nausea, retching & vomiting for group-II (D).

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours
1.	NO	NO	Nausea	NO
2.	NO	NO	NO	NO
3.	NO	NO	NO	NO
4.	NO	NO	NO	NO
5.	NO	NO	NO	NO
6.	Nausea	NO	NO	NO
7.	NO	NO	Nausea	NO
8.	NO	Vomiting	NO	NO
9.	Nausea	NO	NO	NO
10.	Nausea	NO	NO	NO
11.	NO	NO	NO	NO
12.	NO	NO	NO	NO
13.	NO	NO	NO	NO
14.	NO	Nausea	NO	NO
15.	NO	NO	Nausea	NO
16.	NO	NO	NO	NO
17.	Nausea	Vomiting	NO	NO
18.	NO	NO	NO	NO
19.	NO	NO	Nausea	NO
20.	NO	NO	NO	NO

Table-68: Post operative assessment of nausea, retching& vomiting for group-III (M).

Pt. NO.	1ST 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours	Drug delivered
1.	NO	NO	NO	NO	NO
2.	NO	NO	NO	NO	NO
3.	NO	Nausea	NO	NO	NO
4.	NO	NO	NO	NO	NO
5.	NO	NO	NO	NO	NO
6.	Nausea	Nausea	NO	NO	NO
7.	NO	NO	NO	NO	NO
8.	NO	NO	NO	NO	NO
9.	NO	NO	NO	Nausea	NO
10.	NO	NO	NO	NO	NO
11.	NO	NO	NO	NO	NO
12.	NO	Nausea	NO	NO	NO
13.	NO	Nausea	NO	NO	NO
14.	NO	NO	NO	NO	NO
15.	NO	NO	NO	NO	NO
`16.	Nausea	NO	NO	NO	NO
17.	NO	NO	NO	NO	NO
18.	Nausea	NO	NO	NO	NO
19.	NO	NO	NO	NO	NO
20.	NO	NO	NO	NO	NO

Table-69: Post operative data of nausea, retching & vomiting for group-IV (MD).

Pt. NO.	1st 6 hours	2nd 12 hours	3rd 18 hours	4th 24 hours	Drug delivered
1.	NO	NO	NO	NO	NO
2.	NO	NO	NO	NO	NO
3.	NO	NO	NO	NO	NO
4.	NO	NO	NO	NO	NO
5.	NO	NO	NO	NO	NO
6.	NO	NO	NO	NO	NO
7.	Nausea	NO	NO	NO	NO
8.	NO	NO	NO	NO	NO
9.	NO	NO	NO	NO	NO
10.	NO	NO	NO	NO	NO
11.	NO	NO	NO	NO	NO
12.	NO	NO	NO	NO	NO
13.	NO	NO	NO	NO	NO
14.	NO	NO	NO	NO	NO
15.	NO	Nausea	NO	NO	NO
16.	NO	NO	NO	NO	NO
17.	NO	NO	NO	NO	NO
18.	NO	NO	NO	NO	NO
19.	NO	Nausea	NO	NO	NO
20.	NO	NO	NO	NO	NO

Table-70: Postoperative emetic episodes in all studied groups,.

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Mean	1.45	0.550	0.350	0.150
Range	0-3	0-2	0-2	0-1
Std. Deviation±	0.887	0.605	0.587	0.366
P value between group-I and other groups	--	P < 0.001	P < 0.001	P < 0.001

P<0.0001

Table-71: Types and incidence of postoperative emetic episodes in each of the studied groups.

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Nausea	17 episodes (12 pts) (60%)	9 (9) (45%)	8 (7) (35%)	3 (3) (15%)
Retching	4 (4) (20%)	0 (0) (0%)	0 (0) (0%)	0 (0) (0%)
Vomiting	8 (8) (40%)	2 (2) (10%)	0 (0) (0%)	0 (0) (0%)
Total	29 episodes in 16 pts (80%)	11 episodes in 10 pts (50%)	8 episodes in 7 pts (35%)	3 episodes in 3 pts (15%)

Values are expressed as total numbers of episodes (and percentage of patients).

Table-72:. Postoperative IV metoclopramide requirements (mg) in all studied groups,

	Group-I	**Group-D**	**Group-M**	**Group-DM**
Mean	1.50	0.000	0.000	0.000
SD±	3.66	0.000	0.000	0.000
Range	0-10	0.000	0.000	0.000
P value between group-I and other groups	--	P > 0.05	P > 0.05	P > 0.05

P= 0.0232.

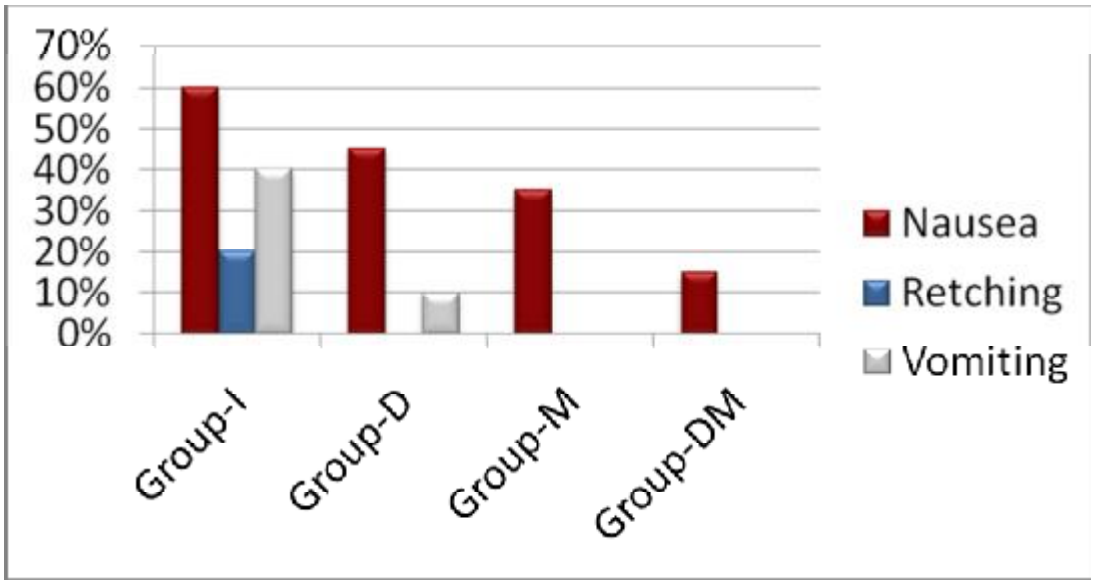

Figure 20 : Postoperative emetic episodes in all studied groups.

Note : Group D retching is 0% (0 episoide).

Group M retching and vomiting is 0% (0 episoide).

Group DM retching and vomiting 0% (0 episoide).

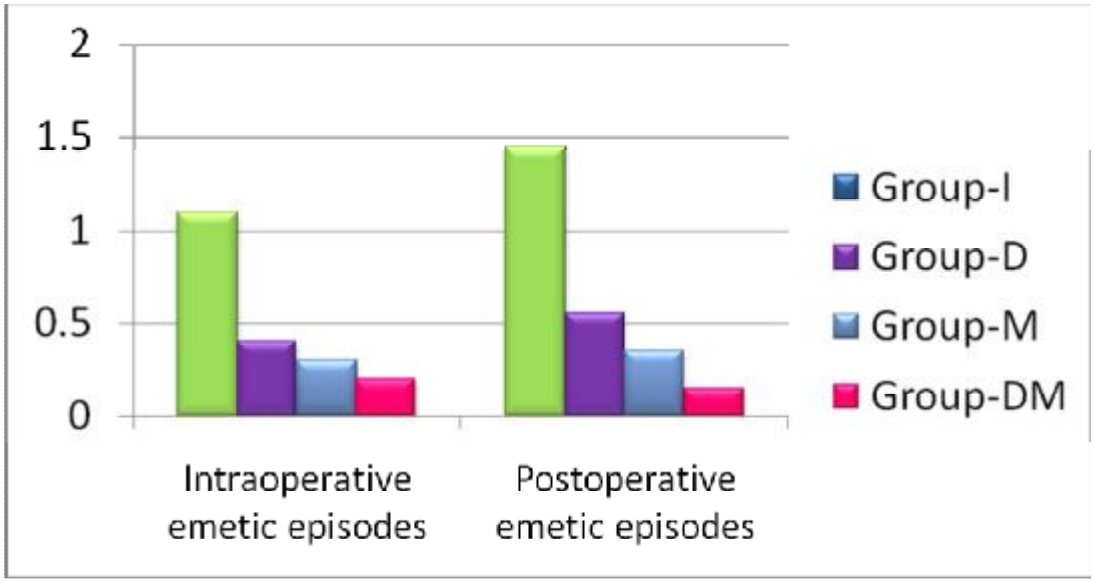

Figure 21 : Summation of intra and postoperative episoides in all groups.

DISSCUSION

Risk factors, such as female gender, anesthetic drugs, type of surgery, and postoperative pain, may all contribute to emetic episodes [117-127]. All these factors were controlled in the current study. All patients were women who underwent Cesarean Section performed under standardized spinal anesthesia. In fact, nausea, retching, and vomiting during spinal anesthesia for cesarean delivery have a complex and multifactorial etiology that may interact and influence the extent of emesis [117, 125]. Spinal anesthesia per se may influence the emetic episodes by inducing maternal hypotension which is directly related to the peak of the block level [125-127]. In this study the mean arterial blood pressure was comparable and the level of the spinal block was similar.

As predicted, the duration of anesthesia and operation were similar among groups. Postoperative wound pain was also similar among groups. Therefore, the differences in the occurrence of emetic episodes among groups can be attributed to the prophylactic antiemetic drugs used in this study.

The current study showed a higher incidence of intra- and post-operative emetic episodes (75% and 80% respectively) in the control group-I, and despite of the prophylactic measures, emesis could not be completely eliminated regardless to the used prophylactic antiemetic. This might be explained by the fact that this study included high-risk patients (pregnant female, obstetric surgery and spinal anesthesia) [117-124-118].

In studies that distinguish between nausea and vomiting, the incidence of nausea ranged from 38% to 52% and that of vomiting from 21% to 33% during the first 24 postoperative hours [128].

Dexamethasone efficacy and safety of as an antiemetic have been previously published [117- 129-133]. The commonly used adult IV doses are 8–10 mg [134]. However,

its role in the prevention and treatment of intraoperative nausea, retching, and vomiting in patients during regional anesthesia for cesarean delivery has not gained wide acceptance because of its pharmacokinetic properties and delayed onset of action [135].

In the present study, dexamethasone significantly reduced the incidence of intra-operative emetic episodes from 23 episodes experienced by 15 patients (75%) to 7 episodes in 7 patients (35%). Postoperatively, it reduced the incidence from 29 episodes occurred in 16 patients (80%) to 11 episodes in 10 patients (50%).

In Subramaniams' study, [136] dexamethasone as a single antiemetic decreased the incidence of PONV from 66.7% to 24.4%. Elhakim et al [137], represented similar results in children after tonsillectomy with significantly reduced incidence of postoperative vomiting from 56% to 20% by preoperative IV dexamethasone administration (0.5mg/kg to maximum dose of 8mg), and concluded that the preoperative dexamethasone administration improves pain scores, reduces analgesic requirements, allows earlier oral fluid intake, and improves postoperative swallowing and the quality of oral intake. They attributed these results to the anti-inflammatory effect produced by dexamethasone, which may reduce local edema and pain. Similarly, Riad and colleagues [134] reported a decreased incidence of postoperative nausea and vomiting from 48% and 52%, respectively, to 32% in children after strabismus surgery by the use of intraoperative prophylactic IV dexamethasone (0.5 mg/kg).

Compared to placebo, dexamethasone 10 mg significantly reduced PONV in the 24 hours following laparoscopic sterilisation from 73% to 34% [14]. Dexamethasone 8 mg was found to be comparable in efficacy to ondansetron 4 mg after day case gynaecological surgery[138]. These doses may be excessive, however, as dexamethasone 2.5 mg was just as effective at preventing emesis after gynaecological surgery as 5 or 10 mg[91]. Wang et al. found that the minimum effective dose of IV dexamethasone in preventing PONV in women undergoing thyroidectomy is 5mg [92].

In three studies, dexamethasone 5-8 mg found to be effective for the prophylaxis against PONV after epidural or spinal morphine for cesarean delivery in parturient [139,140].

In a systematic review and meta-analysis study (136) the authors conclude that dexamethasone (and the serotonergic antagonists) appear to be the most effective agents for preventing postoperative vomiting in children undergoing tonsillectomy. Dexamethasone has many of the features of an ideal antiemetic and clearly deserves greater study and more widespread use[141, 142].

The use of benzodiazepines in the management of PONV has been reported in the literature for both prophylaxis [122, 135, 143] and for treatment [144]. In doses of 35-*75* µg/kg, midazolam has been found as an effective antiemetic that can reduce the incidence and severity of emetic episodes in both adults [143-145] and children [121, 122, 135].

In the present study, midazolam significantly reduced the incidence of intra-operative emetic episodes from 23 episodes experienced by 15 patients (75%) to 6 episodes in 5 patients (25%). Postoperatively, it reduced the incidence from 29 episodes occurred in 16 patients (80%) to 8 episodes in 7 patients (35%).

Although there were no significant statistical differences, midazolam was more effective than dexamethasone in reducing overall incidence of emetic episodes both intra-operatively (6 vs. 7) and postoperatively (8 vs. 11). Also, the number of patients developed emesis was less in the midazolam group both intra- (5 vs. 7) and postoperatively (7 vs. 10).

Midazolam produced similar effectiveness of dexamethasone-midazolam combination in reducing the number of patients with emesis at all studied periods, and was unlike dexamethasone that did differ significantly from the DM postoperatively. Rescue metoclopramide was needed intraoperatively for 2 patients in the D-group, but never for any patient in the M or MD group. Postoperatively, there were two episodes

of vomiting in D group, but no patient vomited in the M or MD groups. These observations are closer to the DM group and are in favor of midazolam that may make it superior to dexamethasone in the current studied patients. However, dexamethasone in this study was given at a fixed dose of 8 mg which could be insufficient for our high risk obstetric patients.

Lee, et alcompared the prophylactic anti-emetic efficacy of IV midazolam (2mg) and IV ondansetron (4mg) administered 30 minutes before the end of minor gynecological or urological surgical procedures, and reported an incidence of PONV of 30% and 27% for the midazolam and ondansetron groups, respectively [(143)]. Unlugenc and colleagues reported 3.3% incidence of PONV after an IV bolus sub-hypnotic dose of midazolam (1-2mg) in adult patients undergoing abdominal or gynecological surgery[(57)]. Midazolam was found to be as effective as ondansetron (4mg) and propofol (15mg) in treating PONV[(57)].

In adult patients undergoing lower abdominal surgery under general anesthesia, Safavi and Honarmand [(145)] found that intraoperative midazolam (35µg/kg) given intravenously 30 minutes before the end of surgery to be more effective in decreasing the incidence of PONV than midazolam premedication (35µg/kg). Following adult open heart surgery, Sanjay and Tauro [(146)] reported a 6% incidence of nausea and no incidence of vomiting by using midazolam infusion (20µg/kg /hr), compared with a 21% incidence of PONV with the ondansetron (0.1 mg/kg) group. After strabismus surgery in children, the use of intraoperative prophylactic IV midazolam (50µg/kg) was found to be effective in decreasing the incidence of postoperative nausea and postoperative vomiting from 48% and 52% to 12% and 0%, respectively [(134)].

None of the currently available antiemetic is entirely effective, perhaps because most of them act through the blockade of one type of receptor. There is increasing evidence that the most effective prophylaxis is achieved by combining multiple antiemetic drugs with different mechanisms of action[(147-152)]. Combination treatment

has often resulted in more than 90% of patients remaining free from PONV during the first 24 hours compared to rates of 60–70% with one antiemetic alone [122, 142, 149-152].

In the present study, combination of midazolam and dexamethasone completely abolished intra- and postoperative vomiting, and resulted in a significant reduction in the incidence of intra-operative emetic episodes from 23 episodes experienced by 15 patients (75%) to 4 episodes in 4 patients (20%). Postoperatively, it reduced the incidence from 29 episodes occurred in 16 patients (80%) to 3 episodes in 3 patients (15%).

Combination of dexamethasone (0.5 mg/kg) and midazolam (50 microg/kg) has been found to be entirely effective in preventing PONV after strabismus surgery in children [134]. Combinations of dexamethasone and 5-HT3 antagonists have similarly been found to be more effective compared to either drug alone, especially with regard to delayed symptoms [149-151]. Most other combinations of antiemetics have been shown to be beneficial, with one notable exception. The addition of metoclopramide to other antiemetics has rarely been shown to achieve any additional benefit [144]. This is consistent with the many studies which have shown prophylactic metoclopramide to be no better than placebo (at least at the commonly-used dose of 10 mg).

Fujii et al,[150] demonstrated that adding dexamethasone 8 mg to propofol at a subhypnotic dose (1.0 mg/kg/h) increased antiemetic efficacy in patients undergoing spinal anesthesia for cesarean delivery, and found an improvement in its efficacy of 15%. The exact mechanism by which dexamethasone increases the effectiveness of propofol as an antiemetic is unknown. Thus, antiemetic therapy with combined granisetron and dexamethasone or combined propofol and dexamethasone is highly effective for the prevention of nausea, retching, and vomiting during regional anesthesia for cesarean delivery [151].

However, Kocamanoglu et al, [152] found no difference in antiemetic efficacy in patients receiving granisetron alone and combined with droperidol and

dexamethasone for the prevention of PONV after general anesthesia for cesarean delivery.

Inconclusive results in other studies may be due to difficulties in standardizing perioperative clinical conditions. PONV are a multifactorial problem and several anesthetic and non-anesthetic factors must be controlled to obtain meaningful results [153, 154].

The results of this study demonstrate that the incidence and severity of intra- and postoperative emetic episodes can be remarkably reduced by the prophylactic use of dexamethasone, midazolam and their combination.

CONCLUSION

1.Prophylactic use of dexamethasone(8mg), midazolam(50mcg/kg) or their combination is effective in reducing the incidence and severity of emetic episodes during and after CS performed under spinal anesthesia.

2- Midazolam(50mcg/kg) is effective as antiemtic addition to sedative and anxiolytic effect.

3- No intraoperative and postoperative adverse effect of agents administered (dexamethasone, midazolam and their combination).

RECOMINDATION

The present study, recommended that:

1- Dexamethasone , midazolam and their combination could be the first drugs of choice in preventing PONV because of its low cost and safety in use.

2- Further research should be done on large scale to evaluate the use of dexamethasone and midazolam in preventing postoperative nausea and vomiting.

SUMMARY

Cesarean section (CS) performed under spinal anesthesia (SA) is associated with a high incidence of intra- (IONV) and post-operative nausea and vomiting (PONV).

None of the available antiemetics are entirely effective when used alone, but using combined antiemetics with different modes of action could be more effective.

To evaluate the efficacy of dexamethasone and midazolam, and their combination in preventing IONV and PONV in parturient undergoing CS.

Eighty parturient scheduled for elective CS under SA were divided into four equal groups to receive one of the following IV agents which diluted in a 10 ml dilution to be injected immediately after umbilical cord clamping: 10ml isotonic saline (group-I), dexamethasone 8mg (group-D), midazolam 50 microgram/kg (group-M), or combined 8mg dexamethasone and 50 microgram/kg midazolam (group-DM). Incidence of IONV and PONV together with the total amount of administered metoclopramide and the analgesic requirements of diclofenac sodium during the first postoperative 24 hours were compared between the groups.

Incidence of intra-operative emetic episodes (nausea, retching and vomiting) was 23, 7, 6 and 4 in the groups I, D, M and MD, respectively. The corresponding postoperative incidence was 29, 11, 8, and 3, respectively . In group-I, metoclopramide was given to 5 patients intraoperatively, and to 3 patients postoperatively. In the other groups, metoclopramide was needed only for 2 patients in group-D.

Prophylactic use of dexamethasone, midazolam or their combination is very effective in reducing the incidence and severity of emetic episodes during and after CS performed under SA

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الخلاصة

فعالية عقاري الديكساميثازون و الميدازولام والجمع بينهما للحد من الغثيان والقئ مابعد الجراحه القيصريه بأستخدام التخدير النصفي

تم عمل هذه الدراسة لمعرفة جدوى استعمال كلا من عقاري الديكساميثازون و الميدازولام للحد من الغثيان والقئ بعد إجراء الجراحه القيصرية تحت التخدير النصفي , وقد تم إختيار عدد 80 حاله وتم تقسيمها الي أربع مجموعات كل مجموعه 20 حاله, المجموعه ألاولي لم يتم أعطائها أي دواء وهي مجموعة للمقارنه , المجموعه الثانية أعطيت 8 مجم من الديكساميثازون ,المجموعة الثالثة أعطيت 50ميكروجرام لكل كيلوجرام من عقار الميدازولام , المجموعة الرابعة أعطيت من كلا العقارين 8مجم من الديكساميثازون و 50ميكروجرام لكل كيلوجرام من الميدازولام , كل ألادوية أعطيت بعد ربط الحبل السري للجنين مباشرة ,وقد تم متابعتهم بالأجهزة القياسية لمراقبة الوظائف الحيوية بإستمرار وتم تسجيل قراءات الوظائف الحيوية كل 5 دقائق طيلة فتره العملية وقد تم تسجيل أربع قراءات لجميع الحالات , وتم متابعة حدوث الغثيان والقئ من عدمه من بعد إعطاء العقار حتي 24 ساعة بعدإجراء العملية لجميع الحالات وتم تدوين النتائج في جداول وتم إعطاء إحصائيات لتلك النتائج .

وبعد إجراء الا حصائيات وجد أن عقار الديكساميثازون و الميدازولام فعالان في الحد من الغثيان والقئ وأن إستعمال كلاهما له فعالية أفضل من إستعمال كل علي حدا.

فعالية الديكساميثازون والميدزولام وكلاهما في تقليل القئ والغثيان أثناء و بعد التخدير النصفي للعمليات القيصرية

رسالة مقدمة لكلية الطب البشري - جامعة بنغازي

إيفاءًا جزئيا لشروط الحصول علي درجة

الماجستير في التخدير والعناية المركزة الجراحية

مقدمة من

الشريف بالقاسم يوسف رجب

بكالوريوس الطب والجراحة

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