IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 4 Ser. 4 (April. 2019), PP 40-46
www.iosrjournals.org

A Comparison of Intrathecal Fentanyl or Placebo Added To Bupivacaine in Prevention of Intra-Operative and Early Post-Operative Emesis in Cesarean Section Performed Under Spinal Anaesthesia

Asif Iqbal
Corresponding Author: Asif Iqbal

Abstract
Background: *The high incidence of intraoperative nausea and vomiting in cesarean section under spinal anaesthesia is distressing to the parturients and disturbing to the surgeons by causing protrusion of abdominal viscera rendering surgery more difficult and increasing the risk of visceral injuries, aspiration being an additional hazard.Many methods have been used to reduce the incidence of nausea and vomiting but they add to cost and side effects. Intrathecal lipophilic opioids added to bupivacaine as an adjuvant have been shown to reduce incidence of nausea and vomiting, it is inexpensive has few serious side effects and is established as adjuvant.Hence could be good alternative for prophylaxis of emetic episodes in cesarean section under spinal anaesthesia, thus basis of our study.*
Material methods: *100 parturients of ASA physical status I and II in the age group 25-40 years undergoing elective cesarean section under spinal anaesthesia were randomized into two groups of 50 each...**Study Group recieved** 0.5% hperbaric bupivacaine 2 ml + fentanyl 12.5 µg in 0.5 ml 0.9% saline.**Control Group recieved** 0.5% bupivacaine 2ml + 0.9% saline 0.5 ml intrathecally,and observations were made. The data was analyzed statistically. All the statistical results have been discussed at 5% level of significance. The p-value <0.05 was considered significant.*
Results *The incidence of nausea in 24hr period was 18% vs 52% (p≤0.007).Retching was 6 % vs 38% (p ≤0.0002). Vomiting was 2 % vs. 26% (p≤0.008) in study and control group respectively rescue antiemetic used in study group (n=3) vs. control group (n=21) (P value≤0.0002). Duration of analgesic was 170min ±8.4 2vs 127min±7.46 (P–value <0.0001). VAS score was 0.52±0.027 vs. 0.86±0.22 (p -value=0.03). Mean Apgar score at 1 min was 7.4vs7.56 respectively and at 5 min interval was 9.3 vs. 9.04 respectively in two groups (p value= 0.317)*
Conclusion *low dose intrathecal fentanyl 12.5µg, when used as adjuvant with 0.5% bupivacaine heavy for spinal anesthesia for parturients undergoing cesarean section, decreases incidence of emesis in perioperative operative period, apart from increasing quality of analgesia with no serious side effects in parturient and new born.*
Key Words*;Nausea, vomiting,cesarean section, spinal anaesthesia,fentanyl,bupivacaine,belville secore,rescue antiemetic.*

Date of Submission: 20-03-2019 Date of acceptance: 06-04-2019

I. Introduction

Regional anaesthesia has been shown to be effective, safe and anaesthesia of choice for elective and emergency cesarean section. But despite major advances in spinal, epidural and combined spinal-epidural anaesthesia techniques, perioperative nausea and vomiting is still present in a significant number of patients. The quoted incidence of nausea/ vomiting in cesarean section under spinal anaesthesia is 66%[1].

Nausea and vomiting may leads to**,** electrolytes imbalance, dehydration. Delayed wound healing, wound dehiscence, bleeding, aspiration of vomits extra. Prolonged hospital stay increasing overall medical cost.[2,3,4]Many drugs have been tried for perioperative nausea and vomiting but all produce adverse effects and add to cost. Drugs like Serotonin (5-HT3) receptor antagonists Ondansetron, dolasetron, tropisetron, granisetron, ramesetrone extra.[5] produce headache ,light headedness and elevated liver enzymes. Dexamethasone causing itching and anal irritation .Dopamine receptor Antagonist may cause QT prolongation and torsades de pointes [6] apart from EPS (extra pyramidal side effects.), anxiety, hypotension ,sedation and dizziness.Phenothiazines like Promethazine and Prochlorperazine causes sedation, dizziness, extrapyramidal symptoms, blurred vision, dizziness and urinary retention. Anticholinergics like Scopolamine cause Sedation, dry mouth, visual

disturbance, renal or hepatic impairment and central nervous effect**.**Diclectin ,Aprepitant are newer agents also have side effects

Acupuncture and Constant pressure by a specific wrist elastic band on the Nei-Guan acupuncture point are non-pharmacologic methods used.[7,8]

Lipophlic opioids like fentanyl and sufentanyl used intrathecally as adjuvant have also been found to reduce episodes of nausea/vomiting, when administered primarily to enhance post operative analgesia.[9]Probabily they reduce emesis by improving quality and duration of analgesia with o.5%bupivacine This combination have been demonstrated to be superior to iv ondansetron in some studies.[10] Low dose Intrathecal fentanyl is inexpensive and has few serious side effects, making it an attractive drug for perioperative nausea and vomiting prophylaxis study.

II. Materials and Methods

This prospective randomized double blind study was conducted in the department of Anaesthesiology and Critical Care, Sher- i -Kashmir Institute of Medical Sciences, Srinagar from december 2011 - december 2013.

After approval from institutional ethics committee and informed consent from all patients, 100 full term parturients with ASA physical status I and II in the age group of 25-40 years, undergoing elective cesarean section under spinal anaesthesia were enrolled for this study.

Following were excluded patients with history of motion sickness,hyperemesis gravidarum, taking antiemetic medication,any contraindication to regional anaesthesia,allergic to study medications.

Day before surgery all patients were clinically evaluated, assessed and investigated.The parturients received ranitidine 150 mg orally and metoclopromide 10mg as premedication 90-100 minutes before surgery with a sip of water. On arrival in operating room, an 18 G intravenous cannula was placed and iv access established. Standard anaesthesia monitoring was instituted and base line blood pressure, heart rate, oxygen saturation and fetal heart rate were recorded. All patients received intravenous hydration with ringer lactate solution 20 ml /kg body weight before performing spinal anaesthesia. Under all aseptic precaution, lumbar puncture was performed with the patient in the sitting position through L3-L4 intervertebral space, using 25 gauge lumber puncture needle. Patients were randomly allocated to two groups, study and control group of 50 patients in each to receive following drug solutions.

Control group (A): received spinal anaesthesia with 0.5% hyperbaric bupivacaine 2ml (10mg) and 0.5 ml normal saline to total volume of 2.5ml.

Study group (B): received spinal anaesthesia with 0.5% hyperbaric bupivacaine 2 ml (10 mg) along with 12.5 microgram fentanyl in normal saline 0.5ml to make a total volume of 2.5ml.

All drug solutions were prepared by an anaesthesia resident not involved in administration of spinal anaesthesia or in data collection. Prior to handling of the drug (for intrathecal injection), the drug was coded by the same resident. Patients were given supine position with wedge under right hip for 15-30 degree left uterine displacement after. The anaesthesiologist performing the block, was unaware of the drug combination injected. A separate observer, who was also not aware of the drug injected, commenced the clinical observations. After spinal anaesthesia, hemodynamic variables like systolic blood pressure, diastolic blood pressure, heart rate and oxygen saturation were recorded every 2 minutes until delivery of baby and then every 5 minutes till the end of surgery. The decrease in systolic blood pressure (more then 20% of base line values and or less then 90mmHg) immediately after the spinal, was treated by increasing the rate of intravenous fluids administration or by ephedrine boluses of 6mg.

Sensory block level testing was performed using a 21 gauge blunt needle in a cephalad to caudal fashion. Dermatome level was tested every 2 minutes, until level stabilized within 3 consecutive tests and a sensory blockade up to T5 was considered as adequate to allow surgery to proceed. Time taken from intrathecal injection to highest level of sensory block was recorded. Motor block in lower limbs was assessed as per Bromage scale[11] .Pain was evaluated with visual analogue scale (VAS).

All patients were catheterized, just prior to surgery after block. The surgical technique was uniform in all the patients and included exteriorization of the uterus. 10 I.U. of oxytocin was given intravenously after delivery of the baby and clamping of the umbilical cord. An attending Pediatrician assessed the neonatal Apgar scores at 1 and 5 min after delivery. Intraoperative and post delivery emetic episodes were recorded by direct questioning. Nausea was defined as subjectively unpleasant sensation associated with awareness of urge to vomit. Retching was defined as labored spasmodic, rhythmic contraction of respiratory muscles without expulsion of gastric contents. Vomiting was defined as forceful expulsion of gastric contents from mouth. Belville's score[12] was used for assessment of emetic episodes 0= no nausea,1= nausea,2=retching 3=vomiting.

Ondansetron 4mg was used as rescue antiemetic with occurrence of two or more emetic episodes. Duration of effective analgesia was recorded from administration of spinal block to the first dose of supplementary analgesia used. Rescue analgesia in the form of paracetamol 1gm IV was given, when VAS score

was > 4 and total number of rescue analgesic doses used in 24 hour period was recorded. Also total dose of rescue emetic used was recorded. Side effects like shivering, respiratory depression, pruritis, bradycardia, and hypotension were recorded.

The data was collected, assessed and statistically analyzed using student t- test, chi-square test, z-test and fisher-exact test. All the statistical results have been discussed at 5% level of significance. The p-value <0.05 was considered significant.

III. Results

The demographic and hemodynamic parameters were comparable in the two groups*(p>0.05*).The incidence of nausea in 24hr period in study and control group was 18% vs 52% (*p*=0.007).Retching episode incidence in 24hr period in study and control group was 6% vs 38% respectively (*p* =0.0002). And incidence of vomiting in study and control group was 2 % vs 26% respectively (*p*=0.0008) all being statistically significant.

The number of patients receiving rescue antiemetic was less in study group (n=3) as compared to control group (n=21) (*P* value≤0.0002). Duration of analgesic in study group was 170min ±8.42 and in control group 127min±7.46 with statistical significant difference.*(P*–value <0.0001).

The mean intraoperative VAS score in study group was 0.52±0.027 and in control group 0.86±0.22 (*p - value*0≤.03).

The mean number of rescue analgesia doses used were less in study group 1.120±0.55 as compared to control group 1.420±0.53 (*p*-value≤ *0.007*) depicting statistical significance.

Mean Apgar score of new born at 1 min in study and control group was 7.4vs7.56 respectively and at 5 min interval was 9.3 vs 9.04 respectively with *(p* value≤0.317) statistically non significant .

None of our patients had significant hemodynamic compromise and none had respiratory depression, either in parturients or newborns. However there were less episodes of shivering in study group as compared to control group athough statistically non significant .

IV. Discussion

Spinal anaesthesia is an easy, rapid and safe technique for cesarean section.[13] It is considered the procedure of choice for elective or emergency cesarean section in countries such as united states, where it is used in up to 41% of cases.[14]

Numerous interventions have been studied for prevention of nausea and vomiting during cesarean section, but none of the available interventions are entirely effective, perhaps because most of them act through the blockade on one type of receptor only, so search for the novel antiemetic is still going on. Palmer et al, [15] Cooper et al[16] in their studies to determine the effect of intrathecally administered fentanyl on the duration of postoperative analgesia in patients scheduled for cesarean section, observed significant less nausea and vomiting in patients who received intrathecal fentanyl. It was just the coincidental finding.

So we designed a prospective randomized controlled comparative study between bupivacaine plus low dose of intrathecal fentanyl (12.5µg) as adjuvant, compared with bupivacaine alone in cesarean section performed under spinal anaesthesia in order to evaluate the effect on incidence of emetic episodes

Demographic parameters The mean age of patients in control group was 31.72yrs ± 3.30 and in study group 32.56yrs ± 2.79 (*p-value=0.172*). The mean weight in control group was 71.12 kg± 6.59 and in study group 70.56kg ± 6.88 *(p-value=0.69)* mean duration of surgery in control group has been 81.17 minutes. ± 15.63 whereas in study group, it was 81.25 minutes ± 16.76 (*p-value*=0.97) and parity in the two groups were all comparable (*p-value=0.43).*

Hemodynamic parameters Mean heart rate in study group was 77.37 bpm ±1.93 and in control group, it was 79.68 bpm±1.32 (*p-value* >0.05). However 3 patients in the study group and 2 patients in control group developed bradycardia requiring treatment with atropine. Our findings were in accordance with studies conducted by Agrawal et al[17] and Dahlgren et al[18]. In our study, 9 patients in study group verses 19 patients in control group had hypotension, but results were statistically non-significant (*p-value=0.61*). Studies conducted by Biswas B N et al[19] also observed non-significant difference in incidence of hypotension in patients receiving bupivacaine or bupivacaine-fentanyl combination intrathecally.

Total emetic episodes in 24hr period. Overall incidence of nausea in study group was (18 %) as compared to (52%) in control group (*p-value*=0.007). (6 %) patients had retching episodes in 24hr period in study group, as compared (38%) in control group (*p-value* =0.0002). Incidence of vomiting was (2%) in study group as compared to (26%) in control group (*p-value=0.0008*) indicating three variables were statistically significant.

Randall et al compared four different subarachnoid solution 0.5% heavy bupivacaine alone, or with adrenaline, or fentanyl and with adrenaline and fentanyl. They observed no nausea and vomiting in patients receiving bupivacaine –fentanyl.[20] There was significant association between the incidence of nausea with the groups receiving adrenaline (*p- value=0.033*). Biswas et al in their study observed (5%) incidence of nausea and vomiting in patients receiving intrathecal fentanyl, whereas it was 40% in control group[19]receiving bupivacaine

alone. Rasooli et al. in their study reduced the dose of fentanyl to 20µg and administered it intrathecally with 6mg of bupivacaine. Out of 22 patients in fentanyl group, no patient had vomiting.[21] Theodore R et al[9] compared intrathecal fentanyl 20µg with iv ondansetron 4mg for prevention of intraoperative nausea and vomiting during cesarean deliveries performed under spinal anaesthesia. They concluded that intrathecal fentanyl as part of spinal anaesthetic for cesarean section is superior to intravenous ondansetron for prevention of intraoperative nausea.

Intraoperative nausea and vomiting during cesarean section under spinal is frequently related to peritoneal traction and exteriorization of uterus[22] accompanied by visceral pain despite adequate dermatomal blockade, that stimulate vagal afferents, hence emetic episodes. Intrathecal administration of fentanyl may provide improved analgesia and there by decreases the discomfort from intraoperative peritoneal manipulation, which may prevent initiation of emetic episodes during spinal anaesthesia for cesarean section hence reduced incidence of emetic episodes.

Effect on maternal and fetal outcome

None of the neonate developed respiratory depression in our study. Mean Apgar score, which was taken as marker of respiratory depression in neonates was 7.4 ±0.67 at 1 min interval in study group and 7.56±0.67 in control group (*p -value*=0.23). At 5 min interval it was 9.3±0.56 in study group and 9.04±0.6 in control group (*p -value*=0.077). Jaishri Bogra et al[23], Dahlgren G et al [18] also observed in their studies that neonatal outcome as judged by Apgar score at 1 and 5 minutes was similar in both groups with no respiratory depression shown in either group .The administration of intrathecal opioids to parturients as adjuvant to local anaesthtics carries a risk of respiratory depression[24] in mothers and new born. In our study none of the parturient in either group experienced respiratory depression probabily using low doses may be the reason.

Side effects

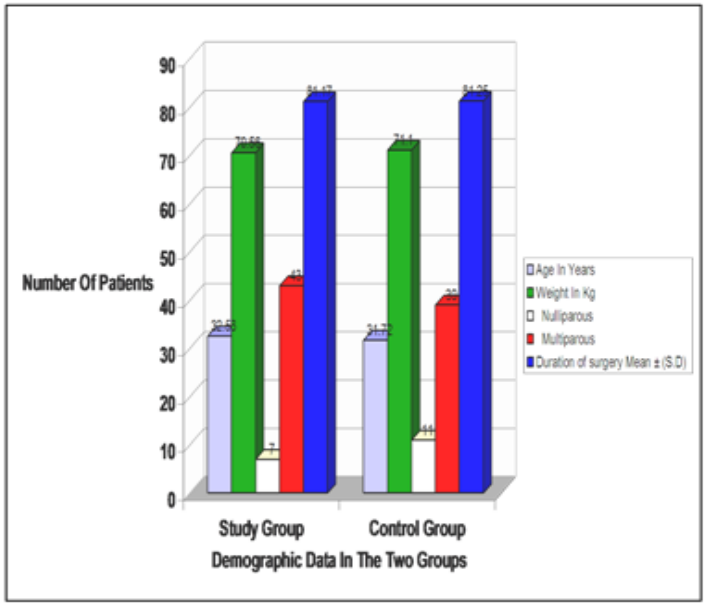
Pruritis was seen in two patients in study group and no patient in control group. Pruritis was mild and did not require any treatment. Belzarena, S.D. et al[25] observed that pruritis and sedation as main side effects of use of intrathecal opioids, but pruritis was of short duration and low to mild intensity and no treatment was needed . Dahlgren et al[18] also noted that pruritis as side effect of intrathecal opioids and was more associated with sufentanil than fentanyl.

None of the patient in the study group had shivering, as compared to four patients in control group in our study. Anchalee et al[26] also observed reduction in shivering episodes with fentanyl used as adjuvant.
Although, urinary retention has been reported with intrathecal opiods,[27] we could not compare the incidence of urinary retention with other studies, as the patients in our study were routinely catheterized for first 24hr as was done in the study by Catherine O Hunt et al.[28]

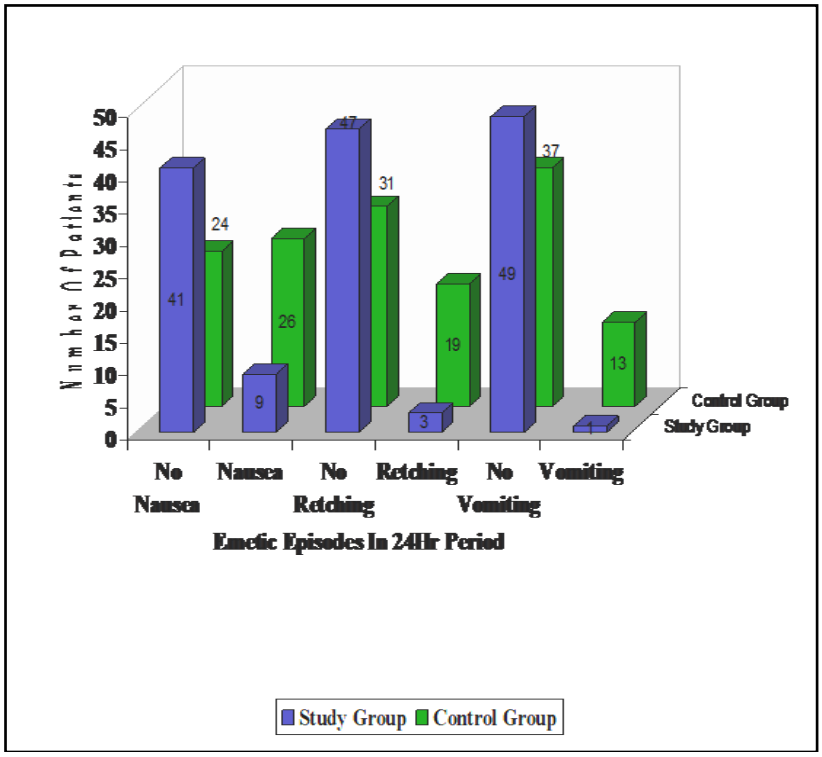
Table-1 Comparison of Mean Age, Weight, Duration of Surgery and Parity in Study and Control Groups

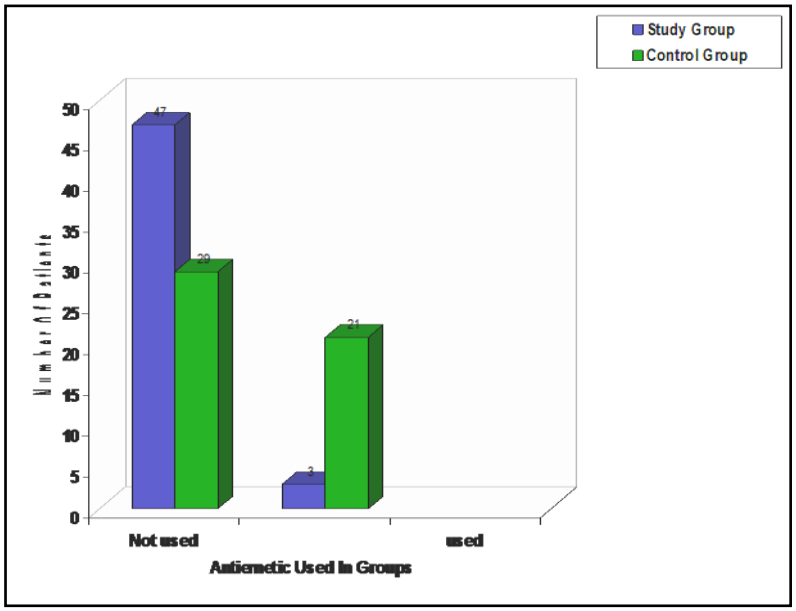
Groups		Study Group Mean ±(S.D)	Control Group Mean ±(S.D)	P -value	Remarks
Age in years Mean ± (S.D)		32.56± 2.79	31.72 ±3.30	0.172	(NS)
Weight in(kg)Mean±(S.D)		70.56 ±6.88	71.12± 6.59	0.679	(NS)
Duration of surgery Mean ±(S.D)		81.17±15.63	81.25±16.76	0.977	(NS)
Parity	Multiparous(n)	43	39	0.4356	(NS)
	Nulliparous(n)	7	11		

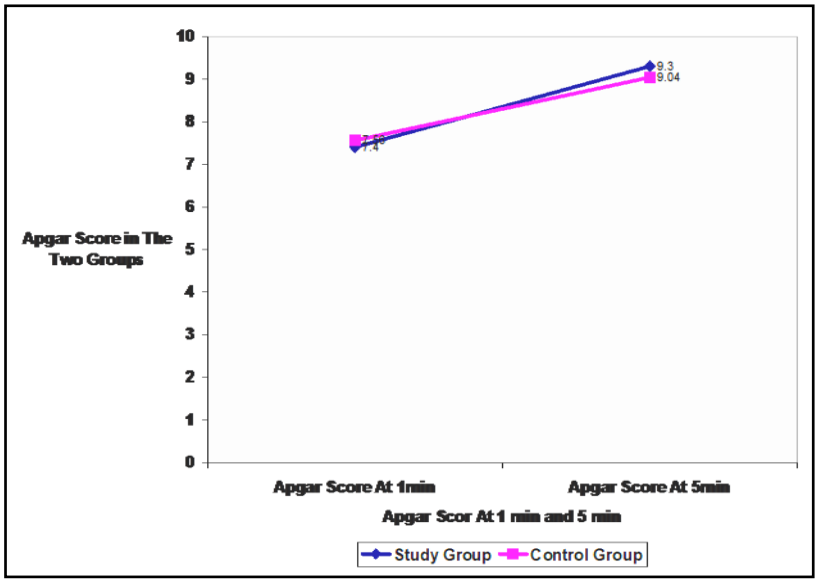
Distribution of Mean Age, Weight, Parity, and duration of Surgery in Groups

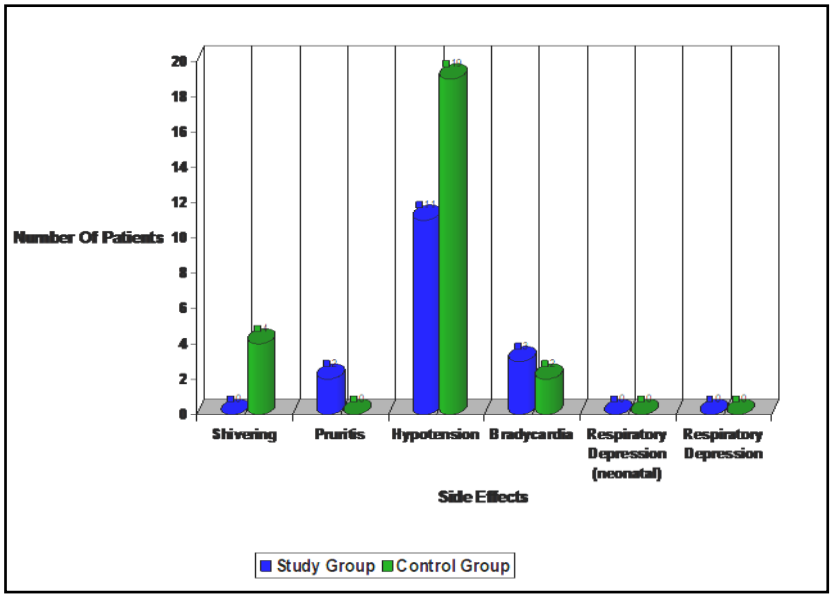


		Study Group		Control Group		Total	P- value	Remark
		n	%	n	%			
Nausea	**No Nausea**	41	82%	24	48%	65	0.007	S
	Nausea	9	18%	26	52%	35		
Retching	**No Retching**	47	94%	31	62%	78	0.0002	S
	Retching	3	6%	19	38%	22		
Vomiting	**No Vomiting**	49	98%	37	74%	86	0.0008	S
	Vomiting	1	2%	13	26%	14		




Study Group
Control Group
50
45
40
35
30
25
20
15
10
5
0
47
29
3
21
Not used
used
Antiemetic Used In Groups


10
9
8
7
6
5
4
3
2
1
0
9.3
9.04
7.4
Apgar Score in The Two Groups
Apgar Score At 1min
Apgar Score At 5min
Apgar Scor At 1 min and 5 min
Study Group
Control Group


20
18
16
14
12
10
8
6
4
2
0
Number Of Patients
Shivering
Pruritis
Hypotension
Bradycardia
Respiratory Depression (neonatal)
Respiratory Depression
Side Effects
Study Group
Control Group

References

[1]. **Lussos S A, Bader A M, Thornhill M L, Datta S**. The antiemetic efficacy and safety of prophylactic metoclopramide for elective cesarean delivery during spinal anesthesia. *Reg. Anesth* 1992; 17: 126–130.

[2]. **Eun Jin Kim, Justin Sang Ko, Chung Su Kim, Sang Min Lee, Duck Hwan Choi.** Combination of antiemetics for prevention of post-operative nausea and vomiting in high risk patients. *J Korean Med Sci* 2007; 22: 878-882.

[3]. **Harmon D, Ryan M, Kelly A, Bowen M**. Acupressure and prevention of nausea and vomiting during and after spinal anaesthesia for cesarean section. *Br J Anaesth* 2000; 84: 463–467.

[4]. **Ky Ho, J W Chiu**. Multimodal antiemetic therapy and emetic risk profiling. *Annals Academy of Medicine Singapore* 2005; 34:196- 205.

[5]. **Balki M, Dhumne S, Kasodekar S, Kingdom J, Windrim R, Carvalho JCA**. Intraoperative nausea and vomiting during cesarean section under regional anaesthesia. *International journal of obstetrics anaesthesia* 2005; 14: 230 -341.

[6]. **Rowbotham D J**. Current management of postoperative nausea and vomiting. *Br J Anaesth* 1992; 69:46S–59S.

[7]. **Coloma M, White P F, Ogunnaike B O, Markowitz S D, Brown P M, Lee A Q, et al.** Comparison of acustimulation and ondansetron for the treatment of established postoperative nausea and vomiting. *Anesthesiology* 2002; 97:1387–92.

[8]. **Heydar Noroozinia, Alireza Mahoori, Ebrahim Hasani, Mohsen Gerami-Fahim.**The effect of acupressure on Nausea and vomiting after cesarean section under spinal anesthesia. *Acta Medica Iranica*, 2013; 51(3): 163-167.

[9]. **Palmer CM, Voulgaropoulos D, Alves D**. Subarachnoid fentanyl augments lidocaine spinal anesthesia for cesarean delivery. *Reg. Anesth*.1995; 20:389 –94.

[10]. **Theodore R, Manullang, Christopher M, Viscomi, and Nathan L, Pace, M D.** Intrathecal fentanyl is superior to intravenous ondansetron for the prevention of perioperative nausea during cesarean delivery with spinal anesthesia *Anesth Analg* 2000; 90:1162–6.

[11]. **Bromage PR,Burfoot MF,Ceowell DE,.**Quality of epidural blockade.Infuence of physical factors.*Br.J.Anaesth*.1964;36:342-52.

[12]. **J.Weldon Bellville MD, William s.Howland,M.D;**Post operative nausea vomiting *jama*.1960;172(14):1488-1493.

[13]. **Juhani T P, Hannele H**. Complication during spinal anaesthesia for cesarean delivery, a clinical report of one year's experience. *Reg anesth*.1993 ;18:128-31

[14]. **Gibbs C P, Krischer J, Peckham B M, Sharp H, Kirschbaum T H**. Obstetric anaesthesia, a national survey. *Aaesthesiology* 1986; 65:298-306.

[15]. **Palmer CM, Voulgaropoulos D, Alves D**. Subarachnoid fentanyl augments lidocaine spinal anesthesia for cesarean delivery. *Reg. Anesth*.1995; 20:389 –94.

[16]. **Cooper D W, Lindsay S L, Ryall D M, Kokri M S, Eldabe S S, Lear. G A.** Does intrathecal fentanyl produce acute cross tolerance to iv morphine.*Br J Aaesth* 1997;78:311-3.

[17]. **Amit Agrawal, Sanjay Agrawal, Veena Asthana, Y S Payal, Jagdish Sharma, V Gupta.** Comparison of intrathecal fentanyl and sufentanil in addition to bupivacaine for cesarean section in spinal. *J Anaesth Clin Pharmacol* 2009;25: 154-156.

[18]. **Dahlgren G, Hultstrand C, Jakobsson J, Norman M, Eriksson E W.** Intrathecal sufentanil, fentanyl, or placebo added to bupivacaine for cesarean section. *Anesth Analg* 1997; 85:1288 –93.

[19]. **Biswas B N, Rudra A, Bose B K, Nath S, Chokarborthy S, Battacherjee S.** Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during cesarean delivery and early post operative period. *Indian J Anaesth* 2002; 46(6):469-472.

[20]. **Randalls B, Broadway J W, Browne D A, Morgan B M**. Comparison of four subarachnoid solutions in a needle-through needle technique for elective cesarean section. *Br J Anaesth* 1991; 66:314–18.

[21]. **Rasooli S, Moslem F, Parish M, Azarfarin R, Fatholahzadeh N.**Minidose bupivacaine-fentanyl spinal anaesthesia for cesarean section in pre-eclamptic parturients. *Medical Journal of Islamic Republic of Iran*. 2006; 20:94-97.

[22]. **Siddiqui M, Goldszmith E, Fallah Kingdom S J, Windrim R, Carvello J C A**. Complication of exteriorized compared with insitu uterine repair in cesarean delivery under spinal anesthesia. *Obstetics & Gynecology* 2007.110:570-575.

[23]. **Jaishri Bogra, Namita Arora, Pratima Srivastava**. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anaesthesia for cesarean section *BMC Anesthesiology* 2005, 5:5 doi: 10.1186/1471-2253-5-5.

[24]. **Etches R C, Sander A N**. Respiratory depression and spinal opioids. *Can J Anaesthesia* 1998;36:165-85.

[25]. **Belzarena SD**. Clinical effects of intrathecally administered fentanyl in patients undergoing cesarean section. *Anesth Analg* 1992; 74:653–7.

[26]. **Techanivate A, Rodanant O, Tachawattanawisal W, Sonsit T**. Intrathecal fentanyl for prevention of shivering. *J Med Assoc Thai* 2005;88:1214-1221.

[27]. **Ronald D, Lars L E, Lee A F, William L Y**. *Miller's Anesthsia*-7th edition. (2009) chapter 27.p.788. Elsevier Churchill Livingstone

[28]. **Hunt C O, Naughty J S, Bader A**. Perioperative analgesia with subarachnoid fentanyl bupivacaine for caesarian delivery. *Anaesthesiology* 1989; 71:535-40.

Asif Iqbal. "A Comparison of Intrathecal Fentanyl or Placebo Added To Bupivacaine in Prevention of Intra-Operative and Early Post-Operative Emesis in Cesarean Section Performed Under Spinal Anaesthesia." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 04, 2019, pp 40-46.