PROPOFOL VERSUS PLACEBO FOR PREVENTION OF EMESIS DURING SPINAL ANAESTHESIA

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Abstract

***Background*:** Spinal anesthesia has been shown to be an easy, rapid and safe technique, nevertheless, it has some minor side effects, including intraoperative nausea and vomiting. Nausea, retching, and vomiting during regional anesthesia are common occurrences. The abrupt diaphragmatic contractions, present in emesis, are uncomfortable to the patient and may cause protrusion of the abdominal viscera, rendering surgery more difficult and increasing the risk of visceral injuries.

***Objectives*:** evaluation the effectiveness of low dose propofol for control of nausea and vomiting during spinal anesthesia.

***Patients and Method*:** After taking written informed consent, 83 Patients (79 males and 4 females) of ASA physical status I or II, aged 23-80 years, scheduled for elective urosurgery in the Sulaimani teaching hospital were enrolled in a single blind prospective study. Patients were divided into two groups to receive either propofol (1 mg/kg/hr) or Intralipid (Placebo). Operations were performed under spinal anaesthesia. Patients were followed up for 24 hours for post operative nausea and vomiting.

***Results*:** Patients who received Propofol had statistically significant less nausea and vomiting than those who received Placebo (Intralipid).

***Conclusion*:** Propofol at a subhypnotic dose is effective in the prevention of nausea and vomiting.

Keywords: Spinal anaesthesia, Nausea, Vomiting, Propofol, Intralipid.

Introduction

Nausea and vomiting has been a problem since the introduction of anesthesia (Hines et al; 1992). Despite the introduction of less invasive surgical procedures and new anesthetic agents, some patients can feel fine, without any problems during the initial period in the postoperative care unit, and then start to feel nauseated and possibly even vomit several hours later. Post operative nausea and vomiting is an important cause of delayed

discharge from the recovery room and decreased patient satisfaction (Pavlin et al; 1998). Nausea and vomiting also associated with complications such as tension on suture lines, wound bleeding and dehiscence, increased intracranial pressure, pulmonary aspiration, dehydration and electrolyte imbalance (Myles et al ; 2000).

Mechanism of post operative nausea and vomiting (PONV) in regional anesthesia:

Hypotension is a common occurrence during neuraxial anesthesia. Low blood pressure may lead to brain stem ischemia, which is thought to activate the circulatory, respiratory, and vomiting centers grouped together in the medulla (Datta et al; 1982). Other investigators have speculated that hypotension rather leads to gut ischemia and the release of emetogenic substances (*e.g.*, serotonin) from the intestines. Consequently, supplemental oxygen can relieve nausea in such circumstances by attenuating the release of serotonin from the vagal afferent nerves in the gastrointestinal tract through increasing oxygen concentration to the tissues, thus enhancing delivery of oxygen to the intestine (Racke & Schworer; 1991)**.** Strategies avoiding hypotension were shown to be effective in reducing emesis (Borgeat et al; 2003).

Neuraxial anesthesia also changes the function of the gastrointestinal (GI) tract (Liu, Carpenter & Neal 1995). Sympathetic blockade by local anesthetics creates unopposed vagal action, resulting in GI hyperactivity. The efficacy of vagolytic agents to relieve nausea during spinal anesthesia has been taken as evidence of the importance of this mechanism (Borgeat et al; 2003).

Visceral pain is a potent stimulus for emetic symptoms during regional anesthesia. Handling of abdominal viscera stimulates sensory vagal fibers and induces emesis by activating the vomiting center (Yoshitaka; 2007).

The choice of local anesthetic used for intrathecal injection does not influence PONV. Most investigations found no difference when comparing local anesthetics (Beilin et al; 2003)**,** the dose of drug does not seem to influence the occurrence of PONV, as long as hypotension is avoided **(**Sheskey et al; 1983).

Propofol possesses direct antiemetic properties, which is not a result of the lipid emulsion in the formulation of propofol (Yoshitaka; 2007**)**.The exact mechanism by which propofol acts as an antiemetic is unknown, but propofol is not considered to have vagolytic properties. In an experimental rat model, there is a possibility that the antiemetic property of propofol is associated with the reduced levels of serotonin in the area postrema and the CSF. Cechetto et al (2001) showed that propofol decreases the concentration

of both serotonin and 5-hydroxyindoleacetic acid within the fourth ventricle at the level of the area postrema.

Patients and Methods

In a prospective, randomised, single blind, placebo-controlled, clinical investigation and after obtaining a written informed consent from the patients, 83 Patients of ASA physical status I or II, aged 22 – 80 years, scheduled for elective surgery in the Urology operating theatre / Sulaimani teaching hospital from 20th May 2009 to 1st October 2009 were enrolled in the study. Patients were randomly assigned into two groups to receive either a continuous infusion of propofol (43 cases) at a subhypnotic dose (1 mg/kg/hr) or intralipid (40 cases). Patients with contraindications for spinal anaesthesia and/or with a history of sensitivity to propofol or intralipid, patients who have gastrointestinal diseases, ear diseases, liver diseases and those who have received drugs with antiemetic properties within 24 hours before surgery were not included in the study.

Every patient received 1 mg lorazepam preoperatively as premedication 2 hours before the operation. All subjects had fasted for at least 8 hours. On arrival in the operating room, routine monitoring devices were attached, and baseline blood pressure, heart rate, and pulse oximetry values were recorded. Each patient received 1 Litre of Ringer's lactate solution before spinal anaesthesia.

Under sterile conditions and via the midline approach dural puncture was performed at the L_3 –L_4 interspace with a 25 gauge spinal needle (Dr.J K-3 point type LUER-Lock HUB Tokyo Japan) in sitting position. After the free flow of CSF, 15-17.5 mg bupivacaine or 70-80 mg lidocaine was injected intrathecally, and then patients were placed in supine position immediately and kept horizontal for the remainder of the study, Oxygen 3 litres per minute administered to the patients via face mask. Following confirmation of sensory block by loss of sensation to cold and pinprick surgery was started. ECG, SpO_2, pulse rate, and arterial blood pressure were monitored and recorded. Blood pressure values of prespinal and 10, 20 and 30 minutes postspinal were recorded for statistical purposes. The decrease in mean arterial blood pressure (more than 20% baseline value) after spinal injection was regarded as hypotension and treated by increasing the rate of intravenous fluid administration, and by 5-10 micrograms increments of adrenaline administered i.v. (every 3-5 minutes) until resolution of hypotension. Heart rate < 60 bpm or 20% less than the baseline was defined as bradycardia and treated with 0.30 mg of i.v. atropine. The patients were advised to lie down in bed for 24 hours postoperatively to decrease the risk of Head ache and PONV.

Within 24 hours of surgery, PONV episodes were identified by direct questioning or by spontaneous complaint by the patients. If two or more

episodes of nausea-vomiting occurred, 10 mg of metoclopromide was provided intravenously as rescue antiemetic treatment. Postoperative analgesia was accomplished by NSAIDS except for those with greater risk of bleeding (20 out of 83 cases) in whom opioids were used instead.

Data were translated into codes using a specially designed coding sheet, and then converted to computerized database. An expert statistical advice was sought and statistical analyses were done using Statistical Package for Social Science (*SPSS*) version 13 computer software. The degree of association between the variables was calculated using Rank correlation i.e. Spearman's rho and/or Kendall's tau rank correlation coefficients. P value was calculated by Chi square and a P value of less than 0.05 was considered as statistically significant.

Results

Patients were divided in to two groups to receive either propofol (51.8% of patients) or intralipid (48.1% of patients), the intrathecal injection of local anesthetic (LA) agent was almost in two-thirds for Bupivacaine and a third for lidocaine, as shown in table 1.

Table 1 shows number and percentage of propofol, intralipid, Bupivacaine and lidocaine receiving patients

Variable	Frequency	Percentage (%)
Research Drug		
Propofol	43	51.81
Intralipid	40	48.19
LA agent		
Bupivacaine	56	67.4
Lidocaine	27	32.6

There was no statistically significant difference between the intrathecally injected local anaesthetic agent in regard to PONV or hypotension as shown in table 2.

Table 2: Shows Lidocaine/ Bupivacaine relation to PONV and hypotension

LA agent	Hypotension		P value	PONV		P value
	No No. (%)	Yes No. (%)		No No. (%)	Yes No. (%)	
Lidocaine	25(92.6)	2(7.4)	0.593	24(88.8)	3(11.2)	0.156
Bupivacaine	54(96.4)	2(3.6)		43(76.78)	13(23.22)	

The frequency and percentage of patients who suffered from hypotension, head ache and PONV is shown in table 3.

Table 3 shows the frequency and percentage of hypotension, PONV and Head ache

Variables	Frequencies	Percentage (%)
Hypotension		
No	79	95.2
Yes	4	4.8
Head ache		
No	70	84.3
Yes	13	15.7
PONV		
No	67	80.7
Yes	16	19.3

Hypotension was not a significant factor in relation to head ache or PONV, Table 4

Table 4: Shows Hypotension relation to head ache and PONV

Variables	Head ache		P value	PONV		P value
	No No. (%)	Yes No. (%)		No No. (%)	Yes No. (%)	
Hypotension						
Yes	4(100.0)	0(0.0)	0.899	3(75.0)	1(25.0)	0.583
No	66(83.5)	13(16.5)		64(81.0)	15(19.0)	

The percentage of female patients who suffered from Head ache and PONV is more than their male counterparts but the results were not statistically significant. These results are shown in table 5.

Table 5: Shows PONV and head ache distribution in relation to gender

gender	Head ache		P value	PONV		P value
	No No. (%)	Yes No. (%)		No No. (%)	Yes No. (%)	
Male	61(84.7)	11(15.3)	0.497	58(80.6)	14(19.4)	0.625
Female	8(80.0)	2(20.0)		8(80.0)	2(20.0)	

Age as a contributing factor was not statistically significant in the occurrence of hypotension, head ache, nausea and vomiting. These results are shown in table 6.

Variables	Age (years) Mean ± Std. Deviation	P value
Hypotension		
Yes	62.00 ± 2.449	0.181
No	53.16 ± 16.626	
Head ache		
No	15.674 ± 54.91	0.087
Yes	46.46 ±18.577	
PONV		
No	52.33 ± 16.472	0.294
Yes	58.88 ± 15.090	

Table 6: Age relation to PONV, head ache and hypotension**.**

Opioid use for control of postoperative pain was associated with a relatively higher incidence of PONV, but the result was not statistically significant. As shown in table 7.

Table 7: Shows Opioid relation to PONV

Opioid options	Research Drug		P value	PONV		P value
	Propofol No. (%)	Intralipid No. (%)		No No. (%)	Yes No. (%)	
Non opioid used	34(54.0)	29(46.0)	0.484	53(84.1)	10(15.9)	0.163
Opioid used	9(45.0)	11(55.0)		14(70.0)	6(30.0)	

Propofol was effective in reducing the incidence of PONV, this result was statistically significant, but there was no statistically significant difference between the relation of propofol or intralipid to headache. These facts are shown in table 8.

Table 8: Shows the effect of Propofol on the incidence of PONV.

Research drug	Head ache		P value	PONV		P value
	No No. (%)	Yes No. (%)		No No. (%)	Yes No. (%)	
Propofol	35(81.4)	8(18.6)	0.455	38(88.4)	5(11.6)	**0.04**
Intralipid	35(87.5)	5(12.5)		29(72.5)	11(27.5)	

Discussion

Reviews dealing with PONV have discussed almost exclusively GA and largely ignored regional anesthesia (Borgeat et al; 2003, Watcha & White; 1992)**.** This contrasts with the increasing popularity of regional anesthesia. A survey in Europe showed that one third of patients are undergoing regional anesthesia for their operative procedure (Borgeat et al; 2003), therefore I planned to investigate PONV among patients who underwent surgery under spinal anaesthesia.

Patients who received propofol had statistically significant lower incidence of PONV than those who received the placebo (Intralipid). This

result agrees with that of studies of Doze et al (1988) observed a 20% incidence of PONV in patients receiving propofol-nitrous oxide versus 40% in those receiving thiopental-nitrous oxide also Raftery and Sherry (1992) assessed the incidence of PONV in 80 patients, they received either total intravenous anaesthesia with propofol or enflurane-nitrous oxide anaesthesia, the former was associated with less PONV.

There was no statistically significant difference between patients who received Lidocaine or Bupivacaine neither in PONV nor in hypotension. This result has been proved in the study of Beilin et al(2003) where they randomized 59 women to receive either spinal lidocaine 30 mg or bupivacaine 5.25 mg for cervical cerclage, they observed that the incidence of the complications of nausea, vomiting, hypotension, and the need for ephedrine did not differ significantly between the Bupivacaine and lidocaine groups.

Patients who used opioid analgesia had relatively more incidence of PONV than others but the difference was not statistically significant, this result disagrees with that observed by Roberts et al (2005) who have confirmed, in a prospective study among 193 patients, that the incidence of nausea and vomiting are both increased in a dose-dependent manner by the amount of opiate administered .This disagreement may be attributed to the small number of patients who received opioid analgesia or the antiemetic effect of propofol in the group where the propofol was used as research drug might have some residual antiemetic effect, yet another reason may be due to the fact that opioid analgesia had been given by i.m. route which has less emetogenic effect (Watcha & White; 1992). The explanation of more PONV in opioid-using patients may be, despite the opioid induced, due to the fact that the operations were more extensive in this group of patients and it is well-known that more visceral manipulation results in higher incidence of PONV (Borgeat et al; 2003, Yoshitaka; 2007**).**[6,8]

Age was not important as a risk factor for PONV or head ache. This agrees with the study of Koivuranta et al (1997) who in a prospective interview-based survey on the incidence of PONV in 1107 in-patients aged 4-86 years found that the most important predictive factors associated with an increased risk for nausea and vomiting were female gender, a previous history of postoperative sickness, a longer duration of surgery, nonsmoking and a history of motion sickness with no effect of age.

Although female patients had more PONV and head ache than their male counterparts but the results were not statistically significant, this result disagrees with that of Larsson et al (1995) who performed a prospective study on 421 patients subjected to routine general-, orthopedic, urologic, gynecological and pediatric surgery to estimate the current incidences of nausea and vomiting during the first 24 hours after surgery. Postoperative

emetic symptoms were not related to age and women had more emetic symptoms than men, this disagreement may be due to the small number of female patients that have been included in our study or for better hemodynamic control.

Hypotension was not significant as a causative agent of head ache or PONV, this result disagrees with the result of Vercauteren et al (2000) who found that avoiding hypotension by ephedrine among 50 parturients undergoing C/S effectively reduce the incidence of PONV**,** this discrepancy may be due to early and effective hemodynamic control or good adherence of patients to our advice in regard to staying in bed.

Conclusion

Propofol infusion at a subhypnotic dose of 1 mg/kg/hr is effective in reducing PONV, in operations under subarachnoid block to gain antiemetic effect.

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