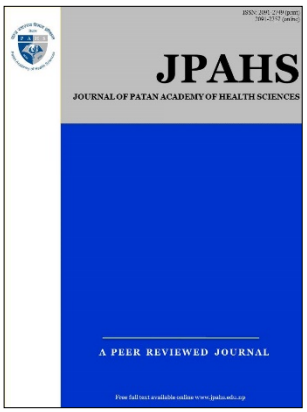

ISSN: 2091-2749 (Print)
2091-2757 (Online)

Maternal hemodynamic effect of prophylactic glycopyrrolate after spinal anaesthesia for elective caesarean section

Roshan Piya[1], Anil Shrestha[1], Manisha Pradhan[1], Shirish Prasad Amatya[2], Niroj Hirachan[2], Binam Ghimire[2]

[1]Asst. Prof., [2]Lecturer, Dept. of Anesthesia, Patan Academy of Health Sciences, Lalitpur, Nepal

Correspondence
Asst. Prof. Dr. Roshan Piya,
Dept. of Anesthesia
Patan Academy of Health Sciences, Lalitpur, Nepal
Email: piyaroshan@hotmail.com

Peer Reviewers
Dr. Sunita Maleku Amatya
Nepal Cancer Hospital and Research Centre, Nepal

Prof. Dr. Nabees MS Pradhan
Patan Academy of Health Sciences, Nepal

Submitted
11 Apr 2020

Accepted
20 Jan 2021

How to cite this article
Roshan Piya, Anil Shrestha, Manisha Pradhan, Shirish Prasad Amatya, Niroj Hirachan, Binam Ghimire. Maternal hemodynamic effect of prophylactic glycopyrrolate after spinal anesthesia for elective cesarean section. Journal of Patan Academy of Health Sciences. 2021Apr;8(1):44-50.

https://doi.org/10.3126/jpahs.v8i1.37012

Abstract

Introduction: Hypotension and bradycardia are the most common complications during spinal anesthesia. Bradycardia decreases cardiac output, resulting in hypotension and even cardiac arrest. Glycopyrronium, an anticholinergic drug increases heart rate and prevents bradycardia during spinal anesthesia by blocking the effects of acetylcholine on the sinoatrial node. The study aims to measure the maternal hemodynamic effect of glycopyrrolate after spinal anesthesia for elective caesarean section.

Method: An intervention, comparative study was conducted in Patan Hospital after approval from Ethical Committee. Eighty-two pregnant women scheduled for elective caesarean section were randomly assigned in two groups by sealed envelope method; Group I received glycopyrrolate 0.2mg intravenous and Group II did not receive glycopyrrolate. The patient's heart rate, blood pressure, mean arterial pressure, a total dose of ephedrine, the occurrence of nausea, vomiting, and dry mouth were recorded. Independent-T test and chi-square test were used for statistical analysis.

Result: Among 82 elective caesarean sections, 41 in each group, Group II (non-glycopyrrolate) reported increased heart rate compared to Group I (glycopyrrolate), but was statistically not significant. The highest recorded diastolic blood pressure was more in Group I compared to Group II and was statistically significant. The highest recorded Mean Arterial Pressure was high in the glycopyrrolate group and was statistically significant. The total dose of ephedrine was lower in the statistically significant glycopyrrolate group. The incidence of dry mouth was more in the glycopyrrolate group and the difference was statistically significant.

Conclusion: Glycopyrrolate reduces the incidence of hypotension but not bradycardia and decreases the need for vasopressor.

Keywords: bradycardia, caesarean sections, glycopyrrolate, spinal anesthesia

Introduction

Spinal Anesthesia is commonly used during caesarean section is associated with hypotension and bradycardia.[1] It decreases blood pressure, accompanied by a decrease in heart rate (HR), cardiac contractility, and even cardiac arrest.[2] Prophylactic glycopyrrolate, an anticholinergic drug is used for preventing intra-operative bradycardia.[3] It does not affect fetal heart rate because it cannot penetrate placental barriers.[4,5]

Glycopyrrolate increases HR by blocking the effects of acetylcholine on the sinoatrial node hence, helps in the prevention of post-spinal hypotension.[6,7] It is predicted to be a safe drug for pregnant women because of its reduced effect on the fetus and effective measure in maintaining heart rate.[8]

The study aims to analyze the maternal hemodynamic effect of glycopyrrolate after spinal anesthesia for elective caesarean section.

Method

A comparative study was conducted on patients undergoing spinal anesthesia for elective cesarean surgery in the Department of Anesthesiology at Patan Hospital, Patan Academy of Health Sciences (PAHS), Nepal during November 2018 - March 2019 after obtaining approval from the Institutional Review Committee of PAHS.

Sample size was calculated[6]41 in each group using mean and standard deviation($N=2(1.96+1.282)^2(15.5)^2/11.8^2=37+$ 10% non-response rate). The effect size of clinical interest was the difference of the mean.

American Society of Anesthesia Physical Status(ASA PS)I or II presenting for elective cesarean section were included after patients' written informed consent. Exclusion criteria were Pregnancy Induced Hypertension (PIH), known abnormality of the fetus detected by USG, cerebrovascular diseases, cardiovascular diseases, pulmonary diseases, coagulopathy, infection at the site of injection, severe spinal deformity, and other contraindications for spinal anesthesia.

Elective cases of caesarean section list were available one day before the operating day. A pre-anaesthetic evaluation of the patient was done one day before surgery. Patients were kept fasting as per the standard Nil Per Os (NPO) guidelines.

Patients were randomly assigned to one of the two study groups(Group I or Group II) by the sealed envelope method. The group was allocated as per the pick by the patient in the anaesthetic preparatory room. Group I received glycopyrrolate 0.2mg with normal saline intravenous and Group II only received normal saline infusion but not glycopyrrolate.

All the patients were prepared as per routine hospital practice. On arrival to the anesthetic preparatory room, vital signs including Blood Pressure (BP), Heart Rate (HR), Mean Arterial Pressure (MAP), and Oxygen Saturation (SpO_2) were recorded three times at five minutes interval while lying comfortably on the bed. The mean of three readings was recorded for a baseline value. After vital signs were recorded, an intravenous line was open with an 18 Gauze cannula, if cannula had not already been inserted in the ward, and preloaded with 500 ml Ringer's lactate solution to all the patients before spinal anesthesia.

In the operating theatre, an Electromyocardiography (ECG) leads, blood pressure cuff, and pulse oximeter were applied and vital signs were recorded every five minutes using an automated device. The highest and lowest recorded values of HR, blood pressure, and mean arterial pressure during the surgery were analyzed as the highest and lowest values. Under all aseptic precautions, spinal anaesthesia was induced by an anaesthesiologist in the subarachnoid space using 25 Gauge Quincke spinal needle and 0.5% hyperbaric bupivacaine 2.5 ml in L3/L4 space through midline approach in

sitting position after a free flow of clear Cerebrospinal fluid (CSF).

The patient's age, weight, and height were analyzed as per record in the patient's chart from the ward. The total dose of ephedrine and volume of intravenous fluid required, nausea, vomiting, and dry mouth were recorded.

Data were analyzed using SPSS version 16 and compared between two groups using the independent-T test and chi-square test with p <0.05 as statistically significant. Continuous data were analyzed as mean, standard deviation, and independent T-test. Chi-square test or Fisher's exact test was done for categorical data.

Result

There was a total of 82 pregnant women,41 Group I (glycopyrrolate)and 41 in Group II(non-glycopyrrolate). The demographics of both the groups, age, height, and weight were matched for both groups.

The mean heart rate, in Group I (glycopyrrolate) and Group II (non-glycopyrrolate)during surgery were statistically not significant, p = 0.87, Table 1.

The total ephedrine used was 14.8±13.8 and 25.0±22.9 in Group I and Group II respectively. Independent T-test showed the differences were statistically significant, p=0.02, Table 1.

Table 1. Comparison of baseline and changes in HR, blood pressure, and mean arterial pressure among Group I (glycopyrrolate, N=41) and Group II (no glycopyrrolate, N=41)

Variable	Group I	Group II	p-value
Demographics			
Age, y	29.55(±3.8)	28.6(±5.0)	0.34
Height, ft#	5.12(±0.32)	5.17(±0.24)	0.49
Weight, kg	69.30(±8.56)	66.90(±9.29)	0.23
Baseline haemodynamic before surgery			
HR beats/min	102(±20.5)	99.5(±15.6)	0.53
SBP mmHg	123.2(±17.1)	120.9(±13)	0.49
DBP mmHg	72.4(±13)	75.6(±10.5)	0.23
MAP mmHg	90.1(±13)	86.4(±13.3)	0.20
Changes in haemodynamic during surgery			
Highest HR	121.2(±15.5)	128.4(±21.3)	0.87
Lowest HR	82.9(±16.5)	79.9(±12.9)	0.36
Highest SBP	137.2(±12.9)	132.2(±13.2)	0.08
Lowest SBP	93(±13.9)	91.1(±15.2)	0.56
Highest DBP	80(±10.5)	85(±10.3)	0.03*
Lowest DBP	49.1(±10)	48.8(±8.9)	0.88
Highest MAP	102.9(±13)	97.3(±9.5)	0.02*
Lowest MAP	64.7(±10.7)	62.7(±11.3)	0.41
Ephedrine required mg	14.8(±13.8)	25.0(±22.9)	0.02*

#ft=feet used for convenience instead of the centimeter, HR=heart rate, SBP=systolic blood pressure, DBP= diastolic blood pressure, MAP= mean arterial pressure, *Statistically significant

Table 2. Incidence of nausea, vomiting, and dry mouth among Group I and II

Variable		Group I	Group II	Total	p-value
Nausea	No	39(52%)	36(48%)	75(100%)	0.43[a]
	Yes	2(28.6%)	5(71.4%)	7(100%)	
Vomiting	No	40(49.4%)	41(50.6%)	81(100%)	1.00[a]
	Yes	1(100%)	0(0%)	1(100%)	
Dry mouth	No	27(41.5%)	38(58.5%0	65(100%)	0.003[b]*
	Yes	14(82.4%)	3(17.6%)	17(100%)	

Fisher's Exact Test[a], Chi-square test[b], Statistically significant*

Among 17 patients reporting dry mouth, 14(82.4%) were in Group I and 3(17.6%) in Group II. Chi-square test result showed a statistically significant value, p=0.003, Table 2.

Discussion

Our results showed that the highest MAP was significantly higher, 102.9±13 vs. 97.3±9.5, (p=0.02) in the intervention group with glycopyrrolate.

Anticholinergics, e.g. atropine is more effective than glycopyrrolate in increasing the heart rate but atropine also has a higher rate of placental transfer than glycopyrrolate.[7] Anticholinergic drugs have been proven to prevent adverse cardiovascular effects and decrease secretion during induction of general anesthesia.[2] Glycopyrrolate has a longer duration of action than atropine and reduces acidity or gastric juice volume in pregnant women.[2,5] Glycopyrrolate increases heart rate by blocking the effect of acetylcholine on the sino-atrial node and helps in the prevention of post-spinal hypotension and is a safe drug for pregnant women.[6,7]

The absorption of glycopyrronium after intramuscular administration was very fast. Glycopyrronium was removed from the circulation rapidly and almost half the dose of the drug was excreted through the urine within three hours. The level of glycopyrrolate in the lumbar cerebrospinal fluid (CSF) after sixty minutes of drug injection was unmeasurable. The concentrations of glycopyrronium in the umbilical venous and arterial after eighty-six minutes of drug injection were low and clinically insignificant in the amniotic fluid.[7] Glycopyrronium does not penetrate through the blood-brain and placental barriers and cardiovascular effects of the neonates were not seen.[5,7,10]

In the present study, there was no bradycardia, but the lowest mean HR was higher in the glycopyrrolate group, 82.9±16.5 vs. 79.9±12.9 (p=0.36).

In contrast, another study revealed prophylactic intravenous glycopyrrolate prevented bradycardia after spinal anaesthesia. The Glycopyrrolate group showed a significant increase in HR than the placebo group.[4,6,9] Another study reported that glycopyrrolate caused increased maternal heart rate and cardiac index which was observed 8-15 mins after induction.[8] Yet another study reported no statistically significant difference in the incidence of bradycardia, tachycardia, and percentage change in HR among glycopyrrolate and saline group.[10] The heart rate was increased significantly and the onset of antisialogogue effect was slow among parturient. But, the duration of the antisialogogue effect was longer than the heart rate effects. The concentrations of inhibition of salivation were high for tachycardia due to the sensitivity of the muscarinic receptor subtypes to glycopyrronium.[7]

Studies have shown a statistically significant decrease in heart rate in the phenylephrine group but showed no significant difference in phenylephrine combined with the glycopyrrolate group.[8] Bradycardia was significantly less in the glycopyrrolate group compared to the ondansetron group and thus, glycopyrrolate decreased the incidence of bradycardia by 30%.[11]

We used the standard dosage of glycopyrrolate i.e. 0.2 mg with normal saline.[5,10,12] But, there are some studies in which 0.4 mg of glycopyrrolate was used.[4,9]

Regional anaesthesia is preferred over general anaesthesia due to reduced pulmonary complications and protection against thromboembolic events.[2] Spinal anaesthesia has become a common and popular technique for caesarean delivery because it is reliable, safe, quick, and offers post-operative analgesia. The most common complications of spinal anaesthesia are hypotension and bradycardia but administration of prophylactic glycopyrrolate during caesarean delivery under spinal anaesthesia increases maternal HR but does not significantly reduce the

incidence of bradycardia.[13] Other common factors causing spinal induced hypotension are systemic vascular reduction, block heights T5 or greater, age 40 y or above, baseline systolic blood pressure less than 120mmHg, spinal puncture above L3-L4 interspace.[14,15] Risk factors of bradycardia are baseline HR less than 60 beats per minute, sympathetic block, use of beta-adrenergic blockers, prolonged PR interval on electrocardiogram, and block height T5 or greater.[3,15] Untreated spinal induced hypotension and bradycardia can cause maternal cardiovascular collapse and fetal acidosis.[13]

Hypotension during regional anesthesia for cesarean section is a common clinical problem because of increased sensitivity to local anaesthesia, aortocaval compression, and increased susceptibility to sympathetic block.[8,9]

Long-term or severe hypotension may cause unconsciousness, pulmonary aspiration, hypoxia, acidosis, and fetal neurological injury due to the reduction of uteroplacental blood flow.[4,8,16] Thus, it has become routine practice to reduce the incidence and the severity of hypotension by administering pre or co-loading of IV fluid, physical methods such as leg compressions and displacing the uterus laterally, and giving vasopressor agents.[17,18,19]

Reduced systemic vascular resistance causes hypotension which is aggravated in the parturient by inferior vena cava compression, partially compensated by increased stroke volume and heart rate. The best method to prevent hypotension is controversial but recent practice recommends prophylactic vasopressors for caesareans section.[19]

In our study, prophylactic glycopyrrolate before spinal anaesthesia for caesarean section reduced the severity of maternal hypotension. The mean arterial pressure was significantly higher with glycopyrrolate than without. Other studies showed the incidence of hypotension was less in the glycopyrrolate group compared to the saline group.[10] Patients with one or more episodes of hypertension were more in the glycopyrrolate group.[9]
The incidence of hypotension was unaffected by glycopyrrolate, but the ephedrine requirement was significantly higher.[5,6] Yet another study reported no statistically significant difference in the severity of maternal hypotension and the dose of ephedrine required in two groups.[4]Another study reported maternal HR was increased in the ephedrine group.[17] Vasopressor reduced the rate of intra-operative hypotension before and after induction of anaesthesia but ephedrine was least effective. The rate of maternal bradycardia was higher in phenylephrine compared to ephedrine and norephedrine infusion.[19] Subarachnoid block induced hypotension have used high dose phenylephrine and is associated with maternal bradycardia and reactive hypertension.[9,18]

The subarachnoid block given for parturients had been associated with hypotension due to a higher level of sympathetic blockade. Maternal hypotension was associated with severe distress in the form of nausea, vomiting, and dizziness. It can also lead to placental hypoperfusion which can affect neonatal outcome. The pre-emptive or proactive vasopressor reduced the incidence and severity of spinal anesthesia induced hypotension.[13,19] Glycopyrrolate was administered intramuscularly to avoid an abrupt increase in heart rate and hypotensive episodes during the subarachnoid block.[10]

Glycopyrrolate in the current study affected blood pressure and mean arterial pressure but not heart rate. Glycopyrrolate, an anticholinergic is used among pregnant women for the prevention of subarachnoid block-induced bradycardia, intra and post-operative nausea, and vomiting.[4,6,16]

Glycopyrrolate, a synthetic quaternary ammonium amino-alcohol ester, has a chronotropic effect through its antimuscarinic activity within one minute of intravenous injection. Glycopyrrolate injection was indicated for the use of pre-operative antimuscarinic to reduce salivary secretions,

free acidity gastric secretions, and block cardiac vagal inhibitory reflexes during induction of anesthesia. The vagal blockades continue for two to three hours. The intravenous glycopyrrolate helps to reverse vagal reflexes and intraoperative bradycardia and protects against the peripheral muscarinic effects of cholinergic agents.[19] When administered to patients undergoing spinal anaesthesia, the muscarinic blockade of glycopyrrolate decreases parasympathetic activity which can prevent bradycardia but increases heart rate.[6,12]

Maternal hypotension after spinal anaesthesia may induce emesis during intra-operative and post-delivery.[20]Antiemetic effect was provoked due to heart rate, increase in cardiac output, and subsequent reduction in hypotension. Hypotension triggers vomiting center to induce emesis due to hypoxia.[5,20]Glycopyrrolate also possess antiemetic properties by inhibiting central muscarinic and cholinergic emetic receptors.[21] It has been reported that glycopyrrolate minimizes the incidence of nausea vomiting during spinal anesthesia for caesarean section without affecting fetal outcome.[5,7]

In the present study, there was no significant difference in nausea and vomiting but a significant difference in the dry mouth between the two groups which was similar to some studies.[4,9,21]In the present study dry mouth was more in the glycopyrrolate group which was statistically significant but another study showed no evidence of dryness of mouth in any of the study patients.[7]

Numerous endocrinal, systemic, and physiological alterations can occur during pregnancy. The aetiology of hypotension and bradycardia in spinal anaesthesia during caesarean section is multifactorial and many interventions were recommended to prevent hypotension and bradycardia. The present study reported that glycopyrrolate had reduced the incidence and severity of hypotension.

In the present study, pregnant women of ASA PS III or IV were excluded, and also use an additional dose of 0.4mg may be extended to find out the dose-dependent effect of glycopyrrolate.

Conclusion

Prophylactic intravenous glycopyrrolate in spinal anaesthesia for caesarean section reduced the incidence and severity of hypotension and the need for vasopressor.

Acknowledgement

We would like to thank all the patients who have participated in the study and also to the Department of Anaesthesia and Department of Obstetrics& Gynecology, Patan Hospital for allowing us to conduct this study.

Conflict of Interest

None

Funding

None

Author Contribution

Concept, designed, and plan- RP, AS, MP, SPA, NH, BG; Literature review- RP, AS, MP, SPA. Data collection and analysis - RP, MP, NH, BG; Draft manuscript- RP, SPA; Manuscript revision AS, NH, BG; All authors read and approved the final manuscript.

Reference

1. Miller RD. Miller's anesthesia. 6th ed. Pennsylvania: Elsevier Churchill Livingstone; 2005. p1661-70. | Weblink |
2. Morgan GE, Mikhail MS, Murray MJ. Clinical anesthesiology. 4th ed. New York: Lange Medical Books/McGraw-Hill Companies. 2006. p240, 317-21. | Weblink |
3. Hasanin A, Mokhtar AM, Badawy AA, Fouad R. Post-spinal anesthesia hypotension during cesarean delivery, a review article. Egyptian J Anaesth. 2017;33(2):189-93. | DOI | Google Scholar | Full Text | PDF | Weblink |
4. Yentis SM, Jekins CS, Lucas DN, Barnes PK. The effect of prophylactic glycopyrrolate on maternal haemodynamics following spinal anaesthesia for elective caesarean section. Int J

ObstetAnesth. 2000;9(3):156-9. | DOI | PubMed | Google Scholar| Weblink |
5. Ure D, James K, McNeill M, Booth JV. Glycopyrrolate reduces nausea during spinal anesthesia for caesarean section without affecting neonatal outcome. Br J Anaesth. 1999;82(2):277-9. | DOI | PubMed | Google Scholar| PDF |
6. Chamchad D, Horrow Jay C, Nakhamchik L, Sauter J, Roberts N, Aronzon B, Gerson A, Medved M. Prophylactic glycopyrrolate prevents bradycardia after spinal anesthesia for cesarean section: a randomized, double – blinded, placebo controlled prospective trial with heart rate variability correlation. J Clin Anesth. 2011;23(5):361-6. | DOI | PubMed | Google Scholar | Weblink |
7. Ali-Melkkila T, Kaila T, Kanto J, Lisalo E. Pharmacokinetics of glycopyronium in parturients. Aneaesthesia. 1990;45(8):634-7. | DOI | PubMed | Google Scholar | Full Text | Weblink |
8. Yoon HJ, Cho HJ, Lee IH, Jee YS, Kim SM. Comparison of hemodynamic changes between phenylephrine and combined phenylephrine and glycopyrrolate groups after spinal anesthesia for caesarean delivery. Korean J Anesthesiol. 2012;62(1):35-9. | DOI | PubMed | Google Scholar | Weblink |
9. Ngan Kee WD, Lee SW, Khaw KS, Ng FF. Haemodynamic effects of glycopyrrolate pre-treatment before phenylephrine infusion during spinal anaesthesia for caesarean delivery. Int J ObstetAnesth. 2013;22(3):179-87. | DOI | PubMed| Google Scholar| PDF| Weblink|
10. Manem A, Krishnamurthy D. Evaluation of pre-emptive intramuscular glycopyrrolate in prevention of spinal anesthesia induced hypotension in elective cesarean sections. Indian J AnesthAnalg. 2019;6(3)(Part-I):705-11. | PDF |
11. Jain R, Sharma R. A comparative study of effects of glycopyrrolate and ondansetron on nausea and vomiting in cesarean section under spinal anesthesia. Anesth Essays Res. 2015;9(3):348-52. | Google Scholar | Weblink |
12. Hwang J, Min S, Kim C, Gil N, Kim E, Huh J. Prophylactic glycopyrrolate reduces hypotensive responses in elderly patients during spinal anesthesia: a randomized controlled trial. Can J Anesth. 2014;61:32-8. | DOI | Google Scholar | PDF | Weblink |
13. Patel SD, Habib AS, Phillips S, Carvalho B, Sultan P. The effect of glycopyrrolate on the incidence of hypotension and vasopressor requirement during spinal anesthesia for cesarean delivery: a meta-analysis. Anesthesia& Analgesia. 2018;126(2):552-8. | DOI| PubMed | Google Scholar| PDF| | Weblink|
14. Liu SS, McDonald SB. Current issues in spinal anesthesia. Anesthesiology. 2001;94:888-906. | DOI| Google Scholar| PDF| Weblink|
15. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. Anesthesiology. 1992;76:906-16. | DOI| PubMed | Google Scholar |
16. Rocklidge MW, Durbridge J, Barnes PK, Yentis SM. Glycopyrronium and hypotension following combined spinal epidural anaesthesia for elective caesarean section in women with relative bradycardia. Anesthesia. 2002;57:4-8. | DOI | Google Scholar | PDF | Full Text |
17. Bhardwaj N, Jain K, Arora S, Bharti N. A comparison of three vasopressors for tight control of maternal blood pressure during cesarean section under spinal anesthesia: effect on maternal and fetal outcome. J Anaesthesiol Clin Pharmacol. 2013;29:26-31. | DOI | PubMed | Google Scholar | Weblink |
18. Ngan Kee WD, Khaw KS, Ng FF. Prevention of hypotension during spinal anesthesia for cesarean delivery: an effective technique using combination phenylephrine infusion and crystalloid cohydration. Anesthesiology. 2005;103(4):744-50. | DOI | PubMed | Google Scholar| PDF | Weblink |
19. Fitzgerald JP, Fedoruk KA, Jadin SM, Carvalho B, Halpern SH. Prevention of hypotension after spinal anaesthesia for caesarean section: a systematic review and network meta-analysis of randomised controlled trials. Anaesthesia. 2020;75(1):109-21. | DOI | PubMed | Google Scholar | PDF | Full Text |
20. Biswas B, Rudra A, Das S, Nath S, Biswas S. A comparative study of glycopyrrolate, dexamethasone and metoclopramide in control of post-operative nausea and vomiting after spinal anaesthesia for caesarean delivery. Indian J Anaesth. 2003;47(3):198-200. | Google Scholar| PDF | Full Text |
21. Amatya BR, Acharya B, Pradhan B, Marhattha M. Effect of glycopyrolate on nausea, vomiting and neonatal outcome during spinal anaesthesia for elective caesarean section. Med J Shree Birendra Hospital. 2016;15(1):2-8. | DOI | Google Scholar | Full Text | Weblink |