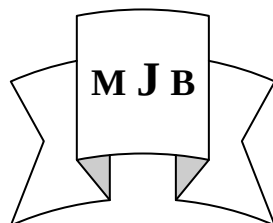


Comparison of the Use of Tropisetron and Metoclopramid in the Prevention of Post-Operative Nausea and Vomiting

Mohammed Jawad
Hilla Teaching Hospital, Babylon General Directory of Health, Hilla, Iraq

Malath Azeez Jebur



Received 28 May 2013

Accepted 20 August 2013

Abstract

Post –operative nausea and vomiting remain among the most common and distressing symptoms occurring after surgery under general anesthesia .In the current study we compare the prophylactic antiemetic effect of Tropisetron, Metoclopramid, and placebo. All are given as identical oral capsules 2 hours pre-operatively . 90 patients undergoing major surgery were divided in to 3groups each group contain 30 patient (15 male and 15 female) and were observed for at least 24 hours after operation . The study revealed that nausea and vomiting occurred was reduced in Tropisetron treated patients than placebo treated patients. And the percentage of nausea and vomiting of Tropisetron treated patients was reduced to 30% while in Metoclopramid treated patients reduced to 43.3% and placebo was 60%.We conclude that post-operative nausea and vomiting were reduced when Tropisetron given prophylactically than Metoclopramid and placebo.

الخلاصة

الغثيان والتقيؤ هي واحدة من أكثر الأعراض إزعاجاً للمرضى الذين يخضعون للجراحة تحت تأثير التخدير العام. في هذه الدراسة نحن نقارن بين تأثير الاستخدام الوقائي لمضادات التقيؤ التروبيسترون والمتوكلوبرومايد ومجموعة العلاج. كل الأدوية أعطيت على شكل كبسولات فموية متشابهة ساعتين قبل إجراء الجراحة. ٩٠ مريضاً يخضعون لجراحة كبرى انضموا للدراسة وقسموا عشوائياً إلى ثلاث مجموعات كل مجموعة تتكون من ثلاثين مريض (١٥ ذكر و ١٥ أنثى) وتمت مراقبتهم لمدة ٢٤ ساعة بعد الجراحة. أظهرت الدراسة أن هناك انخفاضاً في نسبة الغثيان والتقيؤ في المجموعة التي عولجت بالتروبيسترون مقارنة بمجموعة العلاج وأن الغثيان والتقيؤ في مجموعة التروبيسترون انخفض إلى ٣٠% ومجموعة والمتوكلوبرومايد انخفض إلى نسبة ٤٣,٣% بينما مجموعة العلاج كان بنسبة ٦٠%. نستنتج من ذلك أن استخدام التروبيسترون وقائياً قبل الجراحة هو أكثر فعالية في تقليل نسبة الغثيان والتقيؤ بعد الجراحة من المتوكلوبرومايد ومجموعة العلاج.

Introduction

Post-operative nausea and vomiting remain among the most common and distressing symptoms occurring after surgery under general anesthesia [1]. Abdominal and gynecological surgeries are particularly associated with post-operative nausea and vomiting [2]. Furthermore, they are the most frequent factors preventing patients returning home at the end of

day case surgery or necessitating readmission to the hospital [2].

Nausea is often a prodrom of vomiting that is to say, it is a conscious recognition of the subconscious excitation in an area of the medulla closely associated with or apart of the vomiting center [3]. Any part of the gastrointestinal tract can initiate vomiting reflex [4]. Impulses are transmitted by both vagal and sympathetic afferents to the bilateral vomiting centers of the medulla [5].

The receptors involved in the mechanism of vomiting include dopamine (D2) and serotonin (5HT3) in case of chemoreceptor trigger zone, histamine (H2) and cholinergic receptor (M3) in the vomiting center[6]. There are 5HT3 receptor in the small intestine and serotonin secreted by enterochromaffin cells appear to initiate vomiting[7]. The anti emetic drugs acting on the vomiting center have anti muscarinic and antihistaminic action e.g. Hyosin, Promethazin. they alleviate vomiting from any cause but drugs acting on the chemoreceptor trigger zone like Haloperidol and Ondansetron are effective only for vomiting mediated by the chemoreceptors induced by morphine, digoxin, cytotoxics and uraemia. The most efficacious drugs act at more than one site[8].

Factors influence the etiology of post operative nausea and vomiting include : the patients, those who are more prone to motion sickness more likely to vomit[9]. Pre-operative drugs :all opioids drugs possess marked emetic properties[9]. Anesthetic drugs ,site of operation, duration of surgery and condition of the stomach [10].

Metoclopramide

Is a specific anti emetic. it is ad dopamine receptor (D2) antagonist act on the CTZ. At higher dose ,also act on 5HT3 receptors[11,12].

It also, has peripheral action diminishing the sensitivity of visceral nerves to local emetics . and enhance the acetylcholine at the muscarinic nerve endings in the gut also hasten the gastric emptying and increase the tone of lower esophageal sphincter[6,8].

Pharmacokinetics

After oral dose Metoclopramide produce maximum effect in 0.5-2 hr, with plasma half life of 5.7hr. plasma protein binding is 40% while its bioavailability is 30-80%. It is mainly

metabolized in liver and excreted in urine[13]. Side effects

They are mainly related to the blockage of dopamine receptors in the CTZ .disorders of movements can occur in children and young adult and those currently receive other dopamine antagonist .extra pyramidal side effects are produced if the dosage exceeds 0.5 mg/kg. long term use of Metoclopramide may cause tardive dyskinesia in elderly patients. It can stimulate prolactin release and cause galactorrhea and menstruation disorder[14,15].

Tropisetron

It is a selective, competitive , 5HT3 receptors antagonist, that has along elimination half life and need to be given once daily[16]. Its proved to be effective against nausea and vomiting induced by chemotherapy also it shown to be effective in preventing post-operative nausea and vomiting[12]. Pharmacokinetics

After an oral dose Tropisetron produce maximum effect in 1.3 hr with plasma half life of 7.3-8.6hr . it has an oral bioavailability of 50-70% and plasma protein binding of 50-70%. it metabolized in liver by cytochrome P450 and the elimination half life of 8hr in fast metabolizers. Tropisetron can be given orally or intravenously as 5 mg capsule and ampoules[12,17]. Side effect Include headache, sedation ,anxiety and constipation[15].

Patients and Method

90 patients undergoing elective abdominal surgery under general anesthesia in al Hilla Teaching Hospital in Sept.2011 and Mar. 2012 were included in this placebo – controlled study. Age of 20-70 years, weighing 50-70 kg. They were divided to three groups of 30 patients (15 male and 15 female). The patients were randomized to receive Tropisetron, Metoclopramide and placebo, all were

given as identical capsules. Tropisetron 5mg and placebo were given pre operatively while Metoclopramide was given as 10 mg orally 2hr pre operatively and 10 mg every 8hr thereafter.

Diazepam 10mg was given orally at midnight. Anesthesia was induced by sleeping dose of thiopentone (4-6mg/kg), Fentanyl 2 miq/kg , muscle relaxation was achieved by Atracurium 0.6 mg/kg. Anesthesia was maintained by adequate concentration of Halothane in oxygen (1-2%) standard monitoring technique were applied. Nausea and vomiting were assessed by direct questioning and recorded in the following sequence : at the first hour ; 1-4 hours;4-24 hours after recovery from anesthesia . The symptoms were recorded as present or absent.

Results

The incidence of nausea and vomiting during the first 24 hours observation period were 60% (18/30) for patients taking placebo, 43.33% (13/30) for patients treated with Metoclopramide,

and 30% (9/30) for patients treated with Tropisteron. The incidence of post operative nausea and vomiting was less in Tropisteron treated group than the placebo.

The incidence of nausea and vomiting in the Metoclopramide treated group was less than placebo and higher than Tropisteron treated group . (Table 1, figure 1).

The incidence of vomiting (with or without nausea) was higher in the first post operative hour being 53.3% for placebo group, 40% Metoclopramide treated group and 16.66 for Tropisteron treated group. While , in 1-4 hour being 30% for placebo, 23.33% for Metoclopramide treated group and 16.66% for Tropisteron treated group In the period 4-24 hour The incidence of vomiting was 16.6% for placebo group , 13.33% for Metoclopramide treated group and 6.66% for Tropisteron treated group.(Table 2, figure2).

The incidence of nausea and vomiting in female was higher than male in all study groups (Table 3, figure 3).

Table 1 Post-operative nausea and vomiting of patients in different study groups.

Group	Total no. of Nausea & vomiting		Nausea & vomiting %
Placebo	30	18	60%
Metoclopramid	30	13	43.33%
Tropisteron	30	9	30%

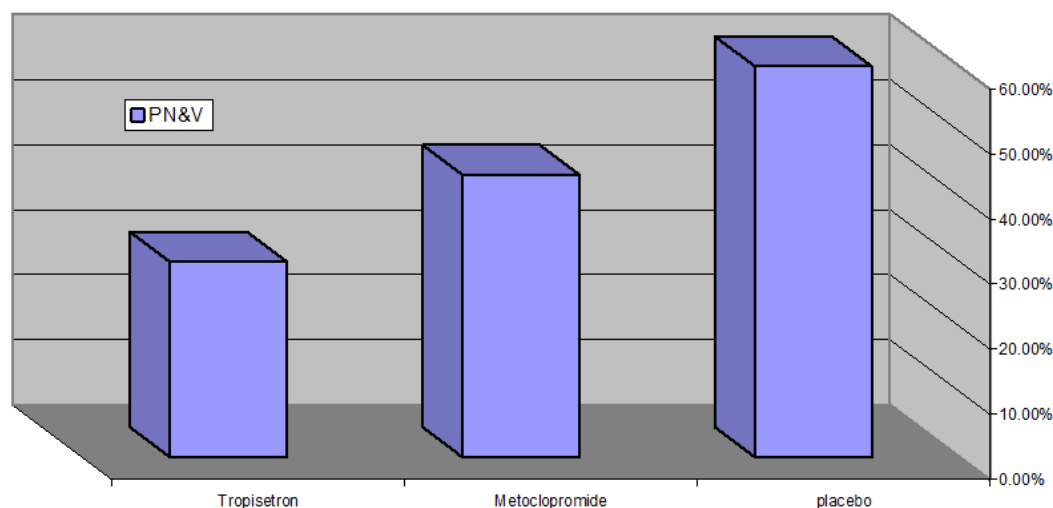


Figure 1 The occurrence of post operative nausea and vomiting of patients in different study groups.

Table 2 The occurrence of post operative nausea and vomiting of patients in different study groups according to time of occurrence.

Time of occurrence	Placebo		Metoclopramid		Tropisteron	
	No./30	%	No./30	%	No./30	%
0-1 hr	9	30%	6	20%	5	16.66%
1-4 hr	7	23.3%	5	16.66%	3	10%
4- 24 hr	2	6.66%	2	6.66%	1	0.333%

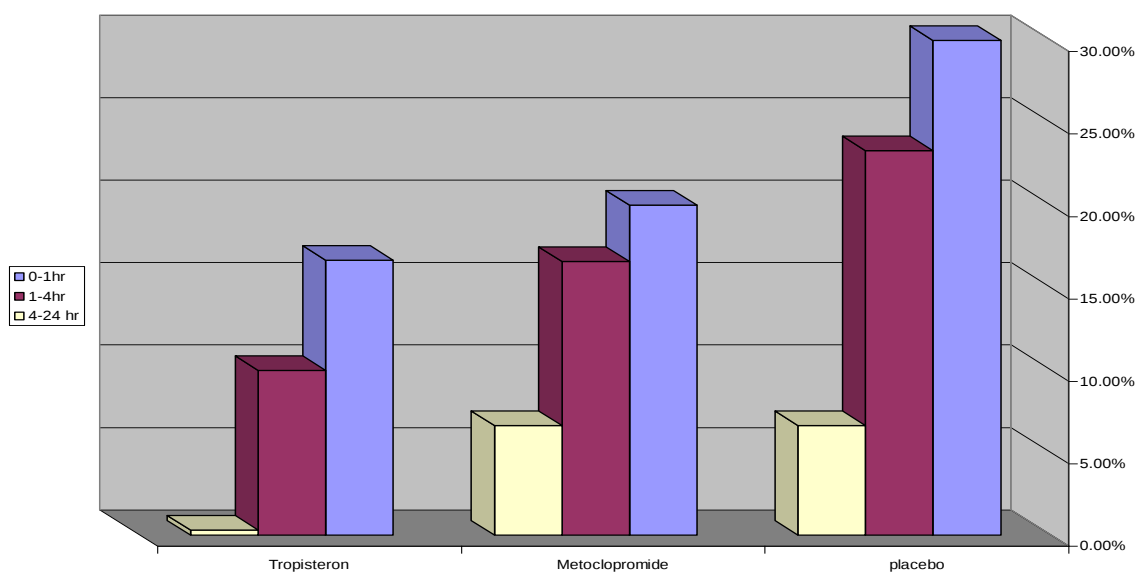


Figure 2 The occurrence of post operative nausea and vomiting of patients in different study groups according to time of occurrence.

Table 3 The occurrence of post operative nausea and vomiting of patients in different study groups according to sex.

Sex	Placebo		Metoclopramide		Tropisteron	
	No/30	%	No/30	%	No /30	%
Male	8	53.3	5	33.3	4	26.6
Female	10	66.6	8	53.3	5	33.3

Discussion

This study was designed to measure the incidence of post operative nausea and vomiting and to compare between the activity of oral Tropisteron and Metoclopramide in the prevention of this post operative complications.

In this study 60% of placebo treated group suffer from post operative nausea and vomiting in the 1st post operative 24hrs and this come with V.T.Churian and I.Smith , 2001[18]. who found that 57% of patients experienced sever post operative nausea and vomiting also with Kaufman .Marcus et al,1994[19] study that measure the incidence of post operative nausea and vomiting during patients controlled analgesia with morphine and go with Purihonin ,Snikka et al,1997 [20]study which found that only 20% of placebo patients are free from post operative nausea and vomiting.

In this study Metoclopramide 10mg orally reduce the incidence of post operative nausea and vomiting. this result goes with Raphael,JH. And Norton1993 [21] and Milans et al,1994 [22] who stated that Metoclopramide reduce the incidence of post operative nausea and vomiting from 50% with placebo to 42% .

In our study Tropisteron reduce post operative nausea and vomiting more than with placebo treated group and when compared with Metoclopramide treated group. Elon .Eli et al,1996[23] found that Tropisteron significantly

reduce post operative nausea and vomiting and vomiting was better controlled and this agree with our finding . On the other hand C.A.ng et al,1998[16] studied the effect of Tropisteron on post operative nausea and vomiting after tonsillectomy in children and they found that Tropisteron had an effective anti emetic effect in children. Also our finding goes with Chan.M.T. et al,1998[24] who state that single dose of Tropisteron is well tolerated and decrease the number of nausea and vomiting episodes after surgery . while, Young Seok Jee et al,2010[25] stated that there are no significant difference between groups treated with Metoclopramide 20mg and dexamethason and other group treated with Ondansetron and dexamethason although, this finding differ in the dose of Metoclopramide and using of dexamethason.

This study revealed that the incidence of nausea and vomiting was higher in female than male. J.P.Dupeyron et al ,1993 [26]. state that female being up to 3 times more likely experience emesis but our study can not demonstrate such difference.

In this study the incidence of post operative nausea and vomiting was higher after operation especially in the first post operative hour and this agree with T.H.Madaj and K.H.Simpson 1986 [27] who found that the incidence of post operative nausea and vomiting occur early in the recovery phase but

not agree with Elon .Eli et al,1996 [23] that state the incidence of post operative nausea and vomiting was rare after 4hours following surgery.

Conclusion

post operative nausea and vomiting are common post operative complication . Tropisteron is more effective anti emetic drug than Metoclopramide in post operative nausea and vomiting.

References

- 1- Naguib Mohamed etal, 1996. Prophylactic anti emetic therapy with Ondansetron, Tropisetron ,Granisetron and Metoclopramide, randomized double blind comparison with placebo. Canadian , J. of Anasth. 34, p 226-231.
- 2-P.J.Zomers etal, 1993. Tropisetron for post operative nausea and vomiting in patients after gynecological surgery. Br.J.of Anasth. 71 ,p 677-680.
- 3-Arthur C.Guyton and Jhon E.Hall 2000. Text book of medical physiology, 10 edition, ch. 66 ,p 764-770.,sounders com. Philadilphia
- 4- Vishwanth R.Lingapand (2000). Physiological medicine ,2nd edition, Ch.25 p 199-256. McGraw-Hill. NY.
- 5-Arthur C.Guyton and Jhon E.Hall. 1997 human physiology and mechanism of disease , 6th edition, ch. 44, p. 537-547. sounders com. Philadilphia.
- 6- M.D,Vicker,M.Morgan, P.Spencer and M.Reed 1999. drug in anesthetic practice , 8th edition , ch.2 p: 61-68. Oxford .
- 7- William F.Ganong. 1999. Review of medical physiology 9th edition , Ch. 14, p 221-244. Appleton and Lang. Stamford.
- 8- D.R.Laurence B.M.Bennet and M.J.Brown (1998). Clinical pharmacology, 8th edition . ch. 32, p 567-578. Churchile Livingstone.
- 9- G .Hobbs1998. complication during anesthesia , text book of anesthesia 3^{ed} edition . Ch.22, p377-407 Churchile Livingstone.
- 10- R.S.Atkinson , G.B.Rushman and N.J.H.Davies . Lee's Synopsis of anesthesia . Ch. 14; p 261-298.
- 11-H.P.Rang, M.M. Dale and Ritter. 2007. Pharmacology 11th edition, Ch. 25, p 391-393 Churchile Livingstone.
- 12- G. Katsung (2009), clinical and basic pharmacology 11th edition Ch.62, McGraw-Hill Companies Lang.
- 13- H.P.Rang, M.M. Dale and Ritter.1998. Pharmacology 7th edition, Ch. 21, p 370-384. Churchile Livingstone.
- 14- Thomas R.Weihrouch 2000. Clinical pharmacology, disorder of G.I.T. Ch . 32; p 339-346. McGraw-Hill. NY.
- 15- R.A.Harvey and Champ 2009. Pharmacology 4¹¹ edition, Ch.25 .p 336-338.Lippincote ellisterated review.
- 16-C .Ang, W.Habrev ,C.Sims .(1998) .Tropisteron reduce vomiting after tonsillectomy in children. Br. J. Anasth.,80, p 338-341.
- 17-. M.T Patikanen et al.1993. The effect of Tropisetron . a5HT3, receptor antagonist on analgesia and nausea after intra thecal morphine . Br.J.Anasthes. vol. 71.p 681-684.
- 18- V.T.Cherien and I.Smith ,2001. prophylactic Ondansetron does not improve patient satisfaction in women use PCAafter casearian section. British J.Anaes.87(3);p:502-504.
- 19- Kaufman ,Markus etal, 1994. Prophylactic anti emetic therapy with patient controlled- analgesia a double blinded placebo controlled comparison of Droperidol, Metoclopramide ,and Tropisetron. Anasth.Anal. 78 .p988-994.
- 20- Purhonen , Snikka etal, 1997. Comparison of Tropisetron ,Droperidol and saline in the prevention of nausea and vomiting in patients after gynecological surgery. Anesthesia. Anal. ;84; p 662-667.

- 21- Raphael , J.H.and Norton A.C. 1993. Anti emetic efficacy of prophylactic Ondansetron in laparoscopic surgery, randomized double blind comparison with Metoclopramide . Br.J.of Anasth. 71; p845-848.
- 22- Malins ,A.F.etal 1994. Comparison of pre medication with oral Ondansetron and Metoclopramide and placebo. Br.J.Anasthes. vol. 72.no. 2.p 231-233.
- 23-Elon-Eli etal, 1996 . Tropisetron for prevention of post operative nausea and vomiting in women undergoing gynecological surgery. Anaes. Anal, 82,p 338-341.
- 24- Chan.M.T. etal,1998. single dose of Tropisetron for prevention of post operative nausea and vomiting after breast surgery. Anaes.Anal.,87(4); p:931.
- 25- Young Seok Jee, Hea-Jo Yoon, and Chang-Ha Jang 2010. Prophylactic antiemetic effects in gynecologic patients receiving fentanyl IV-patient controlled analgesia: comparison of combined treatment with ondansetron and dexamethasone with metoclopramide and dexamethasone. Korian J. of Anesthesiol. Vol. 59(5). Pp 335-339.
- 26- J.P.Duperyon etal, 1993. the effect of Ondansetron in the prevention of post operative nausea and vomiting after major gynecological surgery performed under general anesthesia . Anesthesiology, 48. p: 214-218.
- 27- T.H.Madej and K.H.Simpson 1986. Comparison of the use of Domiperidon, Droperidol, and Metoclopramide in the prevention of post operative nausea and vomiting in patients after gynecological surgery in day case . Br.J.of Anasth, 58; p 879-883.