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A Comparison Study on Effect of Placebo, Dolasetrone and Dexamethasone on Propofol Pain

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Abstract

The pain caused by the injection of propofol during general anesthesia induction have been studied from many researchers during last decade. This work have been done in order to evaluate the effect of dexamethasone and dolasetron on decreasing the injection pain of propofol.

The trial have been conducted on 450 participant female patients, they were divided into three groups randomly, each patient have received 5 mL of saline and intravenously 5 ml of either 1 mg dolasetron) or 0.15 mg/kg of dexamethasone. Following of that was injection of propofol by 0.5 mg/kg.Pain scores and intensity of pain recorded immediately following the injection of propofol. Hemodynamic parameters and O_2sat were recorded 1, 5, 10, and 15 min after propofol injection. A significant decrease of incidence pain have been recorded after the injection of propofol with dolasetron (50.7%) and dexamethasone (49.4%). The dolasetron group score of mean pain was 3.57 ± 1.48, the group of saline was 4.92 ± 1.44and for dexamethasone group was 2.28 ± 1.21, (P = 0.001). The record of mean pain of dolasetron group was 1.58 ± 0.20, for the dexamethasone was 1.36 ± 0.18, and 2.8 ± 0.79 for saline group (P = 0.001).

Similarly, a significant difference have been recorded in the rate of the pulse in the fifth minutes between all groups while in the dolasetron group lesser(P = 0.04). Meanwhile, we have not recorded any significant differences (mean) in both arterial pressure and O_2S at after drugs injection at any time point among the three groups. As a conclusion of this work the use of dolasetron (1 mg) and dexamethasone (0.15 mg/kg) prior to the injection of propofol is reducing the pain effectively and safely.

Keywords: Propofol, Dolasetron, Dexamethasone, Placebo.

Introduction

It is well known that the term Propofol (ICI 35868) is an important anaesthetic agent with special characteristics which has specific properties includes, amenestic, hypnotic and sedative. The onset of action and fast recovery has caused to be introduced as the most common intravenous anesthetic to start and continue anesthesia. Propofol is the drug with Phenol structure whose common complication is pain at the injection site as well as low blood pressure best choice as day care drug for surgeries because of its short elimination half-life, high plasma clearance, and intrinsic anti emetic features (Keskin et al., 2017). Propofol is today considered the most common intravenous drug for the induction of general anesthesia. The most important advantages of using Propofol could be the easy use and control, less PONV comparing to other agents, no anti-reaction, no dysphoria and finally fast recovery (Bujedo 2018). Nevertheless, the Propofol has disadvantages which could be considered as drawback of use, including the

pain at the site of the injection, haemodynamic and depression the respiratory system (Kerker et al., 2010; Chidambaran et al., 2015).To reduce the pain associated with the injection of propofol, various techniques with different results have been applied including cooling propofol, diluting the injected solution, using great antecubital vein, and using topical nitroglycerin and lidocaine (Picard andTramèr, 2000). Among from other drugs used for pain relief from the injection of propofol, are anti-inflammatory nonsteroidal drugs, (El-Radaideh 2007), metoclopramide, (Movafegh2003), narcotic drugs and ketamine and magnesium sulfate (Honarmand and Safavi, 2008). Recent studies have shown that dexamethasone reduces postoperative pain, nausea and vomiting (De Oliveira et al 2013; De Oliveira et al 2011).

Dolasetron is also an irreversible 5-hydroxytryptamine 3 (5-HT3) receptor antagonist with more selective property compared to ondansetron (Piper et al., 2011). In the previous studies, the numbness of subcutaneous injection site of ondansetron which is a (5-HT3) receptor antagonist has been proven, and it has successfully been used to reduce and eliminate the intravenous propofol pain without any side complication in patients (Janicki et al., 2000).

Isik et al (2006), compared the efficacy of ondansetron (0.1 mg/kg), dexamethasone (0.15 mg/kg) and a combination of ondansetron (0.1 mg/kg) and dexamethasone (0.15 mg/kg) for prevention of PONV in a randomized double-blind study involving 90 ASA I and II ½Q12 patients.

They concluded that prophylactic therapy with ondansetron together with dexamethasone is superior to either drug alone.

Another study comparing the efficacy of combining granisetron and dexamethasone to either drug alone yielded similar ½Q13 results. This also holds true in pediatric patients (Alipour et al., 2013).

Thus, the combination of a selective 5-hydroxy tryptamine type 3 receptor antagonist together with dexamethasone is more effective in preventing PONV than either drug alone. Kim et al (2013), compared the antiemetic efficacy of dexamethasone combined with midazolam and concluded that the addition of midazolam did not significantly reduce the overall incidence of PONV compared with dexamethasone alone. However, the addition of midazolam did lower the incidence of vomiting and the need for rescue antiemetic (Kim et al., 2013).

Dexamethasone is used to reduce postoperative pain, nausea and vomiting, and dolasetron to prevent and treat nausea and vomiting in medical research and training hospitals.

Materials and Methods

The following study was carried out after the approval of the Hospital Ethics Committee of Anesthesia Department, NCI, Baqubah General Hospital.

The study was conducted after clear explanation of the method to the participant patients. Four hundred fifty (450) patients with range of age 18–52 years old were selected for this study. The selection followed a written agreement from each patient. The participants in this study were either class 1 or 2 according to the American Society of Anesthesiologists (ASA).

We have excluded patients of specific history diseases including allergy to propofol, analgesia, sedation, mental disorder, heart disease, neuromuscular disease, hypertension, liver disease, coronary artery disease, acute respiratory infection, asthma and chronic obstructive pulmonary disease (Agarwal et al 2013).
We have asked our participant patients to fast for a minimum of 12 hours prior to the surgery time. A special procedures we have follow in order for our patients including injection of lactated Ringer serum, pulse oximetry,non-invasive blood pressure and the patient was connected to electrocardiogram.

The participant patients were divided into three groups randomly, each patient have injected for Dolasetron (1 mg) and Dexamethasone (0.15). A 5 ml Syringes were used for each drug with randomly choice of participant patient according to the number of patient which have been given at the beginning of the trial. The trial started by injection propofol, dexamethasone (152 patients), dolasetron (146 patients), and placebo (152 patients) drugs were injected and the venous drainage was prevented by resident. An examination of incidence and pain evaluation was estimated at the start and end of propofol injection. We have used four categories of measuring the pain as verbal rating scale VRSs (no pain = 0, mild = 1, moderate = 2 or severe = 3) (Hammood et al 2018).

Oxygen mask was used as a ventilation during the surgery. We have recorded the vital signs before the injection of propofol and 1, 5, 10 and 15 min later.

Statistical analysis

Statistical Product for Social Sciences (SPSS) has been used for statistical analyses (software v. 18.0.).
The mean ± SD of data were presented. Categorical data such as gender, ASA status, and the number of patients having pain scores >2 were expressed as number, percent, or both, and were compared using the chi-square test or Fischer's exact test as appropriate. Results were analyzed using One-way ANOVA (Kraemer and Blasey, 2016).

For unrelated data for inter-group comparisons. The p value < 0.05 was considered significant (Murphy et al., 2009).

Results

Our study have been conducted randomly on 450 individual participant patients who were admitted at Al-Betool Teaching Hospitaland randomly divided into three groups: dexamethasone (Group D), dolasetron (Group S), and placebo (Group P). The mean age of showed no significant difference in all three groups (P = 0.84) (P = 0.61) [*Table 1*].

Table 1: Mean age and body mass index in each of the three groups.*Mean ± SD*

Variable	Dexamethasone	Dolasetron	Placebo	Significance (*P*)
Mean age (year)	28.14±5.12	27.84±8.26	26.89±7.66	0.82
Mean BMI (KG/M^2)	24.88±3.12	25.10±1.94	22.86±1.92	0.60

BMI: Body mass index

According to the results of this study, 75 (49.4%) patients, 70 (50.7%) cases, and 135 (88.3%) ones had pain in dexamethasone, dolasetron, and placebo groups, respectively, which shows that there was a significant difference among the three studied groups in terms of pain (P = 0.001) [*Table 2*].

Table 2: Distribution of absolute and relative frequencies of pain in the three groups (n). Mean ± SD

Variable	Pain		Significance (*P*)
	Yes %	No %	
Mean age (year)	29.22±3.45	27.18±8.76	0.82
Mean BMI (KG/M^2)	25.10±3.11	26.29±2.88	0.60

The pain score of group D as mean 2.28± 1.21 and mean of 3.57 ± 1.48 for group mean while the mean score for group P was 4.92 ± 1.44. According to the ANOVA statistical method we have found that there were a significant difference between all groups. Same method of statistical analysis have been used (ANOVA) for pain measurement and the results show a significant differences between S group (dolasetron) and D group (dexamethasone) in pain score with P = 0.78. The difference between groups D (dexamethasone) with group P (placebo) was significant and there were a significant difference in the group S (dolasetron) [*Table 3*].

Table 3: Mean pain score and intensity of pain in the three groups. Mean ± SD

Variable	Dexamethasone	Dolasetron	Placebo	Significance (*P*)
Pain Score	2.33±1.01	3.88±1.53	5.10±1.53	0.001
Intensity of Pain	1.36±0.18	1.58±0.20	2.8±0.79	0.001

There were asignificant difference in intensity of pain injection between all the three groups (P = 0.001).
We have recorded a statistical higher pain intensity in the group P (Placebo) comparing to the other two groups (Group D and Group S).

Meanwhile the blood pressure record have shown no significant difference between groups before and after injection and at 1, 5, 10 and 15 min after injection according to the ANOVA test [*Table 4*].

Table 4: Comparing the mean arterial blood pressure in the three groups (mmHg). Mean ± SD

Variable	Dexamethasone	Dolasetron	Placebo	Significance (*P*)
Blood pressure before the injection	94.13±6.07	95.43±5.96	93.88±5.64	0.23
Blood pressure at 1 min	88.87±6.58	90.36±7.21	89.87±6.19	0.44
Blood pressure at 5 min	82.4±7.66	83.14±7.66	82±7.5	0.64
Blood pressure at 10 min	80.83±8.35	81.71±7.88	80.27±8.36	0.56
Blood pressure at 15 min	84.51±8.33	84.16±7.7	84.45±8.33	0.96

The heart rate (mean) for all groups were non-significant according to ANOVA test, similarly no significant differences of the mean heart rate in all groups at other times with each other. While we have recorded an exceptionalcase for the 5 min since the mean heart rate for the dolasetron receivers was lower with statistically significant (P = 0.04) [*Table 5*].

Table 5: Comparing the mean heart rate in the three groups (n/min). *Mean ± SD*

Variable	Dexamethasone	Dolasetron	Placebo	Significance (*P*)
Heart rate before the injection	94.13±6.07	95.43±5.96	93.88±5.64	0.23
Heart rate at 1 min	88.87±6.58	90.36±7.21	89.87±6.19	0.44
Heart rate at 5 min	82.4±7.66	83.14±7.66	82±7.5	0.64
Heart rateat 10 min	84.51±8.33	84.16±7.7	84.45±8.33	0.96
Heart rate at 15 min	77.8±9.36	75.82±9.54	75.51±9.22	0.26

No significant differences between the three groups regarding the mean O_2Sat before and at 1, 5, 10, and 15 min after injection according. This have been confirmed after the ANOVA test [*Table 6*].

Table 6: Comparing the mean O_2S at in three groups (%).*Mean ± SD*

Variable	Dexamethasone	Dolasetron	Placebo	Significance (*P*)
Heart rate before the injection	98.15±0.87	98.39±2.69	97.44±4.6	0.15
O_2Sat at 1 min	99.42±1.25	99.94±0.66	98.67±4.12	0.08
O2Sat at 5 min	99.94±0.22	99.89±0.05	99.61±2.53	0.33
O2Sat at 10 min	99.98±0.11	99.89±0.39	99.96±0.19	0.06
O2Sat at 15 min	99.97±0.16	99.89±0.42	99.5±3.21	0.26

Discussion

This work have been conducted for a fixed period of 10 months at Baqubah General Hospital.

The results of our work showed that using dexamethasone and dolasetron has significant effect on the intensity of pain caused by injection of intravenous propofol and it could reduce from 88% to 50% in placebo, dolasetron and dexamethasone groups. A statistical significant difference between the intervened and placebo groups was recorder in this trial, meanwhile, there were no significant difference between all groups considering different times of mean blood pressure, heart rate, and arterial oxygen percentage.

Because of discomfort for patient caused by painful irritation of propofol injection and hemodynamic changes in response to pain couldcause a myocardial ischemia in patients (Petros et al., 1993).Many studies have suggested that the releases of Nitric Oxide (NO) is the main mechanism of painful irritations caused by intravenous injection of propofol. The nerve sensitivity ending of human veins to the NO is the main reason of painful irritations (Romero et al., 2011; Gragasin et al., 2013). Furthermore, the NO which is produced by vascular endothelium causing guanylate

cyclase catalyzes the conversion of guanosine triphosphate to guanosine monophosphate which in turn, catalyzes the production of prostaglandin E2 causing hyperalgesia (Kindgen Milles and Arndt, 1996).In addition, Dexamethasone can be effective in reducing the incidence of pain by propofol injection (Holt et al., 2000).

We have used dolasetron in our study as selective on 5HT3 receivers compared to ondansetron. Dolasetron could decrease the injection pain of propofol in differentprocess includes sodium channels blocking, receiver 5HT3antagonizing and the μ receiver stimulating influances which are the same results of previous studies (Gregory and Ettinger, 1998).

Ahmed et al. (2012), have tested the effect of dolasetron on the pain injection of propofol and recorded that the use of dolasteron were significantly reducing the pain in patients. This finding was similar to our study.

The influence of dexamethasone and lidocaine on propofol pain along with saline have been studied by Ahmad et al (2012), compared the effect of dexamethasone and intravenous lidocaine on intravenouspropofol pain. In the present study the effect of dexamethasone on decreasing the pain by propofol was recorder; however, we have used lower doses of dexamethasone (Ahmed et al., 2013).

Ahmed et al (2013)conducted a study of the influence of pretreatment on decreasing the pain by the injection of propofol. The first group received 50 mg tramadol, the second one 4 mg ondansetron in 2 ml normal saline and the third group 2 ml normal saline.

Although the dolasetron is commonly used to prevent postoperative nausea and vomiting during the induction of anesthesia. This study have confirmed the influence of dolasetron on the intravenous propofol pain.

Conclusion

As conclusion to our study, we have found out that reduction of injection propofol pain reached from 85% to 50% in participant patients which is recorded in the studies published before. However, extra doses were used in compared to our doses. Nevertheless, thedolasetron doses used were not observed in all patients. Finally, we suggest further studies with more patients and diverse drug doses for more confidences on the results and the final confirmation of this effect.

References

Agarwal, R. Michael, H. Porter, and G.,O. 2013. Common Medical Illnesses that Affect Anesthesia and Their Anesthetic Management. Oral Maxillofacial SurgClin N Am 25. 407–438.

Ahmad, S. De Oliveira, G., S. Fitzgerald, P., C.and McCarthy, R., J. 2013. The effect of intravenous dexamethasone and lidocaine on propofol-induced vascular pain: A randomized double-blinded placebo-controlled trial. Pain Res Treat. 73: 45-31.

Ahmed, A.Sengupta, S. Das, T.Rudra, A.and Iqbal, A. 2012. Pre-treatment with intravenous granisetron to alleviate pain on propofolinjection: A double-blind, randomized, controlled trial. Indian JAnaesth. 56:135-8.

Alipour, M. Milani, S. Saghafi, N. Eftekharzadeh, S. and Dalouei, M., K. 2013. Comparison of the efficacy of granisetron-dexamethasone versus ondansetron-dexamethasone in prevention of nausea and vomiting following gynecologic laparoscopic surgeries.**IJOGI**.16. 1-8.

Bujedo, M., B. 2018. Current Update in the management of Post-operative Neuraxial Opioid-induced Pruritus. Journal of Clinical Research in Anesthesiology. 1. 1-10.

Chidambaran, V. Costandi, A., J. and D'Mello, A. 2015. Propofol: a review of its role in pediatric anesthesia and sedation. CNS drugs. 29(7):543-63.

De Oliveira, G., S. Ahmad, S. Fitzgerald, P., C. Marcus, R., J. Altman, C., S.and Panjwani, A., S. 2011.Dose ranging study on the effect of preoperative dexamethasone on postoperative quality of recovery and opioid consumption after ambulatory gynaecological surgery. Br J Anaesth. 107:362 71.

De Oliveira, G., S. Castro-Alves, L., J. Ahmad,S. Kendall, M., C. and McCarthy, R., J. 2013. Dexamethasone to prevent postoperative nausea and vomiting: An updated meta-analysis of randomized controlled trials. AnesthAnalg. 116:58-74.

El-Radaideh, K., M. 2007. Effect of pretreatment with lidocaine, intravenous paracetamol and lidocaine-fentanyl on propofol injection pain. Comparative study. Rev Bras Anestesiol. 57:32-8.

Gragasin, F., S, Bourque, S., L. andDavidge, S., T. 2013. Propofol increases vascular relaxation in aging rats chronically treated with the angiotensin-converting enzyme inhibitor captopril. Anesth Analg. 116:775-83.

Gregory, R., E. andEttinger, D., S. 1998. 5-HT3 receptor antagonists for the prevention of chemotherapy-induced nausea and vomiting. A comparison of their pharmacology and clinical efficacy. Drugs. 55:173-89.

Hammood, H., R. Al-Dabooni, S., I. and Al FekhraneT.,R. 2018. A comparative study on different doses of metoclopramide priories alleviates propofol injection pain. Int. J. Adv. Res. Biol. Sci. 5(8): 74-79.

Holt, R. Rask, P.Coulthard, K., P. Sinclair, M. Roberts, G.and Van Der, W., J. 2000.Tropisetron plus dexamethasone is more effective than tropisetron alone for the prevention of postoperative nausea and vomiting in children undergoing tonsillectomy. PaediatrAnaesth. 10:181-8.

Honarmand, A andSafavi, M. 2008. Magnesium sulphate pretreatment to alleviate pain on propofol injection: A comparison with ketamine or lidocaine. Acute Pain. 10:23-9.

Isik, B. Cekmen, N. Arslan, M. Ozsoylar, O. Kordan, A. and Akcabay, M. 2006. Comparison of the antiemetic effects of ondansetron and dexamethasone on middle ear surgery. Saudi medical journal. 27. 646-51.

Janicki, P. Schuler, H. Jarzembowski, T. and Rossi, M. 2006. Prevention of Postoperative Nausea and Vomiting with Granisetron and Dolasetron in Relation to CYP2D6 Genotype. Anesthesia and analgesia. 102. 1127-33.

Kerker, A. Hardt, C. Schlief, H., E. and Dumoulin, F., L. 2010. Combined sedation with midazolam/propofol for gastrointestinal endoscopy in elderly patients. BMC gastroenterology. 10(1):11.

Keskin, G. Akin, M, Senay, Y. Saydam, S. Özmert, S. Kurt, D., K. and Sever, F. 2017. Evaluation of 865 children who underwent magnetic resonance imaging under propofol-midazolam sedation. Medeniye Medical J. 32(3):141-6.

Kim, S. Hong, J. Kim, W. Keum, K., H. Karm, M. and Hwang, Jai. 2013. Palonosetron has superior prophylactic antiemetic efficacy compared with ondansetron or ramosetron in high-risk patients undergoing laparoscopic surgery: A prospective, randomized, double-blinded study. Korean journal of anesthesiology. 64. 517-23.

Kindgen-Milles, D. and Arndt, J.,O. 1996. Nitric oxide as a chemical link in the generation of pain from veins in humans. Pain. 64:139-42.

Kraemer, H., C. and Blasey, C. 2016. How many subjects? Statistical power analysis in research.

Movafegh, A. 2003. A comparison of metoclopramide and lidocaine for preventing pain on injection of propofol. Tehran Univ Med J. 61:274-80.

Murphy, K., R.Myors, B. andWolach, A. 2009. Statistical power analysis: a simple and general model fortraditional and modern hypothesis tests, 3ed ed., Tayler & Francis Group LLC.

Petros, A., J. Bogle, R., G.and Pearson, J., D. 1993. Propofol stimulates nitric oxide release from cultured porcine aortic endothelial cells. Br J Pharmacol. 109:6-7.

Picard, P.and Tramèr, M., R. 2000. Prevention of pain on injection with propofol: A quantitative systematic review. AnesthAnalg. 90:963-9.

Piper, S., N.Röhm, K., D.Maleck, W., H.Fent, M., T. Suttner, S., W.and Boldt, J. 2011. Erratum: Dolasetron for preventing postanesthetic shivering: Retraction (Anesthesia & Analgesia. 94 (106-111).

Romero, T., R.Galdino, G., S.Silva, G., C.Resende, L., C. Perez, A., C.and Côrtes, S., F. 2011.Ketamine activates the L-arginine/Nitric oxide/cyclic guanosine monophosphate pathway to induce peripheral antinociception in rats. Anesth Analg. 113:1254-9.

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