Global Advanced Research Journal of Medicine and Medical Sciences (ISSN: 2315-5159) Vol. 6(6) pp. 111-115, June, 2017
Available online http://garj.org/garjmms


*Full Length Research Paper*

# Comparison of the cost-effectiveness of Propofol intravenous anesthesia and Isoflurane inhalation anesthesia: a randomized clinical Trial

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Accepted 19 June, 2017

**In the recent years, managed care plans have been presented and physicians and health care centers focused on cost-effectiveness of medical procedures. The purpose of this study was comparison of the cost-effectiveness of intravenous Propofol anesthesia versus inhalational Isoflurane anesthesia for maintenance of anesthesia. In this randomized, single-blind, parallel clinical trial, 104 eligible consecutive surgical patients were selected in Imam Hossein hospital of Shahroud and randomly placed into two groups after justification and obtaining informed consent. In intervention group Anesthesia continued with Propofol and Fentanyl and in control group it continued with Isoflurane and Fentanyl. Anesthesia depth monitoring was performed in all patients and Bispectral Index (BIS) was kept between 45 and 60. The outcome measures include systolic blood pressure, heart rate, sweating and pupil size during anesthesia also recovery complications and recovery duration. Price of the used anesthetic for each patient was calculated. In Propofol group were lower nausea and vomiting, after operation and also the average recovery time was significantly lower in Propofol group (p = 0.0001). Other variables such as the cost of anesthesia had not significant difference and were similar in both groups. Induction with Propofol with Bispectral Index control for maintenance of anesthesia is more effective than Isoflurane. Propofol causes less postoperative nausea and vomiting, shorter recovery time, no environmental pollution and it does not impose additional cost to the patient and the hospital.**

**Keywords:** Anesthesia, Isoflurane, Propofol, Cost-effectiveness

## INTRODUCTION

### Background

By the 1990s, hospitals were focused on governmental revenues and the use of technology, drugs and expensive treatments were common and it was believed that leave the cost to others (Dolk et al., 2012). Methods based on state budgets developed inefficient medical systems, operating rooms of hospitals consumed 40 to 60 percent of the hospital budget and the doctors were allowed to use the very expensive equipment and techniques (Dolk et al., 2012; Auerswald et al., 2015). After this date managed care plans were developed and paying per capita was developed instead of the huge

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amount of costs that patient or the insurer must be paid (Dolk et al., 2013). Similar plans were implemented in Iran that one of them is Global Plan which a fixed amount of money is paid by the health insurance organization for each surgical procedure. Due to the limitation of the offered amount, hospital and physicians should control the care cost (Greenhalgh, 2014).

It is necessary that hospital as an economical enterprise provide care with standard quality at the lowest cost to the patients. The one of the patient's costs is the cost of medicine and consumable anesthetic instruments. Due to the fixed payment plan of health insurance any extra charge is a disservice to the hospital and in many cases does not have any profit for patient. So, it is required to consider the cost-effectiveness of every therapeutic procedure (Sloan et al., 2011).

There has long been a vigorous debate between anesthetists over whether inhalational anesthesia or intravenous anesthesia techniques are best for outpatient surgeries (Smith, 2013). Several studies have suggested that total intravenous anesthesia (TIVA) with Propofol reduces the incidence of postoperative nausea and vomiting (PONV) and results in shorter emergence times (Heidvall et al., 2012; Struys et al., 2012). At present, Propofol TIVA is more expensive than inhalational anesthesia with Isoflurane and nitrous oxide (N2O). However, some investigators have suggested that TIVA could be cost-effective because the costs of treating PONV and of increased recovery room stay after inhalational anesthesia offset the additional drug acquisition costs of Propofol TIVA (Boldt et al., 2014; Ozkose et al., 2011).

The aims of this study was comparison of the cost-effectiveness of intravenous Propofol anesthesia versus inhalational Isoflurane anesthesia for maintenance of anesthesia.

## METHODS

**-The aim and design:** One hundred and four eligible consecutive surgical patients. Samples were selected from patients who were prepared for elective open surgical procedures on limbs (orthopedic, reconstructive) and abdominal operations (herniorrhaphy laparotomy, cholecystectomy, appendectomy) at Imam Hossain hospital of Shahroud (northeast area of Iran) for over a period of 8 months (March 2015 to December 2015). After obtaining justification and consent, participants were placed into two groups including Isoflurane (A) and Propofol group (B) based on a predetermined randomized block design. Inclusion criteria consisted of both sex, 18 to 50 years old and ASA physical status 1 or 2 (According to American society of anesthesiologist's classification). Patients with a history of sensitivity to egg (Heidvall et al., 2012), drug abuse, alcohol usage, history of sedative and anticonvulsant medication and complicated anesthesia or surgery were excluded. Monitoring the depth of anesthesia in all patients was carried out with Cerebral State Monitor Model CSM2 (Danameter).

### Anesthesia induction

Premedication in both groups was Fentanyl (1µg/kg) and Midazolam (0.05mg/kg). Induction of anesthesia was done with Propofol (1.5mg/kg) in both groups. In control group maintenance of anesthesia was done by administration of 2% Isoflurane (1.7 MAC) with equal proportions of oxygen and Nitrous oxide and every five minutes, Isoflurane concentration was adjusted so that Bispectral index (BIS) held between 45 and 60 (Dolk et al., 2012). In intervention group, Oxygen and Nitrous oxide in equal proportion sand Propofol (140µg/kg/hour) were administered. In both groups, Fentanyl (1µg/kg/hour) continued throughout the operations.

Intraoperative measurable outcomes in two groups were classified and measured every five minutes. 1-The amount of anesthetic which was regulated by the anesthesiologist (the concentration of Isoflurane and the rate of Propofol infusion), and the depth of anesthesia (Bispectral index) were recorded. 2-Arterial Systolic blood pressure, pulse rate, sweating, pupil reflex and pupil size were recorded every five minutes.

### Record content

1). Recovery complications including pain, restlessness, nausea and vomiting.
2). Recovery length was determined using Modified Alderet scoring system (MASS).

### Calculation method for the anesthetic

In this scoring system, 5 variables of Consciousness, circulation, systemic blood pressure, breathing, SPO2, and activity each take zero to 2 points and 9 score specifies the end of recovery).

### Statistical analysis

SPSS 16.0 was used for analysis. Measurement data were expressed as mean ± standard deviation, chi-square was adopted for comparison of data in the table, and one-way analysis of variance was used for intergroup comparison. $P< 0.05$ was considered statistically significant.

**Table 1.** Distribution of variables in the study groups

| Variable(Preoperative) | *Group Study* Isoflurane, mean(SD*) | Propofol, mean(SD*) | P-Value |
|---|---|---|---|
| Age | 35.19 ± 9.94 | 36.79 ± 9.53 | 0.41 |
| Weight | 70.86 ± 12.44 | 70.51 ± 11.08 | 0.87 |
| Systolic blood pressure | 123.49 ± 19.41 | 121.83 ± 18.07 | 0.65 |
| Diastolic blood pressure | 74.73 ± 10.25 | 75.13 ± 12.17 | 0.85 |
| Heart Rate | 88.69 ± 15.75 | 84.30 ± 14.61 | 0.14 |
| Respiratory Rate | 11.73 ± 1.04 | 11.57 ± 0.82 | 0.39 |
| SPO2 | 98.12 ± 1.83 | 98.84 ± 2.19 | 0.07 |
| $ASA_1$ | 84.3% | 83.0% | 0.86 |
| $ASA_2$ | 15.7% | 17.0% | |

SD; standard deviation

**Table 2.** Comparison of Clinical Outcomes during operation

| Variables | Group Study Isoflurane | Propofol | P-Value |
|---|---|---|---|
| BIS Index | 46.28±5.62 | 45.03±5.83 | 0.27 |
| Systolic Blood Pressure | 130.18±23.04 | 128.00±20.81 | 0.36 |
| Heart Rate | 81.99±13.15 | 78.73±13.15 | 0.20 |
| Pupil Size | 3.14±0.83 | 3.51±1.15 | 0.06 |

**Table 3.** Frequency of Sweating and Light Reflex in study groups

| Variables | Isoflurane | | Propofol | | P-Value |
|---|---|---|---|---|---|
| | yes | no | yes | no | |
| Sweating | 25.5 | 74.5 | 39.6 | 60.4 | 0.13 |
| Light Reflex | 56.9 | 43.1 | 50.9 | 49.1 | 0.55 |

## RESULTS

In this study, 104 inpatients were participated with the mean age of 36.01 ± 9.72 years. 35 (33.7%) patients were female and rest were male. Risk of anesthesia (according ASA classification) was in 87 patients (83.7%) ASA class1 and 17 patients (16.3%) was ASA class2.

12(11.5%) patients were hypertensive, 3 (2.9%) patients were diabetic. The most frequent operations in men were inguinal herniorrhaphy and orthopedic operations and in women were cholecystectomy and orthopedic operations. 51 (49%) patients were in Isoflurane group and 53 (51%) patients were in Propofol group. (Table 1)

Changes in cardiovascular parameters in both groups are shown in Table 2. The average systolic blood pressure changes during and before operation in inhalation anesthesia (Isoflurane) was 8.55±19.11 mmHg and in intravenous anesthesia group (Propofol) was 3.19±11.02 mmHg which the difference between the two group was not significant (p-value = 0.085). Comparing the average heart rate during anesthesia with heart rate before anesthesia in inhaled anesthesia (Isoflurane) was 67.0±11.5 beat/min and in intravenous anesthesia group (Propofol) was 58.0± 10.5 beat/min that the difference between two groups was not significant (p-value = 0.587). This finding was shown in Table 2.

Pupil size was classified as 1 to 10 on for each patient. The minimum size in Isoflurane group was 1 mm and the maximum was 5 mm. In the Propofol group the minimum pupil size was 2 mm and the maximum was 6 mm. The mean pupil size and the pupil reflex to the light in two groups were similar.

Sweating during operation happened in 13(12.5%) patients in Isoflurane group and 21(20.2%) patients had sweating in Propofol group. Bispectral index (BIS) was monitored throughout the anesthesia and was recorded every five minutes. This finding was shown in Table 3.

The concentration of Isoflurane in group 1 and the infusion rate of Propofol in group 2 was adjusted in such a way that the BIS index maintained between 45 and 60. In control group (Isoflurane) mean BIS was 46.28±5.62

**Table 4.** Frequency of postoperative Pain and PONV

| | | Pain and agitation | | PONV | |
|---|---|---|---|---|---|
| | | Frequency | Percent | Frequency | Percent |
| A-Isoflurane | Yes | 14 | 27.5 | 4 | 7.8 |
| | No | 37 | 72.5 | 47 | 92.2 |
| | Total | 51 | 100 | 51 | 100 |
| B-Propofol | Yes | 17 | 32.1 | 2 | 3.8 |
| | No | 36 | 67.9 | 51 | 96.2 |
| | Total | 53 | 100 | 53 | 100 |

**Table 5.** Postoperative Pain and PONV

| | Patient group | N | Mean | Std. Deviation | Sig. |
|---|---|---|---|---|---|
| Pain and restlessness in PACU | A-Isoflurane | 51 | 1.73 | .451 | .061 |
| | B-Propofol | 53 | 1.68 | .471 | |
| Postoperative nausea and vomiting | A-Isoflurane | 51 | 1.92 | .272 | .0378 |
| | B-Propofol | 53 | 1.96 | .192 | |

**Table 6.** Recovery time

| | | N | Mean | Std. Deviation | Sig. (2-tailed) |
|---|---|---|---|---|---|
| Recovery time | A-Isoflurane | 51 | 16.8235 | 1.78556 | .000 |
| | B-Propofol | 53 | 13.5849 | 1.81271 | |

and in intervention group (Propofol) mean BIS was 45.03±5.83 which indicated the adequate level of anesthesia in both groups.

Measurable outcomes after operation including complications and recovery time were recorded and studied. Pain and restlessness during recovery was seen in 14 (27.5%) patients in Isoflurane group and 17 (32.1%) patients in Propofol group. Nausea and vomiting was observed in 4 (7.8%) patients in Isoflurane group and in 2 patients (3.8%) in Propofol group. The difference between two groups was not significant. This finding was shown in Table 4 to 6.

The average length of recovery based on the MASS criteria in Isoflurane group was 16.82 minutes and in Propofol group was 13.58 minutes that the difference between two groups is significant (p-value = .000).

The cost of used inhaled anesthetic in Isoflurane group was 4.87$ and the cost of intravenous anesthetic Propofol drug in Propofol group with 50 ml syringe and infusion set was 5.38$. Although inhalation anesthesia seems cheaper, but changes are not significant (p-value = 0.330).

## DISCUSSION

Comparing the efficacy of intravenous Propofol anesthesia with inhaled Isoflurane anesthesia with control of Bispectral index (BIS) between 45 and 60 showed that cardiovascular changes, sweating, papillary size and reflex in both methods are similar. Pain and restlessness in the recovery in Isoflurane group were 27.5% and in Propofol group were 32.1%. Camci compared intravenous Propofol-alfentanil anesthesia with inhalational Desflurane-alfentanil anesthesia and reported a lower postoperative analgesic requirement in Propofol group (Camci et al., 2014) which is not consistent with our results but in a clinical trial, Ortiz compared Propofol, Isoflurane, and Sevoflurane, Desflurane anesthesia for laparoscopic cholecystectomy and reported that Propofol anesthesia is not associated with less postoperative pain (Ortiz et al., 2014).

Nausea and vomiting was observed 7.8% in Isoflurane and 3.8% in Propofol group. Antiemetic effect of Propofol has been proven (White et al., 2011). Reduction in postoperative nausea and vomiting in Propofol anesthesia has been demonstrated by Camci (Camci et al., 2014) and Sung YF (Loop and Priebe, 2012) (1991) researches.

The recovery time in the Isoflurane group was 16.82 minutes and in Propofol group was 13.58 minutes which the difference is significant (p-value = 0.0001). Similar results also have been reported by Engoren (Engoren et al., 2011) and Camci (Camci et al., 2014).

The average cost of consumed Isoflurane in control group was 4.87$ and the average cost of Propofol,

syringe and infusion set in intervention group was 5.38$. The difference between two groups was not significant and there is not sufficient evidence indicating that intravenous method is more expensive. Epple in similar study reported that Propofol/Remifentanil is more cost-effective than Isoflurane/Fentanyl (Epple et al., 2013).

Engoren in his study reported that Propofol anesthesia in cardiac surgery is more expensive than Isoflurane anesthesia (Engoren et al., 2011). White, his study performed without Bispectral monitoring and the use of BIS monitoring can reduce anesthetics consumption (White et al., 2011). Eger reported that 17 from 19 studies suggested that Propofol based anesthesia was associated with a higher cost than the other agents (Eger et al., 2014).

Generally, intravenous Propofol anesthesia is more effective than Isoflurane anesthesia. It reduces postoperative nausea and vomiting and is associated with faster recovery (Dexter et al., 2013). No significant difference has been shown between Isoflurane and Propofol anesthesia in patient's discharge time (Visser et al., 2011; Gan et al., 2014).

## CONCLUSION

Intravenous anesthesia is more preferred technique for maintenance of anesthesia because of adverse effect of volatile anesthetic vapor on patient and operating room personnel. No sufficient evidence obtained that intravenous anesthesia is more expensive, so by monitoring the depth of anesthesia, Propofol intravenous anesthesia is more cost-effective technique than inhalational Isoflurane anesthesia. Vaporizer and syringe pomp depreciation costs have not been calculated in this study and needs further investigation.

## ACKNOWLEDGEMENTS

The authors are grateful to patients, who participated in the study, for their time to participate in the study. We are also grateful to the Vice Chancellor for Research Affairs at the Shahroud University of Medical Science for their support.

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