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*Original Article*

# ***Cost of general anesthesia during*** **radical gastrectomy using different specifications of propofol: cost-minimization analyses**

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**Abstract:** Background: Recently, the economic cost of anesthesiahas attracted attention. To compare the costs of three methods of general anesthesia (GA), a retrospective 1-year study was designed for patients undergoing radical resection for gastric carcinoma. Methods: A total of 398 patients were originally included in the study. Subjects were divided into three groups according to the mode of anesthesia: balanced anesthesia (BAL; n=258), total intravenous anesthesia (TIVA; n=36), and inhalational anesthesia (INH; n=104). Results: When patients were undergoing elective radical resection for gastric carcinoma, the duration of anesthesia, age, duration of surgery, and postoperative analgesia were positively correlated with the total cost of anesthesia (including wastage of propofol 200 mg:20 mL). Duration of anesthesia and postoperative analgesia were positively correlated with the total cost of anesthesia (including wastage of propofol 500 mg:50 mL). However, the anesthesia group was negatively correlated with the total cost of anesthesia (including drug wastage). When propofol 500 mg:50 mL was used, the total cost of anesthesia and total cost of anesthesia per hour in the BAL group was higher than in the INH group. However, when excluding drug wastage (propofol 200 mg:20 mL), the BAL group was more expensive than the other two groups. Conclusion: Use of propofol 200 mg:20 mL as a GA would save money.

**Keywords:** Gastric cancer, radical resection of gastric cancer, general anesthesia, propofol, cost-minimization analysis

## Introduction

Gastric cancer is the fourth most common cancer and the third most common cause of cancer death worldwide [1]. Radical gastrectomyfor gastric carcinoma can be undertaken using general anesthesia (GA) or epidural anesthesia (EA). GA is preferred by anesthesiologists and surgeons because: (i) it is widely accepted by patients; (ii) it facilitates surgery of long duration; (iii) the airway is secured.

GA is used widely for radical gastrectomy. In general, GA can be divided into three groups: balanced anesthesia (BAL), total intravenous anesthesia (TIVA), and inhalational anesthesia (INH). These different types of anesthesia have important effects upon cost [2-4].

To address these concerns, a retrospective study was designed using a cost-minimization analysis. We wished to compare cost minimization for the three types of GA. Previously, we have shown that the choice of anesthetic method has an impact on cost [2].

From the study by Myles et al. [5], we had expected to find small (but significant) differences in effectiveness against which we could evaluate differences in costs attributable to the higher prices of propofol and sevoflurane, and any differences in total episode costs. When the clinical outcomes were not significantly different, the study that began as a cost-effectiveness study became a cost-minimization analysis.

Literature review revealed that cost comparisons had been made between different methods for spinal anesthesia (SA), EA or GA but that often GA groups were not compared.

**Table 1.** Patients' characteristics n (%)

| | BAL (*n*=258) | TIVA (*n*=36) | INH (*n*=104) |
|---|---|---|---|
| Sex | | | |
| Male | 174 (67.44) | 23 (63.89) | 73 (70.19) |
| Female | 84 (32.56) | 13 (36.11) | 31 (29.81) |
| Pathology | | | |
| Adenocarcinoma | 209 (81.01) | 26 (72.22) | 0 (-) |
| Adenosquamous carcinoma | 3 (1.16) | 0 (-) | 86 (82.69) |
| Interstitialoma | 5 (1.94) | 1 (2.78) | 2 (1.92) |
| Lymphadenoma | 8 (3.10) | 0 (-) | 0 (-) |
| Undifferentiated carcinoma | 9 (3.49) | 1 (2.78) | 7 (6.73) |
| Squamous carcinoma | 1 (0.39) | 0 (-) | 7 (6.73) |
| Signet ring cell cancer | 22 (8.53) | 8 (22.22) | 0 (-) |
| Poorly differentiated neuroendocrine carcinoma | 1 (0.39) | 0 (-) | 0 (-) |
| Underlying diseases | | | |
| Yes | 161 (62.40) | 24 (66.67) | 64 (61.54) |
| No | 97 (37.60) | 12 (33.33) | 40 (38.46) |
| ASA | | | |
| I | 84 (32.56) | 11 (30.56) | 21 (20.19) |
| II | 174 (67.44) | 25 (69.44) | 83 (79.81) |
| Age (years) | 59.67±12.21 | 58.42±12.04 | 58.76±9.95 |
| <65 | 166 (64.34) | 14 (38.89) | 24 (23.08) |
| ≥65 | 92 (35.66) | 22 (61.11) | 80 (76.92) |
| Weight (kg) | 61±10.41 | 60.24±11.86 | 63.15±10.78 |
| Medical insurance | | | |
| Yes | 150 (58.14) | 21 (58.33) | 63 (60.58) |
| No | 108 (41.86) | 15 (41.67) | 41 (39.42) |
| Postoperative analgesia | | | |
| Yes | 233 (90.31) | 30 (83.33) | 96 (92.31) |
| No | 25 (9.69) | 6 (16.67) | 8 (7.69) |

*BAL*, balanced anesthesia; *TIVA*, total intravenous anesthesia; *INH*, inhalational anesthesia; *ASA*, American Society of Anesthesiologists.

Numerous studies [6-9] designed to determine optimal anesthetic methods for outpatient surgery have yielded contradictory data, and this has led to wide variations in practice.

Total costs for anesthesia comprise direct and indirect costs. Hence, an initial step of precise calculation of cost is to maintain an account of the direct costs for the anesthetics used [10]. This is especially important for anesthetics given *via* the intravenous route which are, in part, discarded after use. Furthermore, indirect costs derived from postoperative side effects such as nausea and vomiting should also be assessed [11-13]. Several cost-analysis studies using various anesthetic methods have been published [3, 14-18], but few have focused on the costs associated with GA.

We used a pharmacoeconomic cost minimization analysis to explore the potential economic impact of the choice of GA, and which type of GA was least expensive. The cost associated with waste was taken into account. We also compared anesthesia-related costs when using different specifications of propofol.

Because usually the elderly means ≥65 years old, so we did a subgroup analysis to explore the effect of age to parts of the costs: the cost of anesthetic adjuvant drugs, the total cost of anesthesia per hour (exclution waste) and the total cost of anesthesia per hour (inclusion waste).

Besides postoperative stay in hospital and loss of labor, the cost of these methods has become

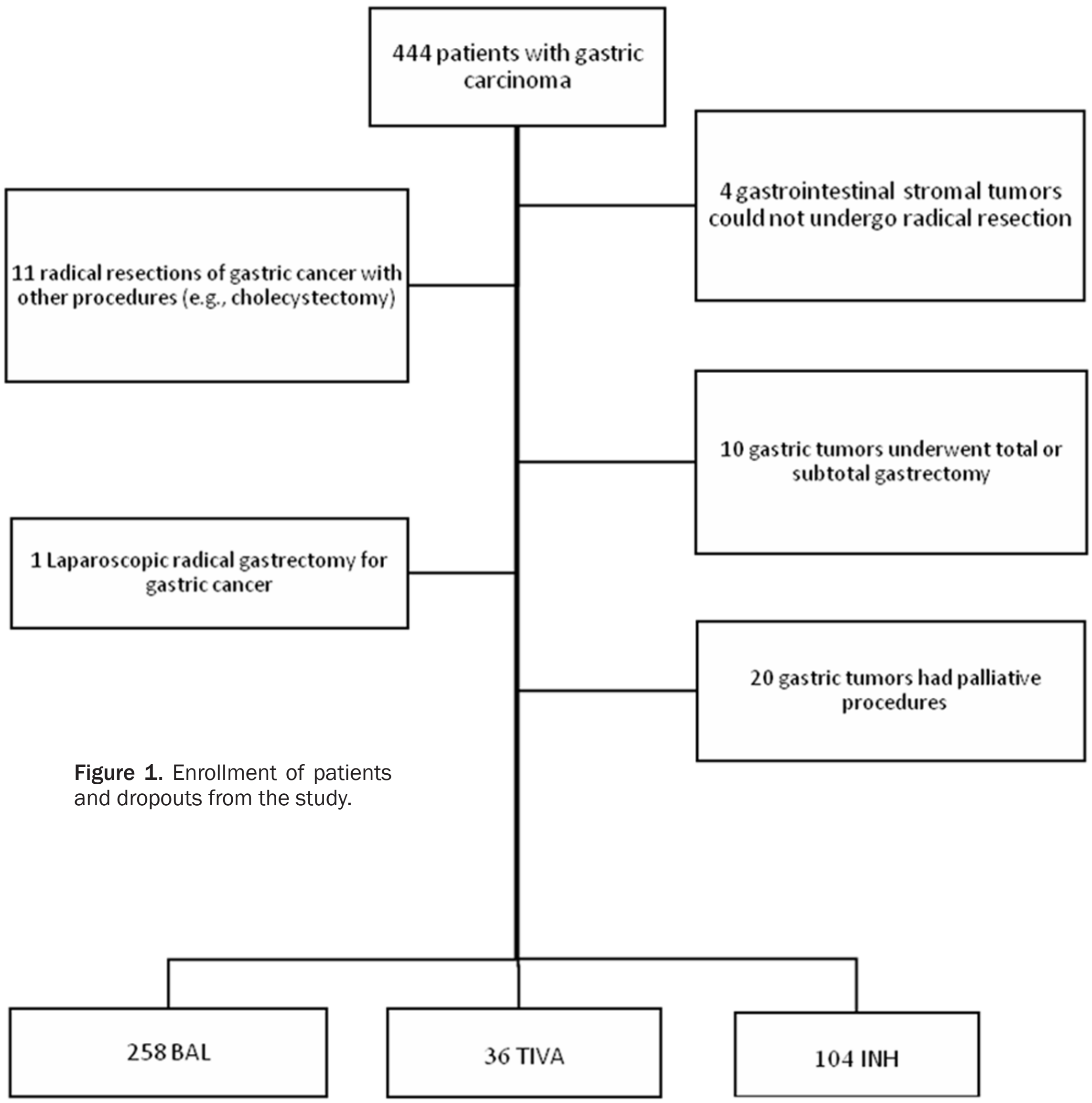


**Figure 1.** Enrollment of patients and dropouts from the study.

much more attractive for government policy-makers recently.

In this present study, applications of GA was compared in terms of the duration of anesthesia, age, operation time, duration of hospital stay, postoperative analgesia and cost analyses.

## Materials and methods

This was a retrospective study. All data were collected from electronic medical records, which were reviewed in detail (including pathology, physical examination, operative reports and anesthesia records). Baseline characteristics of patients were reviewed, including: age; weight; sex; medical insurance; underlying disease (e.g., hypertension, coronary artery disease, diabetes mellitus); postoperative analgesia; duration of surgery (hours); duration of anesthesia (hours); postoperative duration of hospitalization (days); total duration of hospitalization (days); physical status according to criteria set by the American Society of Anesthesiologists (ASA).

Cost data for the entire reconstructive course of each patient were obtained through the Department of Finance at Renji Hospital of the University of Shanghai Jiao Tong (Shanghai, China). From August 2008 to July 2010, 444

**Table 2.** Drug acquisition costs from our hospital's pharmacy list

| Drugs used | Specification | CNY ¥ (US $)[a] |
|---|---|---|
| Midazolam | 5 mg:5 mL | 14.8 (2.38) |
| Fentanyl | 0.1 mg:2 mL | 4.88 (0.79) |
| Remifentanil | 2 mg | 165.2 (26.61) |
| Sufentanil | 50 μg:mL | 98.1 (15.8) |
| Propofol | 200 mg:20 mL | 59.2 (9.54) |
| Propofol | 500 mg:50 mL | 284 (45.75) |
| Etomidate | 20 mg:10 mL | 55.3 (8.91) |
| Penehyclidine hydrochloride injection | 1 mg:1 mL | 75.8 (12.21) |
| Cisatracurium besilate | 10 mg | 120 (19.33) |
| Rocuronium bromide | 50 mg:5 mL | 94 (15.14) |
| Vecuronium bromide | 4 mg:2 mL | 31.7 (5.11) |
| Isoflurane | 100 mL | 627 (101.01) |
| Sevoflurane | 120 mL | 1227 (197.67) |
| Dexmedetomidine | 0.2 g:ml | 172.17 (27.74) |
| Flurbiprofen | 50 mg:5 mL | 90.2 (14.53) |
| Parecoxib | 40 mg | 148 (23.84) |
| Perdipine | 2 mg:1 mL | 25.8 (4.16) |
| Labetalol | 50 mg | 51.1 (8.23) |
| Urapidil | 25 mg:5 mL | 40.8 (6.57) |
| Diltiazem | 10 mg | 54.1 (8.72) |
| Esmolol | 0.2 g:1 mL | 134 (21.59) |
| Tramadol | 0.1 g:2 mLl | 10.16 (1.64) |
| Butorphanol | 1 mg:1 mL | 13.30 (2.14) |
| Metoclopramide | 10 mg:1 mL | 0.2 (0.03) |
| Furosemide | 20 mg:2 mL | 0.45 (0.07) |
| Hypertonic sodium chloride hydroxyethyl starch 40 injection (HSS 40) | 250 mL | 270 (43.5) |
| Gelofusine | 500 mL | 83.22 (13.41) |
| Hetastarch | 500 mL | 102.61 (16.53) |
| Sodium lactate Ringer's solution | 500 mL | 3.5 (0.56) |

[a]US $1=¥ 6.7797 (July 20, 2010).

patients with gastric carcinoma were scheduled for selective radical gastrectomy with general anesthesia. All patients were consecutively incorporated. All anesthesia was performed by three experienced attending doctors. Patient characteristics are given in **Table 1**.

Inclusion criteria were patients: aged ≥18 years and <83 years scheduled for elective radical resection of gastric cancer; with ASA physical status I and II; undergoing no other anesthetic method. No patients underwent premedication. Reasons for not being enrolled are listed in **Figure 1**.

Exclusion criteria were: gastrointestinal stromal tumors (GISTs) that could not undergo radical resection; gastric tumors that had undergone total or subtotal gastrectomy; radical resection of gastric tumors with other types of surgery (e.g., cholecystectomy); palliative procedure for gastric cancer; laparoscopic radical gastrectomy for gastric cancer (laparoscopic procedures increase cost); ASA physical status >III; age <18 years or >83 years; patients undergoing other anesthetic methods; patients with coagulopathy, pulmonary infection, or body mass index (BMI) >25 kg/m$^2$; patients with severe hypertension, midazolam hypersensitivity, chronic obstructive lung disease, increased intracranial pressure or epileptic seizures.

A total of 398 patients were enrolled in the study. Patients were divided into three groups according to the mode of anesthesia: BAL (n=258), TIVA (n=36) and INH (n=104). Char-

**Table 3.** Time in three groups

| | BAL (*n*=258) | TIVA (*n*=36) | INH (*n*=104) |
|---|---|---|---|
| Duration of anesthesia (hours) | 3.37±0.96 | 3.56±0.92 | 3.48±0.98 |
| Duration of surgery (hours) | 2.64±0.85 | 2.8±0.82 | 2.65±0.85 |
| Postoperative duration of hospitalization (days) | 13.88±4.90 | 15.86±7.11* | 13.66±4.03 |
| Total duration of hospitalization(days) | 18.79±5.88 | 20.78±7.17* | 18.43±5.66 |

*P<0.05, different from both *BAL* and INH group. *BAL*, balanced anesthesia; *TIVA*, total intravenous anesthesia; *INH*, inhalational anesthesia.

**Table 4.** Cost of anesthetic adjuvant drugs

| | Cost of anesthetic adjuvant drugs/$ | | *P* |
|---|---|---|---|
| | <65 yr | ≥65 yr | |
| BAL | 447.42±211.4 | 453.09±218.91 | 0.8387 |
| TIVA | 321.81±156.92 | 386.57±226.81 | 0.3176 |
| INH | 411.94±209.44 | 407.92±220.08 | 0.9352 |

*BAL*, balanced anesthesia; *TIVA*, total intravenous anesthesia; *INH*, inhalational anesthesia.

acteristics of the three groups of patients are shown in **Table 1**.

In the three groups, anesthesia was induced using midazolam (0.1-0.4 mg/kg, IV), fentanyl (2-4 μg/kg, IV), sulfentanyl (0.2-0.4 μg/kg, IV) or remifentanil (0.5-1 μg/kg, IV); propofol (1-2 mg/kg, IV) or etomidate (0.2-0.3 mg/kg, IV). All patients underwent oro-endotracheal intubation facilitated *via* administration of rocuronium (0.3-0.6 mg/kg, IV), cisatracurium besylate (0.05-0.1 mg/kg, IV) or vecuronium (0.05-0.1 mg/kg, IV) .

All patients were maintained with 1.0-2.0 L of pure oxygen gas and oxygen saturation in oxygen ($SpO_2$) maintained at >98%. Positive-pressure ventilation was initiated and maintained for the duration of surgery with a tidal volume of 8-10 ml/kg and ventilation rate adjusted to maintain an end-tidal partial pressure of carbon dioxide ($PCO_2$) of 35-45 mmHg.

In the BAL group, anesthesia was maintained with a minimal alveolar concentration of sevoflurane of 1-2 vol% and propofol (1.5-2 mg/kg/min). In the TIVA group, anesthesia was maintained with propofol (5-200 μg/kg/min). In the INH group, anesthesia was maintained with a minimal alveolar concentration of sevoflurane of 1-2 vol%. At the start of skin suturing, sevoflurane was discontinued and the flow of pure oxygen changed to 6 L/min. In BAL and INH groups, at the end of surgery, flow was increased to 6 L/min.

At the maintenance stage, doses of muscle relaxants and anesthetics were: vecuronium (0.8-1.0 μg/kg/min) or cisatracurium besylate (1-2 μg/kg/min) and sulfentanyl (0.25-0.5 μg/kg/min) or remifentanil (0.5-1 μg/kg/min).

Consumption of volatile anesthetics was calculated using the formula of Nakada et al. [19]:

isoflurane liquid dosage (mL)=3.0xFxCxhours

sevoflurane liquid dosage (mL)=3.3xFxCxhours

Where F is fresh gas flow (L/min) and C is monitored concentration (%).

For the same patient, unpolluted residual drugs (e.g., propofol) from the induction phase were allowed to be used during maintenance of anesthesia.

All drugs were from the hospital pharmacy. Price was based on those in Renji Hospital's Pharmacy from 2009 (**Table 2**).

Depth of anesthesia was adjusted in all three groups to maintain heart rate and blood pressure within 10-15% from baseline. Titration of anesthesia was as light as possible without causing movements that could disrupt the surgical procedure. Maintenance of anesthesia was discontinued when the final skin suture was completed in all three groups. Thirty minutes before the end of the procedure, the bolus or continuous infusion of non-depolarizing muscular relaxant was stopped. The final bolus of sufentanil was injected ≥30 min before the expected end of the procedure, but remifentanil was stopped at the end of the procedure.

Neuromuscular blockade was reversed by administration of neostigmine (0.04 mg/kg, IV) and atropine (0.02 mg/kg, IV). Patients were extubated when they met the criteria for tracheal extubation (respiratory rate >8; spontaneous breathing with a minimum of 8 mL/kg of

**Table 5.** Total cost of anesthesia per hour (exclution waste) at different ages

| | *The total cost of anesthesia per hour (exclution waste, Propofol 200 mg:20 mL)/$* | | P | *The total cost of anesthesia per hour (exclution waste, Propofol 500 mg:50 mL)/$* | | *P* |
|---|---|---|---|---|---|---|
| | <65 yr | ≥65 yr | | <65 yr | ≥65 yr | |
| BAL | 686.05±157.24 | 728.44±153.24 | 0.0373 | 750.00±224.88 | 770±162.78 | 0.4775 |
| TIVA | 648.46±189.17 | 635.27±150.89 | 0.8273 | 734.74±197.25 | 716.41±152.22 | 0.7691 |
| INH | 635.91±145.71 | 724.66±203.75 | 0.0195 | 648.08±148.7 | 731.84±203.91 | 0.0293 |

*BAL*, balanced anesthesia; *TIVA*, total intravenous anesthesia; *INH*, inhalational anesthesia.

**Table 6.** The total cost of anesthesia per hour (inclusion waste) at different ages

| | *The total cost of anesthesia per hour (inclusion waste, Propofol 200 mg:20 mL)/$* | | *P* | *The total cost of anesthesia per hour (inclusion waste, Propofol 500 mg:50 mL)/$* | | *P* |
|---|---|---|---|---|---|---|
| | <65 yr | ≥65 yr | | <65 yr | ≥65 yr | |
| BAL | 715.68±165.61 | 762.21±161.85 | 0.0302 | 805.66±205.04 | 843.05±173.01 | 0.2036 |
| TIVA | 689.54±201.34 | 672.19±168.48 | 0.7905 | 812.45±232.43 | 785.54±157.94 | 0.7063 |
| INH | 663.38±153.63 | 755.38±206.66 | 0.0199 | 729.14±168.89 | 821.97±216.13 | 0.0295 |

*BAL*, balanced anesthesia; *TIVA*, total intravenous anesthesia; *INH*, inhalational anesthesia.

body weight; ability to sustain a 5-s head lift; sustained hand grip; sustained arm lift).

Age, sex, and ASA physical status were recorded preoperatively. Heart rate (HR) and mean arterial blood pressure (MABP) were recorded before initiation of anesthesia, after initiation of surgery, after surgery was completed, and after anesthesia was completed. These parameters were not recorded upon admission to the post-anesthesia care unit (PACU).

Duration of anesthesia (time from the entry into the operating room until transfer to the PACU) and duration of surgery (time from incision to placement of surgical dressing) were recorded for each patient. However, duration in the PACU (total time in the PACU) was not recorded.

The cost of anesthesia for each patient, including supplies (tracheal catheter, central venous puncture bag, arterial transducer, analgesia pump), analgesic drugs, monitoring of vital signs, and analgesic gases, were recorded from the start of anesthesia to discharge from the operating room. For each patient, all open vials were considered to be fully consumed when calculating the total cost of anesthesia. The amount of anesthetic consumed was monitored carefully for each patient. Subgroup analyses were done to assess the cost per hour of anesthesia for different age groups. Costs associated with monitors and anesthetic machines were not included in the calculated anesthesia costs, nor were physician labor costs (because they are paid a fixed monthly income).

Statistical analyses were done using SPSS v15.0 (IBM, Armonk, NY, USA). Continuous data were compared by analysis of variance (ANOVA). The Kolmogorov-Smirnov test was used to determine the distribution of variables. After testing for normal distribution, data were compared using the unpaired Student's *t*-test and chi-square test. Non-parametric statistical methods were used to analyze heterogeneous variables. The Mann-Whitney U-test was used to analyze non-parametric variables. Multivariate logistic and linear regression analyses of factors associated with cost were also undertaken. $P<0.05$ was considered significant.

## Results

Two-hundred and seventy males (67.84%) and one hundred and twenty-eight females (32.16%) with a mean age of 59.31±11.60 years were the study cohort. There was no significant difference among groups for patient characteristics (**Table 1**). Adenocarcinoma had the highest prevalence in the study cohort. More patients had ASA physical status II than ASA physical status I. There was no significant difference in terms of mean age, but there were more patients aged <65 years in the BAL group ($P<0.05$). A large proportion of patients had

**Table 7.** Cost comparisons of different anesthetic methods (\$, $\bar{x}$ ± s)

| | BAL (*n*=258) | TIVA (*n*=36) | INH (*n*=104) | *F* value | *P* |
|---|---|---|---|---|---|
| Anesthetic drug | | | | | |
| Induction (*Propofol 200 mg:20 mL*) | 297.36±41.39 | 203.27±57.63 | 185.35±38.69* | 3.77 | 0.0239 |
| Induction (Propofol 500 mg:50 mL) | 412.61±58.10 | 428.06±57.63# | 403.41±54.48 | 2.61 | 0.0751 |
| Maintenance (*Propofol 200 mg:20 mL*) | 589.88±248.28 | 639.78±180.30 | 521.55±221.04* | 4.53 | 0.0114 |
| Maintenance (*Propofol 500 mg:50 mL*) | 669.27±703.75 | 822.72±271.35 | 516.88±216.66* | 4.39 | 0.013 |
| Adjuvant drug | 449.44±213.70† | 236.99±186.83 | 411.02±210.86 | 4.31 | 0.014 |
| Wasted drug (*Propofol 200 mg:20 mL*) | 97.71±48.95 | 130.88±64.81* | 91.62±44.30 | 8.73 | 0.0002 |
| Wasted drug (*Propofol 500 mg:50 mL*) | 195.76±135.21 | 243.54±101.76 | 268.32±70.08* | 14.69 | <.0001 |
| Monitor, medical consumables | 620.98±167.37 | 665.88±187.01 | 631.53±190.80 | 1.07 | 0.3456 |
| Postoperative analgesia | | | | | |
| Excluding analgesia pump | 229.28±112.32 | 213.48±127.47 | 237.76±100.24 | 0.66 | 0.1517 |
| Including analgesia pump | 507.38±186.23 | 470.12±228.78 | 521.93±167.99 | 1.04 | 0.3543 |
| Wasted drug | 1.65±7.72 | 0 | 2.33±9.18 | 1.2 | 0.3012 |
| Total wasted drug (including postoperative analgesia) | | | | | |
| *Propofol 200 mg:20 mL* | 99.37±49.45 | 130.88±64.81* | 93.95±45.44 | 7.59 | 0.0006 |
| *Propofol 500 mg:50 mL* | 197.42±135.88* | 243.54±101.76 | 270.66±68.95 | 14.76 | <.0001 |
| Total anesthesia drug | | | | | |
| Including wasted drug (*Propofol 200 mg:20 mL*) | 1236.6±346.37# | 1190.04±291.84 | 1117.91±318.97 | 4.68 | 0.0098 |
| Including wasted drug (*Propofol 500 mg:50 mL*) | 1531.33±756.94 | 1597.78±357.87 | 1331.31±324.95* | 4.21 | 0.0155 |
| Excluding wasted drug (*Propofol 200 mg:20 mL*) | 1138.97±333.85# | 1059.16±267.38 | 1026.29±312.46 | 4.86 | 0.0082 |
| Excluding wasted drug (*Propofol 500 mg:50 mL*) | 1355.57±747.94 | 1354.24±358.13 | 1062.98±320.17* | 7.23 | 0.0008 |
| Total anesthesia cost | | | | | |
| Including wasted drug (*Propofol 200 mg:20 mL*) | 2365.05±481 | 2326.06±541.73 | 2271.39±428.17 | 1.46 | 0.2339 |
| Including wasted drug (*Propofol 500 mg:50 mL*) | 2659±852.62# | 2733.80±570.23 | 2484.79±429.47 | 2.52 | 0.0816 |
| Excluding wasted drug (*Propofol 200 mg:20 mL*) | 2267.34±468.43 | 2195.18±508.25 | 2179.77±421.09 | 1.51 | 0.2217 |
| Excluding wasted drug (*Propofol 500 mg:50 mL*) | 2463.93±844.53# | 2490.26±545.02 | 2216.46±427.23 | 4.51 | 0.0116 |
| Total cost of anesthesia per hour | | | | | |
| Including wasted drug (*Propofol 200 mg:20 mL*) | 732.27±165.47# | 682.79±186.92 | 684.61±170.75 | 3.69 | 0.0259 |
| Including wasted drug (*Propofol 500 mg:50 mL*) | 818.99±225.96# | 801.99±204.58 | 750.56±183.99 | 3.8 | 0.0233 |
| Excluding wasted drug (*Propofol 200 mg:20 mL*) | 701.16±156.85* | 643.32±173.12 | 656.39±164.21 | 4.18 | 0.016 |
| Excluding wasted drug (*Propofol 500 mg:50 mL*) | 757.95±219.04# | 727.62±178.97 | 667.41±165.83 | 7.38 | 0.007 |
| Operation cost | 3754.02±679.78* | 4144.32±841.30 | 3823.31±725.28 | 4.84 | 0.0084 |
| Total hospitalization cost | 31010.93±14873.60 | 39007.95±12532.26 | 36099.73±14662.49* | 7.76 | 0.005 |

*BAL*, balanced anesthesia; *TIVA*, total intravenous anesthesia; *INH*, inhalational anesthesia. Total anesthesia cost is composed of the cost of total anesthetic drugs, cost of adjuvant drugs, and cost of monitoring. Average anesthesia cost of per hour contains the cost of wasted drugs; compared with other two groups: *P<0.05; compared with the INH group: # P<0.05; compared with the TIVA group: †P<0.05.

**Table 8.** Regression coefficient (including wasted drug; Propofol 200 mg:20 mL)

| | Parameter estimation | Standard error | t | Sig | Standard partial regression coefficient |
|---|---|---|---|---|---|
| a | 558.84 | 119.07 | 4.69 | <0.0001 | 0 |
| b1 | 143.2 | 51.12 | 2.8 | 0.0053 | 0.29104 |
| b2 | -59.15 | 18.71 | -3.16 | 0.0017 | -0.10881 |
| b3 | 5.86 | 1.39 | 4.2 | <0.0001 | 0.14353 |
| b4 | 182.45 | 58.48 | 3.12 | 0.0019 | 0.32388 |
| b5 | 611.2 | 54.39 | 11.24 | <0.0001 | 0.38346 |

a: constant; b: partial regression coefficient.

medical insurance and agreed to have postoperative analgesia.

A comparison of the duration of anesthesia, surgery, hospital stay after surgery, and hospital stay are shown in **Table 3**. There were no significant difference induration of anesthesia and duration of surgery among the three groups. Duration of hospital stay after surgery and duration of hospital stay (in days) in the TIVA group was 15.86±7.11 and 20.78±7.17, respectively, and significantly longer than in the other two groups (P<0.05).

Patients in the three GA groups were divided into two new groups based on age. One group

Table 9. Regression coefficient (including wasted drug; Propofol 500 mg:50 mL)

| | Parameter estimation | Standard error | t | Sig | Standard partial regression coefficient |
|---|---|---|---|---|---|
| a | 1008.15 | 157.08 | 6.42 | <0.0001 | 0 |
| b1 | 356.45 | 32.83 | 10.86 | <0.0001 | 0.46176 |
| b2 | -106.74 | 36.26 | -2.94 | 0.0034 | -0.12515 |
| B5 | 626.77 | 106.18 | 5.9 | <0.0001 | 0.25064 |

a: constant; b: partial regression coefficient.

was aged <65 years and the other ≥65 years. There was no significant difference inthe cost of anesthetic adjuvant drugs (**Table 4**). From **Tables 5**, **6**, we found that if patients were aged ≥65 years, the BAL group and INH group had a higher total cost of anesthesia per hour (irrespective of inclusion or exclusion of waste) when propofol at 200 mg per 20 mL was used ($P<0.05$). However, if propofol at 500 mg per 50 mL was used, only INH-group patients aged ≥65 years had a higher total cost of anesthesia per hour (irrespective of inclusion or exclusion of waste) ($P<0.05$).

More information is given in **Table 7**. Cost of drugs for the induction of anesthesia when propofol (200 mg per 20 mL) was used was lower in the INH group than in the other two groups ($P=0.0239$). However, the TIVA group cost more than the INH group when propofol (500 mg:50 mL) was used. For the maintenance of anesthesia, irrespective of the specification of propofol, the cost of the INH group was lower ($P<0.05$). Cost of adjuvant drugs was higher in the BAL group (449.44±213.70) than in the TIVA group (236.99±186.83) ($P=0.014$).

The difference was more pronounced when the cost associated with waste was taken into account. The TIVA group was the most expensive when propofol (200 mg:20 mL) was used. However, if using propofol (500 mg:50 mL), the INH group was more expensive. There were no significant differences in the cost of postoperative analgesia, monitoring, and medical consumables. When comparing the total cost of drugs wastage (including postoperative analgesia), the TIVA group remained the highest (when propofol 200 mg:20 mL was used) and the BAL group the lowest (when propofol 500 mg:50 mL was used).

Total cost of anesthetic drugs is the drug cost from induction to maintenance stages. Regardless of whether the drug was wasted, when using propofol 200 mg:20 mL, the BAL group was more expensive than the INH group. However, if using propofol (500 mg:50 mL), the INH group was less expensive than the other two groups.

Besides the cost of drugs, the total cost of anesthesia also included monitoring and medical consumables. Irrespective of whether wasted drugs were excluded (propofol 500 mg:50 mL), the BAL group had a higher cost than the INH group.

Comparing the total cost of anesthesia per hour, when including wasted drugs and excluding wasted drug (propofol 500 mg:50 mL), the BAL group had a higher cost than the INH group. However, when excluding wasted drugs (propofol 200 mg:20 mL), the cost in the BAL group was higher than in the other two groups ($P=0.016$).

Operation cost was highest in the TIVA group ($P=0.0084$). A too-long operation time can delay postoperative recovery, thereby increasing the cost of anesthesia. Our study did not account for the cost in the PACU. Though the duration of operation time affected the total cost of hospitalization, it had no effect on the total cost of anesthesia per hour. In fact, the duration of the operation did not affect the cost of anesthesia per hour. Total hospitalization cost in the INH group was less than in the other two groups ($P=0.005$).

Total cost of wasted drug (including postoperative analgesia; propofol 200 mg:20 mL) accounted for 4.29% oftotal anesthesia cost (including wasted drug; propofol 200 mg:20 mL). However, the proportion of total cost of wasted drug (including postoperative analgesia; propofol 500 mg:50 mL) was 8.42% of total anesthesia cost (including wasted drug; propofol 500 mg:50 mL).

Total cost of anesthesia (including wasted drug), when propofol 200 mg:20 mL was used, was 7.09% of the total hospitalization cost. However, when propofol 500 mg:50 mL was used, the cost accounted for 7.93% of the total hospitalization cost.

Multiple linear regression analysis was undertaken to assess the relationship among total

**Table 10.** Types of economic analysis applicable to anaesthesia

| | Input | Output | Output examples |
|---|---|---|---|
| Cost minimization (cost identification) | Direct costs | Not applicable | Outcomes assumed equal |
| Cost-benefit | All costs | Economic benefits (benefits as monetary units) | Money saved, production gains or return to work |
| Cost-effectiveness | All costs | Natural units (measured outcomes used directly) | Numbers free from nausea, successfully treated cases |
| Cost-utility | All costs | Utility units (outcomes converted to common unit) | Quality adjusted life years |

Adapted with permission from [20].

**Table 11.** Definition of different types of costs

| Term | Definition |
|---|---|
| Costs | Irreversible use of a resource |
| Direct costs | Costs of the material and labour used for production |
| Fixed costs | Costs that remain the same no matter how many goods or services are produced |
| Indirect costs | Costs related to the consequences of an event to society or an individual |
| Intagible costs | Costs of pain and suffering as a result of illness or treatment |
| Variable costs | Costs that change with the number of goods or services are produced |

Adapted with permission from [22].

anesthesia cost (including wasted drug; propofol 200 mg:20 mL) (y1), total anesthesia cost (including wasted drug; propofol 500 mg:20 mL) (y2),duration of anesthesia (x1), anesthesia group (x2), age (x3), duration of surgery (x4), postoperative analgesia (x5), medical insurance (x6), weight (x7), pathology (x8), ASA physical status (x9) and underlying diseases (x10).

Data in **Table 8** show that the duration of anesthesia (x1), age (x3), duration of surgery (x4) and postoperative analgesia (x5) were positively correlated with total anesthesia cost (including wasted drug; propofol 200 mg:20 mL), but that anesthesia group (x2) was negatively correlated with it. The regression equation was

$$y1=558.84 + 143.2x1-59.15x2 + 5.86x3 + 182.45x4 + 611.2x5$$

According to **Table 9**, we obtain the equation

$$y2=1008.15 + 356.45x1-106.74x2 + 626.77x5$$

The dose of drugs is often calculated by referring to patient weight (i.e., anesthesia is positively correlated with weight-related cost). However, our study did not come to the same conclusion.

## Discussion

Being aware of cost in medicine is becoming increasingly important. Different types of economic analysis applicable to healthcare are summarized in **Table 10** [20]. The choice of analysis depends on how benefits/outputs are treated. A cost-identification analysis is an element of all medical economic studies but can be seen as synonymous with cost-minimization studies [21].

According to **Table 11**, hospitalization costs can be divided into variable costs and fixed costs (costs that do and do not change with patient volume, respectively). Costs can be partitioned further into direct costs and indirect costs (costs that can and cannot be linked directly to a patient, respectively) [22].

GA can be maintained using intravenous agent alone, inhaled agents alone, or a combination of both. We wished to undertake a cost-minimization analysis of three GA methods for scheduled elective radical resection of gastric cancer.

We are aware of the difficulties in comparing costs between centers because of national traditions, reimbursement systems and culture. Nevertheless, studying healthcare from an economic viewpoint, and sharing experiences to produce best-value healthcare, is important. Effect data are more variable than cost data, so detecting differences at the same level of inferential error is difficult [23].

Propofol can lead to faster sedation and recovery, so is used widely. It has been found to have anti-emetic properties and to be associated with a low prevalence of postoperative nausea and vomiting (PONV) [24], which could reduce GA costs. Propofol is more expensive than most drugs. Usually, there are two specifications of propofol: 200 mg:20 mL and 500 mg:50 mL. However, no study has focused on cost variance using propofol.

The present showed that total anesthesia time and operation time was not significantly different in the three groups (**Table 3**). Different anesthesiologists, different surgeons and different degree of surgical procedure influence anesthesia time and operation time. Decreasing discrepancies among groups is difficult.

When patients were divided into two groups based on age (<65 years and ≥65 years), there was no significant difference in the cost of adjuvant drugs for anesthesia (**Table 4**). In the ≥65 years group, the total cost of anesthesia per hour was significantly different, and the cost of INH and BAL (Propofol 200 mg:20 mL) were higher (**Tables 5**, **6**). Usually, aged patients have poor tolerance for anesthesia, so they need less anesthetic drugs than younger patients, and the cost should be reduced. However, we did not see this effect.

In our study, the cost associated with waste was taken into account (**Table 7**). Waste included drugs used in induction and maintenance stages. When propofol was used in different specifications, the result was different. Using propofol 200 mg:20 mL, the cost of waste in the TIVA group was higher than in the other two groups. However, when propofol 500 mg:50 mL was used, the cost of waste in the BAL group was higher. We compared anesthesia-related costs using different specifications of propofol. Irrespective of whether we considered the cost of wasted propofol or if propofol was used in the maintenance stage, the cost of propofol 500 mg:50 mL group was always higher than propofol 200 mg:20 mL. Hence, a higher specification of propofolis appropriate for procedures of long duration rather than those of short duration.

Kumar et al. [25] concluded that the cost of propofol as a maintenance anesthetic was significantly higher than that of desflurane or sevoflurane. No study has calculated the total cost including ancillary equipment or waste. Weinger et al. considered that the total cost should include the cost of drug wastage [26]. Nowadays, propofol is usually packaged as a preservative-free, single patient-use agent, so it may cost even more [27]. Therefore, any opened vial of propofol remaining at the end of the surgical procedure would have been wasted. Although the cost saving per patient was small, the potential for savings over 1 year would be large. Whether this saving would be negated by the potential extra need for anti-emetic agents with inhalational anesthesia (or other infusion equipment) has not been studied [28].

Macario et al. [29] estimated that ≈3% of total inpatient surgical costs are under immediate control of anesthesia providers. Hence, they argued that choosing less costly alternatives can reduce such costs as long as the quality of care is not decreased. Jackson et al. [30] concluded that propofol and sevoflurane do not offer significant economic advantages over thiopental and isoflurane in adults undergoing elective inpatient surgery.

In the present study, the total cost of wasted drugs (including postoperative analgesia) accounted for 4.29-8.42% of total anesthesia cost (including wastage of propofol). The proportion of cost of wasted drugs cost was not low. We should minimize such waste so that savings can be made. Though the saving-per-patient would be small, savings over 1 year would be considerable [29].

Hospital stay for patients undergoing radical gastrectomy in the TIVA group was longer. This phenomenon could have been because 66.67% of patients in that group had underlying disease, which was higher than for the others. Underlying disease (e.g., diabetes mellitus) often leads to long recovery times. GA rarely used long-acting drug, so has little impact upon hospital stay.

Duration of hospital stay is another critical issue for selection of anesthesia type. In recent years, policymakers have paid more attention to increasing healthcare expenditures. Saving money and providing high-quality healthcare simultaneously are important issues. However, standardized and comparative studies related to this topic in the literature are lacking.

Nursing and physician labor costs were not included in our analysis because they receive a fixed monthly income. We found that total anesthesia cost (including drug wastage) was 7.09% (propofol 200 mg:20 mL) and 7.93% (propofol 500 mg:50 mL) of total hospitalization cost. However, Macario et al. [29] reported that the costs of intraoperative anesthesia account for only 5.6% of total hospital costs. 49% of total hospital costs were variable. 57% were direct costs. The largest category of hospital cost was the operating room (33%), followed by the patient ward (31%). Reducing the cost of anesthesia will have minimal impact on total costs. The method for obtaining the minimum cost is to achieve cooperation among nurses, anesthesia personnel, surgeons, and administrators to develop effective strategies to enhance productivity and minimize inefficiency.

An important and unique aspect of this present study was integration of cost data into the analysis. Cost data may be criticized for institution-specific derivations and lack of professional fees. However, we hope that it can be used as a reference for choosing GA for radical gastrectomy in healthcare systems. To ascertain the intraoperative factors associated with cost, a linear regression analysis with cost as the dependent variable and several intraoperative factors as independent variables was done (**Tables 8**, **9**). Multivariate linear regression of factors associated with total cost was carried out and demonstrated that duration of anesthesia (x1), age (x3), duration of surgery (x4) and postoperative analgesia (x5) were positively correlated with the total cost of anesthesia (including wasted drug; propofol 200 mg:20 mL). Duration of anesthesia (x1) and postoperative analgesia (x5) were positively correlated with the total cost of anesthesia (including wasted drug; propofol 500 mg:50 mL). Our findings demonstrated that anesthesia, age, duration of surgery, and postoperative analgesia had a positive effect upon total GA cost. Interestingly, the anesthesia group (x2) was negatively correlated with the total cost of anesthesia (including drug wastage). These findings are likely related to duration of stay in these two subpopulations, but exceed the scope our analysis. No studies have assessed the cost minimization of GA using different specifications of propofol. These findings are important and must be assessed carefully [31].

Our study had six main limitations. First, we excluded nursing and physician labor costs. Second, duration of surgery was closely related to surgeon experience. Experienced surgeons usually had shorter operation times, and patients had shorter hospitalization times and faster postoperative recovery. These factors indirectly reduced the total cost. Third, this was a retrospective study. Fourth, during the induction and maintenance of anesthesia, drug types change considerably, which is not conducive for comparing costs. Anesthetic drugs used to calculate the cost of anesthesia are based on anesthesia records rather than the actual amount, so errors are inevitable. Fifth, these results were derived from a single, university hospital setting. We realize that different hospitals are likely to vary in terms of commonly used GA drugs, drug cost, consumables, monitoring, and surgical procedure. Finally, it isargued that differences in anesthetic outcomes can influence the entire episode of hospitalization [3, 29, 32-35]. However, our study focused on the use and costs of drugs. We did not report on comparisons of the costs of care, and doses were not included in the cost in the PACU or related cost of anesthesia after leaving the PACU to admission on the ward. We limited the costing to the perspective of anesthesia departments rather than institutions or higher-level decision-makers.

## Conclusion

When patients were undergoing elective radical resection for gastric carcinoma, the duration of anesthesia, age, duration of surgery, and postoperative analgesia were positively correlated with the total cost of anesthesia (including wastage of propofol 200 mg:20 mL). Duration of anesthesia and postoperative analgesia were positively correlated with the total cost of anesthesia (including wastage of propofol 500 mg:50 mL). However, the anesthesia group was negatively correlated with the total cost of anesthesia (including drug wastage). When propofol 500 mg:50 mL was used, the total cost of anesthesia and total cost of anesthesia per hour in the BAL group was higher than the INH group. However, when excluding drug wastage (propofol 200 mg:20 mL), the BAL group was more expensive than the other two groups. Use of propofol 200 mg:20 mL as a GA would save money.

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## Disclosure of conflict of interest

None.

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## References

[1] Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D and Bray F. GLOBOCAN 2012 v1. 0, cancer incidence and mortality worldwide: IARC CancerBase No. 11 [internet]. International Agency for Research on Cancer, Lyon. globocan. iarc. fr (accessed 10 October 2014) 2013.

[2] Jakobsson I, Heidvall M and Davidson S. The sevoflurane-sparing effect of nitrous oxide: a clinical study. Acta Anaesthesiol Scand 1999; 43: 411-414.

[3] Boldt J, Jaun N, Kumle B, Heck M and Mund K. Economic considerations of the use of new anesthetics: a comparison of propofol, sevoflurane, desflurane, and isoflurane. Anesth Analg 1998; 86: 504-509.

[4] Watcha MF and White PF. Economics of anesthetic practice. Anesthesiology 1997; 86: 1170-1196.

[5] Myles PS, Hendrata M, Bennett AM, Langley M and Buckland MR. Postoperative nausea and vomiting. Propofol or thiopentone: does choice of induction agent affect outcome? Anaesth Intensive Care 1996; 24: 355-359.

[6] Raeder J, Gupta A and Pedersen FM. Recovery characteristics of sevoflurane- or propofol-based anaesthesia for day-care surgery. Acta Anaesthesiol Scand 1997; 41: 988-994.

[7] Jellish WS, Lien CA, Fontenot HJ and Hall R. The comparative effects of sevoflurane versus propofol in the induction and maintenance of anesthesia in adult patients. Anesth Analg 1996; 82: 479-485.

[8] Dexter F and Tinker JH. Comparisons between desflurane and isoflurane or propofol on time to following commands and time to discharge. A metaanalysis. Anesthesiology 1995; 83: 77-82.

[9] Stevanovic PD, Petrova G, Miljkovic B, Scepanovic R, Perunovic R, Stojanovic D and Dobrasinovic J. Low fresh gas flow balanced anesthesia versus target controlled intravenous infusion anesthesia in laparoscopic cholecystectomy: a cost-minimization analysis. Clin Ther 2008; 30: 1714-1725.

[10] Vitez TS. Principles of cost analysis. J Clin Anesth 1994; 6: 357-363.

[11] Hirsch J. Impact of postoperative nausea and vomiting in the surgical setting. Anaesthesia 1994; 49 Suppl: 30-33.

[12] Carroll NV, Miederhoff PA, Cox FM and Hirsch JD. Costs incurred by outpatient surgical centers in managing postoperative nausea and vomiting. J Clin Anesth 1994; 6: 364-369.

[13] Watcha MF and Smith I. Cost-effectiveness analysis of antiemetic therapy for ambulatory surgery. J Clin Anesth 1994; 6: 370-377.

[14] Bach A, Bohrer H, Schmidt H, Motsch J and Martin E. [Economic aspects of modern inhalation anesthetics with sevoflurane as an example]. Anaesthesist 1997; 46: 21-28.

[15] Weiskopf RB and Eger EI 2nd. Comparing the costs of inhaled anesthetics. Anesthesiology 1993; 79: 1413-1418.

[16] Broadway PJ and Jones JG. A method of costing anaesthetic practice. Anaesthesia 1995; 50: 56-63.

[17] Newson C, Joshi GP, Victory R and White PF. Comparison of propofol administration techniques for sedation during monitored anesthesia care. Anesth Analg 1995; 81: 486-491.

[18] Alhashemi JA, Miller DR, O'Brien HV and Hull KA. Cost-effectiveness of inhalational, balanced and total intravenous anaesthesia for ambulatory knee surgery. Can J Anaesth 1997; 44: 118-125.

[19] Nakada T, Ikeda D, Yokota M and Kawahara K. Analysis of the cost-effectiveness of remifentanil-based general anesthesia: a survey of clinical economics under the Japanese health care system. J Anesth 2010; 24: 832-837.

[20] Rowe WL. Economics and anaesthesia. Anaesthesia 1998; 53: 782-788.

[21] Sperry RJ. Principles of economic analysis. Anesthesiology 1997; 86: 1197-1205.

[22] Suttner S, Kumle B and Boldt J. Pharmacoeconomic considerations in anaesthetic use. Expert Opin Pharmacother 2002; 3: 1267-1272.

[23] Cartwright WS. Methods for the economic evaluation of health care programmes, second edition. By Michael F. Drummond, Bernie O'Brien, Greg L. Stoddart, George W. Torrance. Oxford: Oxford University Press; 1997. J Ment Health Policy Econ 1999; 2: 43.

[24] Hofer CK, Zollinger A, Büchi S, Klaghofer R, Serafino D, Bühlmann S, Buddeberg C, Pasch T

and Spahn DR. Patient well-being after general anaesthesia: a prospective, randomized, controlled multi-centre trial comparing intravenous and inhalation anaesthesia. Br J Anaesth 2003; 91: 631-637.
[25] Kumar G, Stendall C, Mistry R, Gurusamy intravenous anaesthesia using propofol with sevoflurane or desflurane in ambulatory surgery: systematic review and meta-analysis. Anaesthesia 2014; 69: 1138-1150.
[26] Weinger MB. Drug wastage contributes significantly to the cost of routine anesthesia care. J Clin Anesth 2001; 13: 491-497.
[27] Ravenelle F, Gori S, Le Garrec D, Lessard D, Luo L, Palusova D, Sneyd JR and Smith D. Novel lipid and preservative-free propofol formulation: properties and pharmacodynamics. Pharm Res 2008; 25: 313-319.
[28] Eikaas H and Raeder J. Total intravenous anaesthesia techniques for ambulatory surgery. Curr Opin Anaesthesiol 2009; 22: 725-729.
[29] Macario A, Vitez TS, Dunn B and McDonald T. Where are the costs in perioperative care? Analysis of hospital costs and charges for inpatient surgical care. Anesthesiology 1995; 83: 1138-1144.
[30] Jackson T and Myles PS. Part II: total episode costs in a randomized, controlled trial of the effectiveness of four anesthetics. Anesth Analg 2000; 91: 1170-1175.
[31] Bonnet F and Marret E. Influence of anaesthetic and analgesic techniques on outcome after surgery. Br J Anaesth 2005; 95: 52-58.
[32] Smith I, Terhoeve PA, Hennart D, Feiss P, Harmer M, Pourriat JL and Johnson IA. A multicentre comparison of the costs of anaesthesia with sevoflurane or propofol. Br J Anaesth 1999; 83: 564-570.
[33] Suttner S, Boldt J, Schmidt C, Piper S and Kumle B. Cost analysis of target-controlled infusion-based anesthesia compared with standard anesthesia regimens. Anesth Analg 1999; 88: 77-82.
[34] Fazi L and Watcha MF. The economics of newer anaesthetic drugs: should we take the Rolls-Royce or the bicycle today? Paediatr Anaesth 1999; 9: 181-185.
[35] Tagliente TM. Pharmacoeconomics of propofol in anesthesia. Am J Health Syst Pharm 1997; 54: 1953-1962.