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Drug Cost Analysis of Three Anesthetic Regimens in Prolonged Lumbar Spinal Surgery

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Background: Drug cost analysis has not been performed to compare different anesthetic techniques used in prolonged procedure surgery under auditory evoked potential (AEP) monitoring. We compared the costs of propofol-based total intravenous anesthesia (TIVA), sevoflurane (SEVO) anesthesia and desflurane (DES) anesthesia in prolonged lumbar spine surgery lasting more than 4 h. **Methods:** We studied 75 patients (ASA class I-II) scheduled to undergo elective lumbar spine surgery. Patients were randomized into TIVA, SEVO, or DES groups. The AEP index was maintained at 15-25. After completing surgery, emergence time from anesthesia was measured and the anesthetic costs were calculated in New Taiwan dollars (NTD). **Results:** Demographic factors were not significantly different between groups. The total cost was significantly higher in the SEVO group than in the TIVA and DES groups (NTD 2052±485, 1327±316 and 1439±313, respectively; $P < 0.001$). The main anesthetic drug was significantly cheaper in the TIVA than in the SEVO and DES groups (NTD 846±216, 1616±456 and 969±304, respectively; $P < 0.001$). The cost of perioperative fentanyl and cisatracurium were higher in the TIVA group than in the SEVO and DES groups. The TIVA group had faster recovery than the DES and SEVO groups (9.7±4.0, 26.8±11.9 and 23.1±11.6 min, respectively; $P < 0.001$). **Conclusions:** Patients undergoing prolonged procedure recover faster after TIVA than after DES or SEVO anesthesia. The TIVA and DES regimens were significantly cheaper than SEVO-based anesthesia.

Key words: cost, prolonged procedure surgery, propofol, sevoflurane, desflurane

INTRODUCTION

In the era of economic management of health care, it is necessary to identify the cheapest optimal anesthetic techniques. At the same time, cost control is of major importance in today's climate of economic consciousness and the choice of anesthetic can have an important impact on total costs for an anesthesia department.

Propofol-based total intravenous anesthesia (TIVA) was reported to cost less than sevoflurane (SEVO) or desflurane (DES) anesthesia during gynecological laparoscopic surgery because of the low cost of propofol[1]. However, the surgery episodes analyzed in that study were short, lasting around 100 min. The cost of different anesthetic techniques used in prolonged procedure surgery is not clear in Taiwan. In the present study, we compared the costs of TIVA, SEVO and DES anesthesia used in lumbar spine surgery lasting than more 4 h.

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METHODS

After obtaining approval from the Ethics Committee of Tri-Service General Hospital (Taipei, Taiwan) and after obtaining written informed consent from the patients, we studied 75 patients (ASA class I-II) scheduled to undergo elective lumbar spine surgery. We excluded patients with known neurological or psychiatric disorders, patients currently using anticonvulsants or other centrally active medications, prolonged procedure users of drugs or alcohol and patients with a body weight more than 50% higher than their ideal body weight.

The patients were randomized to three groups using sealed envelopes: the TIVA group received propofol induction and propofol maintenance, the SEVO group received propofol induction and SEVO maintenance, and the DES group received propofol induction and DES maintenance.

Patients were not premedicated and the same anesthesiologist attended to every patient. Before induction of anesthesia, electrocardiography (ECG), pulse oximetry and noninvasive blood pressure monitoring were applied and three A-Line® Auditory Evoked Potential (AEP) electrodes (Danmeter, Odense, Denmark) were positioned at the mid-forehead (+), left forehead (reference) and left mastoid (-). In the TIVA group, anesthesia was induced with 2 μg/kg fentanyl, 2% lidocaine (1.5 mg /kg) and 2 mg cisatracurium. Afterwards, continuous infusion of propofol was begun by using a target-controlled infusion (TCI) system (Fresenius Orchestra Primea®, Fresenius Kabi AG, Bad Homburg, Germany) with the plasma target set at 4.0 μ g/mL. When the patient lost consciousness, 1.5 mg/kg succinylcholine was given. The trachea was intubated until the AEP index (AAI) decreased to 20[2] and mechanical ventilation was then started. The anesthesia was maintained using TCI with propofol and a gas flow of 0.3 L/min oxygen. In the SEVO and DES groups, anesthesia was induced with 2 μg/kg fentanyl, 2% lidocaine (1.5 mg/kg), 2 mg cisatracurium and 2 mg/kg propofol. After loss of consciousness, 1.5 mg/kg succinylcholine was administered and tracheal intubation was performed until the AAI decreased to 20[2]. The anesthesia was maintained with SEVO and DES after 15 min washing in at 2 L/min and then kept at 1 L/min (SEVO) or 0.3 L/min (DES) in 100% oxygen, as is our practice. Respiratory and cardiovascular functions were monitored and recorded at preinduction (baseline), 1 min intervals during induction of anesthesia and subsequently at 5 min intervals throughout the anesthesia and recovery periods. Heart rate (HR) was measured using a continuous lead type II ECG; mean arterial blood pressure was measured noninvasively using an automatic oscillometer and partial oxygen saturation (SpO_2) was measured by pulse oximetry. Respiratory function was monitored by recording the respiratory rate (RR) and SpO_2 and end-tidal carbon dioxide ($ETCO_2$) by capnometry. Propofol, desflurane and sevoflurane during maintenance of anesthesia were adjusted continuously to keep the AAI between 15 and 25. Adverse hemodynamic responses of at least 1 min duration were recorded and were classified as "hypertension" (mean arterial pressure, MAP > 20% above preoperative baseline value), "hypotension" (MAP < 60 mmHg), "tachycardia" (HR > 20% above preoperative baseline values) or "bradycardia" (HR < 50 bpm). An AAI over 25 or hypertension and tachycardia were initially treated by concentration of effect(Ce) with 0.2 μg/mL , 0.2% and 1% increments of propofol, SEVO and DES, respectively. If two increments were unsuccessful, the propofol, SEVO and DES were increased by 0.5 μ g/mL, 0.5% and 2% increments, respectively. Hypertension and tachycardia were treated with fentanyl (1 μg/kg i.v.) if the AAI was in the set range. Hypotension was treated initially with fluids and 5 mg ephedrine was given i.v. if the AAI was in the set range. If the AAI was less than 15 and associated with hypotension, we applied 0.2 μ g/mL, 0.2% and 1% decrements in propofol, SEVO and DES, respectively. Atropine (0.5 mg) was given if the heart rate decreased to <50 beats per min and was accompanied by hypotension.

Respiratory frequency and end-tidal volume were adjusted to maintain the $ETCO_2$ at 35-45 mm Hg. Muscle relaxation was maintained with cisatracurium. At the last three stitches of surgery, administration of the maintenance anesthetics was discontinued and the oxygen flow was adjusted to 6 L/min until the patient was returned to the supine position. Muscle relaxation was reversed with intravenous neostigmine (2 mg) combined with atropine (1 mg). Emergence from anesthesia was assessed by measuring the time until spontaneous eye opening and removal of the endotracheal tube.

The acquisition costs of anesthetic drugs and the disposables associated with their administration were recorded. The costs of disposable material associated with the administration of IV drugs (appropriately sized syringes, infusion tubing and three-way stopcocks) were also recorded. Syringes were reused whenever repeat doses of the same drug were required in the same patient. Consumption of inhalation anesthetics was calculated by weighing the vaporizer using a precision weighing machine (SG 16001; Mettler Toledo, Greifensee, Switzerland; accuracy 0.1 g). Conversion from grams to milliliters was performed using the specific weights of the inhalation anesthetics (desflurane 1.465 g/mL and sevoflurane 1.52 g/mL). Prices for all used substances were taken from our hospital pharmacy list (Table 1). Anesthetic drugs included opioids, propofol, inhalation anesthetics, neuromuscular blocking drugs and antagonists. The intraoperative cost of drugs was calculated in New Taiwan dollars (NTD; Sevoflurane NTD 20.5/g; Desflurane NTD 10.7/g; propofol NTD 85/200 mg; cisatracurium NTD 139/10 mg). The costs of oxygen, staff (physician, nurses) and other overhead costs (e.g., anesthesia machines, monitoring) were not calculated.

Statistical Analysis

Based on retrospective data in the same surgical popu-

Table 1 Basic Cost Assumptions for the Economic Analyzes

Drug Acquisition Costs	TSGH(NTD)	USA(NTD)	European(NTD)
Propofol 1%	85(20 mL)	220(20 mL)[19]	368(50 mL)[4]
Desflurane(240 mL)	3750	2168[19]	3078[4]
Sevoflurane(250 mL)	7800	5145[19]	7762[4]

Note: Data are based on the direct cost to our institution from the manufacturer in April 2007 and the exchange rate was NTD 33 and 45 in USD and Euro.

Table 2 Patient characteristics

	Group TIVA (n = 25)	Group SEVO (n = 25)	Group DES (n = 25)
Gender (M/F)	13/12	14/11	13/12
Age (yr)	63.8±15.4	58.4±9.8	59.9±10.0
Weight (kg)	69.2±12.3	66.4±11.8	65.1±9.5
Height (cm)	162.5±9.5	164.0±7.1	165.4±10.3
Surgery time (min)	245.6±67.4	243.5±67. 8	249.1±67.1
Anesthetic time (min)	285.4±65.4	270.7±67.9	280.5±73.7

There were no significant differences between groups. TIVA, propofol-based total intravenous Anesthesia; SEVO, sevoflurane-inhalation Anesthesia; DES, desflurane-inhalation Anesthesia.

lation from our institution, a power analysis was performed using cost as the primary variable. We calculated a sample size so that a between-group difference in cost difference of NTD 500 would permit a one-tailed type I error rate of $\alpha = 0.05$ with a power of 80%. This analysis indicated that a sample size of at least 23 patients per group was necessary.

Data are expressed as the median with range. Continuous variables were analyzed using analysis of variance or the Kruskal-Wallis test, depending on the distribution or significant difference in variances, followed by posttests if indicated. The frequency distributions were subjected to chi-squared tests. In all tests, $P < 0.05$ was considered significant.

RESULTS

The patient demographics and anesthetic characteristics are summarized in Table 2. There were no significant differences between groups in terms of hemodynamics, fluid management, blood loss or AEP levels (data not shown). The total cost was significantly higher in the SEVO than in DES and TIVA groups (NTD 2052 ± 485, 1327 ± 316 and 1439 ± 313, respectively; $P < 0.001$; Table 3). In addition, the main anesthetic drug was significantly cheaper in the TIVA than in the DES and SEVO groups (NTD 846 ± 216, 969 ± 304 and 1616 ± 456, respectively; $P < 0.001$; Table 3). The cost of perioperative fentanyl and cisatracurium were higher in the TIVA group (NTD 42 ± 16 and 387 ± 146, respectively) than in the SEVO and DES groups (NTD 30 ± 10 and 295 ± 61; 30 ± 12 and 312 ± 83, respectively; both P < 0.001; Table 3). The time to clinical recovery was 9.7±4.0, 26.8±11. 9 and 23.1 ± 11.6 min in the TIVA, DES and SEVO groups, respectively (TIVA vs DES and SEVO; $P < 0.001$; Table 3).

Table 3 Extubation time and cost analysis

	Group TIVA (n = 25)	Group DES (n = 25)	Group DES (n = 25)
Extubation time (min)	9.7±4.0***	23.1±11.6	26.8±11.9
Cost of Main drugs (propofol, sevoflurane, desflurane) (NTD)	846±216**	1616±456	969±304
Intraoperative fentanyl (μg)	195±73*	136±40	139±54
Cost of fentanyl (NTD)	42±16**	30±10	30±12
Intraoperative cisatracurium(mg)	24±11*	16±5	18± 6
Cost of cisatracurium (NTD)	387±146*	295±61	312±83
Total Cost (NTD)	1327±316	2052±485[#]	1439±313

Values are mean ± SD. Group TIVA, propofol-based total intravenous anaesthesia; Group SEVO, sevoflurane-inhalational anaesthesia; Group DES, desflurane-inhalational anaesthesia; NTD, New Taiwan dollars.
* $p<0.05$ compared with group DES and group SEVO;
** $p<0.01$ compared with group DES and group SEVO;
*** $p<0.001$ compared with group DES and group SEVO;
[#] $p<0.001$ compared with group TIVA and group DES.

DISCUSSION

Safety of anesthesia is the first priority in surgery and cost control in anesthesia becomes important gradually. We found that the cost of TIVA was similar to that of DES-based anesthesia under low-flow anesthesia. This result conflicts with a previous study[1] that demonstrated a lower cost associated with TIVA than with DES anesthesia in gynecological laparoscopic surgery. This difference may be explained by the duration of surgery. We speculate that the economic effect of low-flow anesthesia is not prominent in short surgery. The initial washing-in to fill the lungs and circuit is necessary in inhalation anesthesia, even in short-term surgery. Our current results support our hypothesis that the difference in the anesthetic cost of DES anesthesia under low-flow anesthesia becomes more apparent in prolonged than in short-term surgery. Thus, the lower cost of the initial inhalation wash-in is offset by prolonged procedure anesthesia.

In a similar study, Rohm et al.[3] presented significantly higher costs for TIVA than for DES anesthesia. There are several possible reasons for the differences between our data and that study. First, Rohm et al. used a continuous infusion of remifentanil (REM) as an anesthetic adjuvant in TIVA and we used a bolus of fentanyl because REM is unavailable in our country. Loop et al.[4] found higher costs of REM-based anesthesia compared with conventional anesthesia and they concluded that the high costs of anesthetics and disposable i.v. anesthetics contributed to this result. Therefore, anesthesia combined with REM increases the costs of TIVA. Second, the low price of propofol contributes to the overall lower cost, because propofol is cheaper in our country than in European countries and this is an important contributor to the differences between our cost analysis and that by Rohm et al.[3]. However, the prices of anesthetics and anesthetic techniques vary greatly from area to area, and even from hospital to hospital. Moreover, controversial results had also been reported and previous authors have questioned the differences of anesthetic depth among anesthesia techniques; they were either not clear or unequal as to when titration of anesthesia was commenced under the guide of autonomic and somatic responses[1]. In comparison with previous studies, the difference may be caused by the price difference among propofol, desflurane and sevoflurane. In the USA and Europe, propofol is more expensive than that in our country; on the other hand, desflurane and sevoflurane are cheaper than in our country (Table 1). Furthermore, the prices of anesthetics and anesthetic techniques vary greatly from area to area, even from hospital to hospital. The price of propofol is decreasing now that propofol has been taken off license and a number of companies have introduced a generic propofol brand.

In addition, compared with DES and SEVO anesthesia, TIVA involved more consumption of cisatracurium and fentanyl. Previous reports have demonstrated that, compared with propofol, inhalation anesthesia reduces the need for and prolongs the effect of neuromuscular blocking drugs[5,6]. Moreover, the use of such drugs prolongs the need for neuromuscular blockade by closed-circuit inhalation anesthesia[7]. SEVO and fentanyl exhibit a high degree of synergistic antinociceptive interaction in dogs[8]. Therefore, even though the main anesthetic cost is lower in TIVA, the additional cost of analgesic and neuromuscular blocking drugs is higher than in inhalation anesthetics. In this study, SEVO anesthesia cost more than the other two anesthetic techniques for both prolonged and short-term surgery. We performed SEVO anesthesia under a fresh gas flow of 1 L/min, which was higher than that used for DES anesthesia. The present study further supports the economic benefit of DES in low-flow anesthesia[9,10]. Taken together, these data indicate that many factors contribute to the costs of anesthesia in prolonged procedure surgery involving either TIVA or DES with low-flow anesthesia.

Here we applied AEP monitoring as a guide to titrate the level of anesthesia. AEP monitoring makes it easy to control this, given that our objective was to perform a cost analysis of the different anesthetic regimens. AEP monitoring was more precise than in previous studies that used titrated anesthetics according to the hemodynamic or autonomic responses[11,12]. Use of TCI with TIVA has benefits, especially in prolonged procedure surgery, TCI uses averaged pharmacokinetic models to control the infusion rate and to control the calculated plasma concentration directly, rather than the indirect control provided by adjusting the infusion rate[13]. Comparative studies between TCI and manual infusion show better hemodynamic stability, faster recovery[14] and lower induction doses[15] with TCI. These factors contribute to the lower cost of TIVA when used with TCI.

Another objective of our study was to compare the recovery time between groups. Many factors can affect this, such as anesthetic time, gas flow rate, ventilation and use of N_2O and opioids. We found that patients on TIVA had a faster emergence time than those on inhalation anesthesia, although the emergence times in this study were longer than those in a previous study[1] using the same anesthetic techniques. Our explanation for this difference is that prolonged procedure anesthesia increases the emergence time because the inhaled anesthetics are redistributed in the fatty tissue and muscle. The delayed emergence time is not obvious in the TIVA group because we used TCI for TIVA, as the optimal effective site concentration of propofol can be maintained and less propofol accumulates.

We did not analyze various prognostic profiles such as postoperative nausea and vomiting (PONV), time to discharge from post-anesthetic room (PAR), hospitalization days and total hospital costs. First, our case number was sufficient for a cost comparison study, but not to compare PONV[16]. Second, the time to discharge from PAR was dependent on many nonmedical and administrative issues[17]. Third, spine surgery always needs a relatively long hospitalization and huge total hospital costs; it is not easily controlled because of many factors. Therefore, in the present study, we compared the costs of anesthesia concentrate solely on the acquisition costs of the drugs used and did not investigate the financial consequences of the anesthetics compared. In addition, we did not calculate the costs of oxygen, staff (physicians and nurses), overhead costs【e.g., anesthesia machines such as TCI pumps and vaporizers, monitoring such as AEP and BIS (Bispectral index)】and disposables (e.g., anesthesia circuits and pulse oximeter probes), as the costs of these aspects of surgery typically are not calculated in such studies[3,12,18-21].

In conclusion, patients undergoing prolonged procedure surgical procedures recovered faster after TIVA than after DES or SEVO anesthesia. The costs of the TIVA and DES regimens were significantly lower than that a SEVO-based anesthetic technique in this series involving prolonged spinal surgery.

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