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Original Research Article

Comparative effect of propofol and sevoflurane on chronic postsurgical pain and cognitive function after cardiac surgery in Chinese elderly patients: A preliminary clinical study

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Abstract

Purpose: *To compare the effects of propofol and sevoflurane on chronic post-surgical pain and cognitive function after cardiac surgery in Chinese elderly patients.*
Methods: *A total of 200 Chinese patients (aged > 65 years) with confirmed diagnosis of severe chronic artery disease who underwent cardiac surgery were given either propofol or sevoflurane. The following efficacy variables were assessed in both treatment groups: pain using an 11-point NRS after surgery; cognitive function, using Severe Impairment Battery (SIB), Clinician Interview-Based Impression of Change (CIBIC), Mini Mental State Examination (MMSE) scale; as well as psychological well-being and disability, using K10 Psychological Distress Scale K-10 and WHO Disability Assessment Schedule (WHODAS) scale. Incidence of complications and duration of hospital stay were also compared.*
Results: *Pain severity score was significantly lower in patients treated with propofol than in those who received sevoflurane (6.1 vs 8.4; $p < 0.05$). Psychological well-being measured using K-10 score was similar in both groups ($p > 0.05$). Similarly, there were no meaningful differences in disability score between the two treatment groups ($p > 0.05$). The severity of signs and symptoms of dementia were similar at baseline visit ($p > 0.05$). Propofol-treated patients had numerically greater relief in signs and symptoms of dementia/cognitive impairment, when compared to the Sevoflurane-treated patients ($p > 0.05$). However, incidence of complications (including adverse events) was comparable in both groups ($p > 0.05$).*
Conclusion: *Propofol produced significantly greater improvement in post-surgical pain and cognitive functions than sevoflurane after cardiac surgery in Chinese elderly patients.*

Keywords: *Propofol; Sevoflurane; Cardiac surgery; Chronic postsurgical pain; Cognitive functions*

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INTRODUCTION

Cardiac surgery is a major form of surgical intervention in patients with chronic heart diseases who account for up to 56 % of cases of chronic post-surgical pain (CPP) [1,2]. It has been reported that CPP arises mainly from the anterior thorax due to physiological changes that occur after cardiac surgery. Chronic post-surgical pain (CPP) affects the quality of life, mood and

sleep of patients who underwent cardiac surgery under anaesthesia [2]. The cognitive complications after surgical intervention can last for weeks or several months. This negatively affects the quality of life as a result of loss of patients' ability to focus, recall, or undertake activities of daily living. Cognitive dysfunction is one of most common complications associated with major surgical interventions [3-5].

Patients who opt for elective cardiac surgery must undergo general anaesthesia using either intravenous (iv) or inhalation anaesthetics. Studies have found that propofol affects pain signaling via impairment of cytokines and NMDA receptor involved in pain signaling [6-9]. Meta-analyses have shown that propofol is effective in reducing postoperative pain in patients who underwent major surgeries [10]. In addition, propofol produces favorable postoperative cognitive outcomes [7-9,10,12]. No studies have been conducted to compare the effect of intravenous anaesthesia with that of inhalation anaesthesia on chronic post-surgical pain and cognitive function in Chinese elderly patients who underwent cardiac surgery. The present preliminary clinical study was designed as a comparative investigation on the effects of propofol and sevoflurane on chronic postsurgical pain and cognitive function after cardiac surgery in Chinese elderly patients.

METHODS

Patients and ethics

Chinese patients aged > 65 years, with confirmed diagnosis of severe chronic artery disease, and who met the ASA I/II criteria for cardiac surgery, were randomly assigned equally to two groups treated either with propofol or sevoflurane. Written informed consent was obtained from each enrolled patient. All study-related documents including protocol, ICFs and CRFs were willingly obtained. The study was initiated after getting ethical approvals from the institutional ethics committee of Shandong University, *vide* approval no. IEC-SU-QH-2019/09-Q1, and was implemented in line with the ethical principles laid down in the Helsinki Declaration and its later amendments [13].

Patients with a history of severe renal impairment, liver disease, lung disease, and thyroid disease were excluded. Moreover, patients with any other pathology likely to affect the outcome of study, and patients who received concomitant and contra-indicated medications, as well as patients undergoing any other form of surgery, were excluded.

Propofol was administered at an infusion rate of 3 – 8 mg/kg/h, while sevoflurane was administered at a minimum end-tidal concentration of 0.5 – 2. Fentanyl was administered as pre-anaesthetic medicine in both treatment groups. Other pre-anaesthetic medicines were administered in both groups when required.

Determination of efficacy and safety of treatments

The following efficacy variables were assessed in the two treatment groups: time before onset of anaesthetic effect (measured as time taken to achieve pain-free status after administration of intravenous or inhalational anaesthesia); loss of reflex, and loss of intubation. After surgery, pain was measured using an 11-point NRS scale (0 = no pain, 10 = severe pain). The analgesics received by patients were recorded. Moreover, changes in cognitive score from baseline in both treatment groups were recorded using the SIB scale (0= severe, 100= least affected). Each of the enrolled patients was interviewed to assess their functional status using the CIBIC scale. The CIBIC scale recorded data from the patients and their caregiver on a seven-point scale (low score denoted improvement, while a high score indicated low improvement and worsening of symptoms). In addition, the ADCS-ADL scale was used to evaluate daily living score as an index of treatment outcome/benefit. The cognitive function of each subject was tested using the MMSE scale which ranged from 0 to 54, where 0 indicated severely impaired or severely-affected, while 54 indicated minimally affected/impaired. Safety data were also assessed. Mean arterial blood pressure (mm Hg), heart rate and oxygen saturation (SpO2) were measured during induction, immediately after intubation, and 3 min post-intubation. Moreover, the lengths of time taken to reach pain-free status, loss of reflex (eye), and intubation were measured for both study drugs. Pain was measured using the modified Brief Pain Inventory short form which incorporated Numerical Rating Scale (NRS) pain scores out of 100 for average, worst pain and least pain in the last 24 h. Disability was measured using the World Health Organization Disability Assessment Schedule (WHODAS), while the Kessler K-10 Psychological Distress Scale (K-10) was used to measure mood and psychological well-being.

Statistical analysis

The present investigation was designed as a pilot study. Thus, there was no formal calculation of sample size. Numerical category data showing bell shaped curve were analysed using unpaired

t-test, while numerical category data with non-bell shape characteristics were analysed using Mann Whitney test after normality assessment. Quantitative data are presented as mean ± SD, while categorical data are presented as percentage/proportion of patients, and were analysed using Fisher exact test or chi-square test based on size of data.

RESULTS

Data from a total of 220 patients were analysed. As shown in Table 1, demographic and baseline characteristics were similar in the two groups of patients.

Pain severity score was significantly lower in patients treated with Propofol than in those treated with Sevoflurane. Psychological well-being as measured using K-10 score, was similar in both groups of patients. Similarly, there were no meaningful difference in disability between patients in the two groups, based on measurement with WHODAS (Table 2).

The severity of signs and symptoms of dementia were similar at baseline visit. However, significantly greater relief in signs and symptoms of dementia/cognitive impairment was observed in patients treated with Propofol, relative to those treated with Sevoflurane. There were statistically significant differences in SIB, CIBIC, and MMSE scores between the two treatment groups. In addition, severity of functional status was similar at baseline visit. However, the difference was not statistically significant between the two treatment groups.

Table 1: Demography and baseline characteristics of Chinese elderly patients who underwent cardiac surgery

Outcome variable	Sevoflurane group (n = 110)	Propofol group (n = 110)
Age (mean ± SD)	67.3±4.1	67. 4±2.2
BMI (mean ± SD)	27.2±1.3	26.6±2.1
Gender (M/F; %)	75/25	70/30
Waist (cm, mean ± SD)	111.3±4.1	123.1±5.1
SBP (mean ± SD)	113.43±5.1	119.3±2.1
DBP (mean ± SD)	8.2±3.1	83.1±1.3
Hypertension (% of patients)	53.1	45.7
Baseline computerized total cognitive score (mean ± SD)	83.3±2.3	82.4±2.4
DM (% of patients)	74	77.3
SIB (mean ± SD)	53±1.4	54±1.4
CIBIS+/CIBIC (mean ± SD)	61±3.1	63±2.9
ADCS-ADL (mean ± SD)	66±4.4	64±2.5
MMSE (mean ± SD)	64±3.1	66±4.1
Mental illness status (%) Mild	60	65
Moderate	40	34
Severe	10	11
Living status (%) Living with friend	10	20
Living with caregiver	30	9
Living with relative or friend	70	81

Values are presented as mean ± SD for quantitative variables, whereas categorical variables are presented as proportion/percentage of patients

Table 2: Summary of pain, psychological wellbeing and disability score in Chinese elderly patients who underwent cardiac surgery

Outcome variable	Sevoflurane group (n=110)	Propofol group (n=110)	*P*-value
Cumulative 72 h NRS pain score (mean ± SD)	8.4±1.1	6.1±1.2	<0.05
K-10 (median)	12.4	13.7	>0.05
Change in K-10 (median)	1.2	1.3	>0.05
WHODAS (median)	3.2	3.5	>0.05
Change in WHODAS, median	1.5	1.6	>0.05

P < 0.05 denotes statistically significant difference

In addition, the ADCS-ADL scale which was used to evaluate daily living score, showed a similar trend of results, favoring both study treatments. However, improvement in daily living scores was significantly greater in patients treated with Propofol than in patients treated with Sevoflurane (Figure 1).

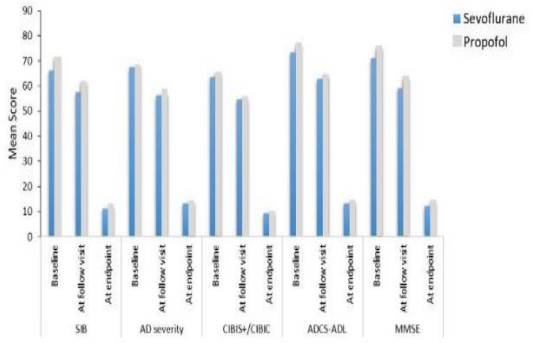

Figure 1: Comparative effectiveness of Propofol and Sevoflurane on cognitive function in Chinese elderly patients who underwent cardiac surgery

The duration of time for attainment of pain-free status was significantly shorter in patients treated with Propofol than in those who received Sevoflurane ($p < 0.05$; Table 3). In addition, the time taken for loss of reflex pertaining to eye and intubation was slightly shorter in patients treated with Propofol than in patients treated with Sevoflurane (Table 3).

In the Sevoflurane group, mean arterial pressure values during induction, intubation (before treatment), immediately after intubation, and 3 min after intubation were slightly lower than the corresponding values for Propofol. Similarly, heart rate values at these time points were slightly lower in patients treated with Sevoflurane than in the Propofol-treated group. However, the differences between both groups were not statistically significant. Furthermore, oxygen saturation (SpO_2) levels during induction, intubation (before treatment), immediately after intubation, and 3 min after intubation were comparable in both treatment groups (Figure 2).

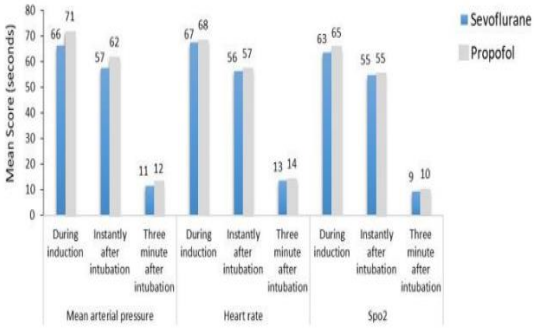

Figure 2: Mean arterial pressure, heart rate and SpO_2 during induction, immediately after intubation, and 3 min after intubation in both groups

The time taken for cardiopulmonary bypass, duration of anaesthesia, and duration of surgical intervention (operating time) were shorter in patients treated with Sevoflurane than in those treated with Propofol (Table 4). The differences in time taken for cardiopulmonary bypass, anaesthesia duration, and duration of surgical intervention (operating time) between both groups were not statistically significant. Urine output was comparable between patients in the two groups. In addition, the duration of hospital stay was shorter in patients treated with Propofol than in those treated with Sevoflurane ($p < 0.05$). The number of patients with return of spontaneous heart rate was significantly higher in the Propofol group than in Sevoflurane group. In addition, there were no significant differences between the two groups with respect to incidence of complications including adverse events.

DISCUSSION

This is the first study designed and carried out to compare the effects of intravenous and inhalational anaesthesia on chronic post-surgical pain and cognitive function after cardiac surgery in Chinese elderly patients.

Table 3: Comparison of durations of time to attain pain-free status, loss of reflex and intubation in Chinese elderly patients who underwent cardiac surgery

Outcome variable	Sevoflurane group (n=110, mean ± SD)	Propofol group (n=110, mean ± SD	*P*-value
Time taken to reach pain-free status (s)	72. 7±3.6	61.4±2.1	<0.05
Loss of reflex: Eye (s)	47.1±3.3	46.2±3.1	>0.05
Intubation (s)	86.1±2.1	85.1±3.5	>0.05

Values are presented as mean ± SD. $P < 0.05$ denotes statistically significant difference

Table 4: Anaesthetic parameters in Chinese elderly patients who underwent cardiac surgery

Outcome variable	Sevoflurane group (n=110)	Propofol group (n=110)	*P-value*
Time taken for cardiopulmonary bypass (min; mean ± SD)	54.3±3.1	74 2±2.6	>0.05
Anaesthesia time (min; mean ± SD	37.4±4.2	55.6±3.5	>0.05
Operating time (min), mean ± SD	113.1±1.5	122.6±3.2	>0.05
Urine output (ml)	823.34±23.21	833.14±20.11	>0.05
Hospital stay interval (days; mean ± SD)	8.2±1.2	9.1±1.1	>0.05
Return of spontaneous heart rate (n)	78%	62%	>0.05
Incidence of complications including adverse events	12%	11.29%	>0.05

Values are expressed as mean ± SD for numerical variable, whereas data for categorical variables are presented as % of patients. P < 0.05 denotes statistically significant difference

Overall, improvements in post-operative pain and cognitive functions were significantly better in patients treated with Propofol than in those treated with sevoflurane. However, the two study drugs were similar with respect to patients' scores for psychological well-being and disability. Moreover, both drugs were similar in clinical outcomes such as operating time, hospital stay, return of spontaneous heart rate, and incidence of complications, including adverse events. However, the duration of time for attaining pain-free status was significantly lower in propofol-treated patients than in sevoflurane-treated patients. In addition, NRS pain severity score was significantly lower in patients treated with Propofol. Psychological well-being, as measured using K-10 score, was similar in both groups of patients. Similarly, there were no significant differences in disability between the two treatment groups. Overall, the two study drugs were comparable with respect to their effects on important anaesthetic parameters.

The propofol-treated patients had numerically greater relief from signs and symptoms of dementia/cognitive impairment than patients treated with Sevoflurane. In addition, propofol produced numerically greater improvement in daily living scores than Sevoflurane. The results on effect of propofol on cognitive score are consistent with other published studies. It is well known that elderly patients who underwent a major surgical intervention such as cardiac surgery under anaesthesia are likely to experience confusion or cognitive impairment within a few days after surgical intervention. The results of the present study are consistent with previous reports [6-12].

Safety outcome parameters such as incidence of complications/adverse events were comparable between the two treatment groups. In both groups, there were changes in vitalssigns. However, there were no observed abnormalities in either group. These findings are consistent with previously published reports.

Propofol produced significantly greater improvement in postsurgical pain and cognitive functions in the elderly Chinese patients who underwent cardiac surgery than sevoflurane. The finding of present study may be of benefit to the scientific community in China, and may be of help in the design of large clinical trials to evaluate the efficacy and safety profiles of propofol in Chinese elderly population after undergoing cardiac surgery.

Limitations of the study

The only limitation of the present preliminary investigation is that the study was conducted at a single centre. Thus, the results cannot be generalized to the entire Chinese population. There is need for further studies on a larger sample size to confirm the finding of present preliminary investigation.

CONCLUSION

Propofol produced significantly greater improvement in postsurgical pain and cognitive functions than sevoflurane after cardiac surgery in Chinese elderly patients.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors included in this manuscript met all 4 criteria for authorship.

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