THE IMPACT OF ANESTHETIC TECHNIQUES ON COGNITIVE FUNCTIONS AFTER UROLOGICAL SURGERY

Mahtab Poor zamany Nejat kermany*, Mohammad Hossein Soltani**, Khazar Ahmadi***, Hoora Motiee***, Shermin Rubenzadeh*** and Vahid Nejati***

Abstract

Background: Postoperative cognitive dysfunction (POCD) is a well-recognized complication of cardiac and noncardiac surgery. However, contradictory results concerning postoperative mental function have been reported. The aim is to determine the effect of anesthetic techniques (general or spinal) on cognitive functions using more sensitive neuropsychological tests in patients undergoing urological surgery.

Material and Methods: A total of thirty patients were enrolled in the study and assigned to receive either general (n=15) or spinal (n=15) anesthesia. A battery of neuropsychological tests including Wisconsin Card Sorting Test, Iowa Gambling Task, Stroop Color-Word Test, N-back Task and Continuous Performance Test was performed preoperatively and three days later.

Results: The two experimental groups were similar at baseline assessment of cognitive function. Although there were no statistically significant differences between general and spinal anesthetic groups with respect to Wisconsin Card Sorting Test and Iowa Gambling Task, a significant intergroup difference between pre-and postoperative N-back scores was detected in the general anesthesia group (p=0.001&p=0.004). In addition, patients within this group had significantly higher error rates on the Stroop Color-Word (p=0.019) and Continuous Performance Tests (p=0.045). In contrast, patients receiving spinal anesthesia exhibited little change or marginal improvement on all subscales of the battery.

Conclusions: Our findings indicate significant decline in specific aspects of mental function among patients who were administered general anesthesia compared with the other technique. It seems that spinal anesthesia contributes to lower disturbance after surgery.

Key word: Anesthesia - Cognitive function - Urology.

* Anesthesiology Department of Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences (SBMU), Tehran, I.R. Iran.
** Urology Department of Shahid Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences (SBMU), Tehran, I.R. Iran.
*** Neuroscience department of Shahid Beheshti University of Medical Sciences (SBMU), Tehran, I.R. Iran. Address: No#99, 9th Boston St., Pasdaran Ave, Tehran, Iran.Tel & Fax: 0098-21-22588016 . Corresponding author: Vahid Nejati , Urology Department of Shahid Labbafinejad Medical Center, Email : v_nejati@sbu.ac.ir
Introduction

Postoperative cognitive dysfunction (POCD) is a common complication in adult patients undergoing surgical procedures which refers to decline in variety of neuropsychological domains such as verbal or visual memory, executive functioning, language comprehension, attention and concentration. Although primarily observed after cardiac surgery, it has also been detected following major noncardiac surgeries. While POCD is presumed to be transient and the long-term effects are considered uncertain, recent studies suggest that the symptoms of neurocognitive change may persist long after the operation and diminish quality of life. Patients with POCD are more likely to withdraw from employment and social activities that will lead to premature dependency. The ISPOCD 1 study (International Study of Post-Operative Cognitive Dysfunction) of 1,218 elderly patients (60 yr or older) scheduled for major noncardiac surgery showed that cognitive impairment was present in 25.8% patients one week after the operation and in 9.9% of them after 3 months. Furthermore, postoperative cognitive decline has been associated with significantly higher risks of postoperative morbidity and mortality, particularly in elderly. A similar study revealed that patients with POCD at hospital discharge were more likely to die within 3 months of the discharge. In general, the rate of cognitive dysfunction has been positively correlated with mortality risk. Several studies show an increased risk of early mortality in elderly individuals with cognitive deterioration.

The etiology of POCD is likely multifactorial with type of surgical procedure (due to differences in duration) metabolic/endocrine stress response, imbalance of neurotransmitter system (particularly acetylcholine and serotonin), hypoxia and hospitalization, all potentially playing a role. Advanced age, history of cerebral vascular accident with no residual impairment, lower educational level, evidence of cognitive dysfunction at hospital discharge and alcohol abuse also contribute to the pathogenesis of POCD. With further identification of preoperative risk factors for POCD, patients and healthcare providers can be better informed before making a decision to proceed with major surgery.

It has been speculated that POCD risk could be reduced by performing certain surgical procedures under regional anesthesia. Results of a study indicated that the maintenance of mental function in an elderly population was better following spinal anesthesia when compared with general anesthetic technique. Similarly, another report showed that the incidence of cognitive deterioration was lower after epidural anesthesia. A recent study found that general anesthesia posed a significant risk for the occurrence of early POCD in elderly patients that could persist for 3 days after surgery. However, review of the existing literature has not revealed a significant difference between the two intraoperative anesthetic techniques. The heterogeneity of procedures used to measure cognitive deficits and methodological inconsistencies make the limited literature on POCD difficult to interpret.

Most of these tests are subsets of test banks used to assess the memory and intelligence of adults. The use of more sensitive neuropsychological tests may elucidate more prolonged damage to cognitive performance. In addition, the majority of previous investigations have primarily focused on elderly patients, a population with an increased vulnerability to neurological deterioration after exposure to anesthesia. As a result, the cognitive effects of anesthesia and surgery in young and middle-aged adults are poorly understood. The objective of this study was to evaluate post-operative mental function of patients who had undergone general or spinal anesthesia for a urologic surgery, and to compare the effect of these two anesthetic techniques on mental function.

Material and Methods

From July to September 2011, 30 patients undergoing urological surgery following either general or spinal anesthesia were participated in the study at Shahid Labbafinezhad Hospital. Written informed consent was taken from all patients and university ethics committee approved the study structure. Entry criteria included age (24+ yr), normal mental status, speaking and reading fluency in the Persian language and the absence of any serious vision or hearing impairment that would preclude neuropsychological testing. Participants were excluded if they had any...
prior history of dementia, central nervous system disease, psychiatric disorders, alcoholism and drug abuse. In addition, any patients with history of allergy to anesthetic drugs were also excluded. Information about the demographic status, medical history, education and occupational history of the subjects were documented.

**Anesthetic techniques and agents**

All patients received 5cc/kg normal saline serum before anesthesia. In the group of patients who underwent general anesthesia, the following agents were used for the induction of anesthesia: Fentanyl (2µ/kg), Midazolam (1mg), Lidocain (1.5mg/kg), Propofol (2mg/kg) and Atracurium (0.5mg/kg). For maintenance phase of general anesthesia, Propofol (100-200µ/kg) and Remifentanil (0.1 µ/kg/min) were used. Spinal Anesthesia was done by injection of 2.5 to 3 cc bupivacaine 0.5% (Marcaine®) in the subarachnoid space. For post-operative pain control, intravenous pethidine (25-50 mg) was administrated in the recovery room and Diclofenac 100mg suppository was given in the ward as needed.

**Neuropsychological Assessment**

The cognitive function evaluation was performed in an undisturbed room with only the patient and the psychometrician present. Patients completed the tests one day prior to surgery and at hospital discharge (three days after the operation). The psychological measures included Wisconsin Card Sorting Test, Stroop Color-Word Task, Continuous Performance Test, N-Back Task and Iowa Gambling Test that were administered in about 30 minutes. These measures primarily focus on executive functions and memory, elaborated as follows:

Wisconsin Card Sorting Test is commonly regarded as “the gold standard executive function task”\(^\text{26,27}\). Patients were asked to match response cards to reference cards according to three dimensions of sorting principle (color, form and number)\(^\text{28}\). Stroop Color-Word Test estimates the patient’s ability to concentrate and ignore distracting stimuli\(^\text{29}\). Continuous Performance Test (CPT) requires subjects to maintain vigilance and react to the presence or absence of specific stimuli within a continuously presented set of distracters\(^\text{30,31}\). N-Back Task is one of the most popular experimental paradigms for studies of working memory, in which subjects are asked to monitor the identity or location of a set of verbal or nonverbal stimuli and to indicate when the currently presented stimulus is the same as the one presented in trials previously\(^\text{32,33}\). Iowa Gambling Task evaluates decision-making under initially ambiguous conditions. It simulates real-life decision making by testing the ability of subjects to learn to sacrifice immediate rewards in favor of long-term gains\(^\text{34,35}\).

**Statistical Analysis**

Given the large number of dependant variables, comparison of the cognitive function between the two anesthesia groups was performed with multivariate analysis of covariance (MANCOVA) using SPSS (version 18). Follow-up tests were conducted when warranted by multivariate results with ANOVA and paired t-tests. Pre-test scores were considered to be covariate variables in order to control for the practice effect. The customary two-tailed α level of significance was set at 0.05.

**Results**

Thirty patients (13 women and 17 men) were recruited. The subjects had a mean age of 44.6 (±12.66). 36.6% subjects were classified as young (24-39yr), 53.33% were middle-aged (40-59) and 10% were elderly (60-65). General anesthesia was used in 15 patients (50%), and the remaining subjects received spinal anesthesia.

The baseline characteristics of the patients included in the study are listed in table 1. Data analysis revealed that the two groups did not differ in preoperative scores. However, statistically significant differences were observed when postoperative scores were compared with the baseline levels. Results indicated significant association between general anesthetic technique and damage to particular domains of cognitive functions. Although subtests of the Wisconsin Card Sorting Test and Iowa Gambling Task did not change significantly...
between the two groups, separate univariate analysis and paired t-test showed that patients were more likely to have worse 1-and 2-back test performance after general anesthesia ($p=0.001$ & $p=0.004$). These patients also had significantly higher omission error score on the Continuous Performance Task ($p=0.045$) and considerable error rates on the $3^{rd}$ part of the Stroop Color-Word Test ($p=0.019$). It is worth noting that patients receiving spinal anesthesia showed little change or slight improvement on all subscales of the battery. The mean pre-and postoperative neuropsychological test scores are exhibited in Table 2.

**Discussion**

This study is one of the few investigations of postoperative cognitive function that includes younger population. In the current study, we used some of the most popular neuropsychological tasks to assess executive functions. Comparison of the two arms of the study was based on MANCOVA which provided more statistical power. Our data revealed that general anesthesia was associated with weaker performance in the memory and concentration domains. These results are in accordance with the findings of Chung et al, who found that patients receiving general anesthesia performed worse on digit-symbol substitution for 2-3 days after surgery. Herbert and colleagues also noted that choice reaction time was impaired for 36 hours after administration of general anesthesia. Findings of another study indicated that general anesthesia patients perceived residual impairment of their cognitive faculties after 3 days.

Previous research addressing the role of anesthesia on cognitive deterioration has yielded conflicting results. The absence of a consistency regarding the operational definition of POCD may contribute to this issue. Our findings are inconsistent with the vast majority of existing evidence demonstrating no significant difference between intraoperative regional and general anesthesia in preserving postoperative

<table>
<thead>
<tr>
<th>Table 1</th>
<th>General characteristics of the patients, compared in two groups (general vs. spinal anesthesia.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General Anesthesia</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>46.9</td>
</tr>
<tr>
<td><strong>Age Groups</strong></td>
<td></td>
</tr>
<tr>
<td>24-39 (Young)</td>
<td>6</td>
</tr>
<tr>
<td>40-59 (Middle-aged)</td>
<td>8</td>
</tr>
<tr>
<td>60 and above (Elderly)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>Less than High school</td>
<td>4</td>
</tr>
<tr>
<td>High School</td>
<td>6</td>
</tr>
<tr>
<td>More than High school</td>
<td>5</td>
</tr>
<tr>
<td><strong>Type of surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Lithotripsy</td>
<td>4</td>
</tr>
<tr>
<td>Intravesical injection</td>
<td>1</td>
</tr>
<tr>
<td>Radical Nephrectomy</td>
<td>2</td>
</tr>
<tr>
<td>Varicocelectomy</td>
<td>2</td>
</tr>
<tr>
<td>Bladder Stone Removal</td>
<td>2</td>
</tr>
<tr>
<td>TUL</td>
<td>1</td>
</tr>
<tr>
<td>TURT</td>
<td>1</td>
</tr>
</tbody>
</table>
cognitive function. For instance, in a prospective, randomized study, Williams-Russo et al, compared the effect of epidural versus general anesthesia on the incidence of POCD in patients undergoing elective unilateral total knee replacement and found no significant difference postoperatively\textsuperscript{20}. In another randomized trial, no significant differences were found in the postoperative mental abilities between patients who received general, regional or combined anesthetic techniques\textsuperscript{39}. O’Hara et al, observed no clinically important impacts on major outcomes in patients who were administered general or spinal anesthetic techniques after the hip surgery\textsuperscript{40}. In a systematic review, Wu et al, found that intraoperative neuraxial anesthesia does not decrease the incidence of POCD when compared with general anesthesia\textsuperscript{41}.

Detection of POCD requires two crucial elements: a sensitive battery of tests and controlling for the practice effect. We used some of the well-known psychological measurements to determine more subtle defects. The enhancement observed in this trial cannot be attributed to practice effect. In as much as, pretest scores were considered as covariate variables.

There may be several factors that might have a negative impact on cognitive function after general anesthesia. Some agents that are used to induce and maintain anesthesia may deteriorate cognition and memory\textsuperscript{10}. In addition, there may be a possibility of hemodynamic instability, hypoxia and stress induced response due to prolonged intubation; the factors that are not commonly related to regional anesthesia\textsuperscript{15}.

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General</td>
<td>Spinal</td>
</tr>
<tr>
<td></td>
<td>(n-15)</td>
<td>(n-15)</td>
</tr>
<tr>
<td>Achieved Clusters</td>
<td>1.66±0.61</td>
<td>1.60±0.63</td>
</tr>
<tr>
<td>Number of Total Errors</td>
<td>37.93±6.39</td>
<td>38.2±5.79</td>
</tr>
<tr>
<td>Perseverative Errors</td>
<td>15.46±3.62</td>
<td>14.86±2.13</td>
</tr>
<tr>
<td>Iowa Gambling Task</td>
<td>25.20±2.48</td>
<td>23.53±3.29</td>
</tr>
</tbody>
</table>

N-Back Task

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General</td>
<td>Spinal</td>
</tr>
<tr>
<td></td>
<td>(n-15)</td>
<td>(n-15)</td>
</tr>
<tr>
<td>1-back</td>
<td>19.93±6.71</td>
<td>16.26±6.30</td>
</tr>
<tr>
<td>2-back</td>
<td>8.13±3.29</td>
<td>8.73±3.97</td>
</tr>
</tbody>
</table>

Continuous Performance Test

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General</td>
<td>Spinal</td>
</tr>
<tr>
<td></td>
<td>(n-15)</td>
<td>(n-15)</td>
</tr>
<tr>
<td>Omission Error</td>
<td>16.06±8.67</td>
<td>16.33±8.10</td>
</tr>
<tr>
<td>Commission Error</td>
<td>1.06±0.51</td>
<td>1.157±0.94</td>
</tr>
<tr>
<td>Hit Reaction Time</td>
<td>0.548±0.06</td>
<td>0.562±0.04</td>
</tr>
</tbody>
</table>

Stroop Color-Word Task

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General</td>
<td>Spinal</td>
</tr>
<tr>
<td></td>
<td>(n-15)</td>
<td>(n-15)</td>
</tr>
<tr>
<td>Error Rates 1</td>
<td>1.33±0.97</td>
<td>1.40±0.82</td>
</tr>
<tr>
<td>Reaction Time 1</td>
<td>0.46±0.45</td>
<td>0.33±0.37</td>
</tr>
<tr>
<td>Error Rates 2</td>
<td>0.53±0.74</td>
<td>0.53±0.63</td>
</tr>
<tr>
<td>Reaction Time 2</td>
<td>0.34±0.55</td>
<td>0.27±0.34</td>
</tr>
<tr>
<td>Error Rates 3</td>
<td>17.40±7.91</td>
<td>19.33±7.006</td>
</tr>
<tr>
<td>Reaction Time 3</td>
<td>1.85±0.93</td>
<td>1.34±0.55</td>
</tr>
</tbody>
</table>

Values are given as mean±SE. “*” mark indicates significant difference in the assigned group before and after the operation.
This study was limited by two major factors. Firstly, patients were not allocated randomly to the general or spinal anesthesia groups. Secondly, we were unable to include a control group of healthy volunteers matched with the experimental groups in the present study. Hospitalized patients not undergoing surgery or any other intervention were also considered as a better control group, but a sufficient sample size for comparison could not be attained due to lack of participation. Our findings should therefore be interpreted with caution. A more extensive study with follow-up testing is required to determine the precise profile of the postoperative cognitive impairment.

In conclusion, our results suggest a linkage between general anesthesia and weaker postoperative mental function. Local anesthesia might have an advantage over general anesthesia in terms of neuropsychological functioning.

Acknowledgments

The authors thank the hospital staff and patients for taking part in this study. Their assistance was essential for data collection and the coordination of the research protocol.

Conflict of interest:

The authors have no conflict of interest.
References


35. Linnet J, Möller A, Peterson E, Giede D, Doudet D: Dopamin release in ventral striatum during Iowa Gambling Task performance is associated with increased expression levels in pathological conditions.


The key to

Lock-up

Postoperative Pain

**STEP I**
Initial bolus
Inject 1 ampoule Tramal® 100 mg
i.v. or i.m. slowly over 2-3 minutes

**STEP II**
Ways of administration after initial bolus

- **Infusion**
  - Inject 2 ampoules Tramal®, each 100 mg, in 500 mL of infusion solution.
  - Infusion rate 12-24 mg Tramal®/h (10-20 mL/h or 30-60 mL/h).
  - If needed further doses of Tramal® 50 mg up to a total of 200 mg (including the initial bolus) within the first 60 min.

- **PCA**
  - Subsequent increments of 50 mg with a lock-out time of 5 minutes.
  - Uptitration dose is 50 mg or 100 mg 4-6 hourly up to a total daily dose of 400 mg except in special clinical situations which might necessitate daily doses up to 600 mg.

- **Injection**
  - If needed further doses of Tramal® 50 mg up to a total of 200 mg (including the initial bolus) within the first 60 min.

**STEP III**
Follow-up
- 50 mg
  - 1-2 capsules every 4-6 hours
  - 20-40 drops every 4-6 hours
  - 1 suppository every 4-6 hours

- 100 mg
  - Slow release 100 mg, 150 mg, 200 mg
  - 1 tablet every 12 hours

---

**Intra-Operative**

- **Loading Dose**
  - 2.5 - 3 mg/kg
  - at wound closure

**Post-Anaesthesia Care Unit**

- If intra-operative dose not given then:
  - BOLUS I.V.
  - 100 mg over 2-3 mins

An intra-operative loading dose of Tramal® will reduce PONV rates

---

For patients with localized
BURNING
SHOOTING
STABBING
Neuropathic pain

WORKS WHERE IT HURTS
BRIDION—for optimal neuromuscular blockade management and improved recovery

Predictable and complete reversal

- 98% of BRIDION patients recovered to a TOF* ratio of 0.9 from reappearance of T\textsubscript{2} \textsuperscript{+} within 5 minutes\textsuperscript{2}
- 97% of BRIDION patients recovered to a TOF* ratio of 0.9 from 1 to 2 PTCs \textsuperscript{1} within 5 minutes\textsuperscript{3}

Rapid reversal

- BRIDION rapidly reversed patients from reappearance of T\textsubscript{2} \textsuperscript{+} in 1.4 minutes\textsuperscript{2}
- BRIDION rapidly reversed patients from 1 to 2 PTCs \textsuperscript{1} in 2.7 minutes\textsuperscript{3}

BRIDION is indicated for the reversal of neuromuscular blockade induced by rocuronium or vecuronium. In children and adolescents (aged 2-17 years), BRIDION is only recommended for routine reversal of moderate rocuronium-induced neuromuscular blockade.\textsuperscript{1}

Important safety information

BRIDION is not recommended in patients with severe renal impairment. Studies in patients with hepatic impairment have been conducted and, therefore, patients with severe hepatic impairment should be treated with great caution. Caution should be exercised when administering BRIDION to pregnant women as no clinical data on exposed pregnancies are available.

BRIDION has not been investigated in patients receiving rocuronium or vecuronium in the Intensive Care Unit (ICU) setting.

If neuromuscular blockade is required within 24 hours of BRIDION administration, a nonreversal neuromuscular blocking agent should be used instead of rocuronium or vecuronium. The most commonly reported adverse reactions were dysgeusia (metal or bitter taste) and anesthetic complications (movement, coughing, grimacing, or suctioning on the endotracheal tube). In patients treated with BRIDION, a few cases of awareness were reported. The relation to BRIDION was uncertain. In a few individuals, allergic-like reactions (i.e., flushing, erythematous rash) following BRIDION were reported. Clinicians should be prepared for the possibility of allergic reactions and take the necessary precautions. In a trial of patients with a history of pulmonary complications, bronchospasm was reported in 2 patients and a causal relationship could not be fully excluded.

Volunteer studies have demonstrated a slight (17%-22%) transient (<30 minutes) prolongation of the prothrombin time/activated partial thromboplastin time (PT/aPTT) with BRIDION; however, clinical studies have demonstrated no clinically relevant effect on peri- or postoperative bleeding complications with BRIDION alone or in combination with anticoagulants. As BRIDION has demonstrated an in vitro pharmacodynamic interaction with anticoagulants, caution should be exercised in patients on antiocoagulation for a pre-existing or comorbid condition. This pharmacodynamic interaction is not clinically relevant for patients receiving routine postoperative prophylactic anticoagulation. Although formal interaction studies have not been conducted, no drug interactions were observed in clinical trials. Preclinical data suggest that clinically significant drug interactions are unlikely with the possible exceptions of toremifene, fusidic acid, and hormonal contraceptives.


Please see summary of product characteristics for full prescribing information.
TAP Block And InfiltraLong
For Effective Treatment Of Long And Deep Incisions

Sono Cannulas
For Single Shot UltraSound Guided Nerve Blocks

SonoSystem And SonoLong Curl
For UltraSound Guided Nerve Blocks

Sprotte® 2.G
The New Generation Dura Puncture In Minimum Time

SonoEye Ophtalmic Block
For Peribulbar And Retrobulbar Blocks Under Ultrasonic Monitoring

www.mediline-lb.com Tel:+961 1 697500