CHAPTER III

RESEARCH METHODOLOGY

Target Population

The target population of this study are any patients undergoing elective gynecologic diagnostic laparoscopy.

Population Sampled

The study enrolls the patients undergoing elective gynecologic diagnostic laparoscopy at Siriraj Hospital during the study period.

Inclusion criteria:

1. Patients undergoing elective gynecologic diagnostic laparoscopy
2. ASA class I, II (see appendix I)
3. No premedication
4. Aged 16-60 years

Exclusion criteria:

1. Patients having neurological or psychiatric problems
2. Illiterate patients
3. Patients having history of allergic reactions to any of the study drugs
4. BMI $\geq$ 30 kg/m^2 because halothane highly deposits in fat tissues and leads to delay in recovery.

Sampling Technique

Simple randomization

Sample Size Calculation

Sample size is calculated by this formula

$$n/group = \frac{2\,(Z\alpha + Z\beta)^2 \sigma^2}{\Delta^2}$$

$Z\alpha$ = Type I error 5% (two tail) = 1.96

$Z\beta$ = Type II error 10% = 1.28

σ^2 = Pooled variance

Δ = Difference of recovery time

We considered half an hour to be the minimum significant difference that resulted in more rapid turnover rate of bed.

This study needed a pilot study to estimate sample size, and test the overall feasibility and logistics of the study.

From pilot study :

$\sigma^2 = 0.32$

$$n/gr = \frac{2\,(1.96 + 1.28)^2\ 0.32}{(0.5)^2} = 26.87$$

This study needed at least 27 patients/group.

Experimental Maneuver

The patients who met the eligible criteria were randomly assigned to either the halothane or isoflurane group by random number table.

Before induction of anesthesia, patients were moved to a screened area of the recovery room. Here the psychomotor and cognitive tests were explained to the patients (Ball Bearing Test and Digit Symbol Substitution Test), and ten minutes were allowed so the patients could practise and demonstrate to an observer that they understood their task. To obtain baseline data, the patients were asked to perform each test 3 times and the best score was selected to be the control value. The same recovery area were used for subsequent postoperative testing.

In the Ball Bearing Test[14], the patient was asked to transfer ball bearing from the glass dish to the vertical tube as quickly as possible using a pair of forceps. The score was the number of ball bearings inserted in 40 seconds. In the Digit Symbol Substitution Test (DSST)[15,16,17] the patient was asked to substitute single digits, 1-9, each with its specific symbol. The correct matching of the symbols with the corresponding digits completed in a 90-sec.period of time were counted. All aspects of recovery room assessment were conducted by an observer unaware of the anesthetic technique used.

After baseline testing, a fast running IV. infusion of crystalloid solution was commenced (at non-dominant hand) , and patients were transferred to the operating room. Intraoperative monitoring consisted of heart rate, blood pressure, oxygen saturation, EKG., the end-tidal concentrations of halothane, isoflurane and carbon dioxide.

The general anesthetic technique consisted of propofol 2 mg./kg. iv. for induction and succinyl choline 1.5 mg./kg.iv. was administered to facilitate tracheal intubation. Vecuronium 0.08 mg./kg. iv. was administered initially and then intermittently 1 mg. every 20-30 min. to maintain adequate muscle relaxation. In the control group, anesthesia were maintained with halothane 0.5-0.75 % end tidal and N_2O 67 % in O_2 (2L/min : 1L/min), and the treatment group received isoflurane 0.75-1.2 % end tidal and N_2O 67 % in O_2. Ventilation was controlled and end tidal CO_2 tension was maintained in the range of 30-40 mm. Hg.

At the end of operation, residual neuromuscular blockade was reversed with a combination of neostigmine 2.5 mg. and atropine 1.2 mg. iv. Halothane,isoflurane and N_2O were discontinued immediately after skin closure. Patients'lungs then were ventilated with 100 % O_2 at a total gas flow rate of 4 L/min, and end tidal CO_2 is maintained at 30 -40 mm. Hg.

The time of discontinuation of anesthetic agents was noted as time zero (end of anesthesia) for all subsequent measurements. The times to the first response to verbal command to open eyes and orientation to age, name and body parts (left VS right) were assessed in a uniform method at 1- min. interval and recorded. The time of extubation was also recorded.

After this initial wake-up assessment, patients were returned to the recovery area. The Ball Bearing Test and the Digit Symbol Substitution Test were performed every 30 minutes after the end of anesthesia until the patients could perform both tests at control level $\pm$ 10 % and all tests were performed with the patients in the sitting position, wearing spectacles when appropriate. At these times , the observer also asked the patients to sit up, stand up and walk and the times the patient could perform these were recorded. In addition, the

observer obtained a visual analogue pain score from the patient and asked the patient about postoperative complications such as nausea, vomiting,dizziness and so on. Severe postoperative pain was managed by the use of diclofenac 75 mg.intramuscularly. Droperidol would be given 0.5 mg.iv.to patients with severe vomiting. This dose does not prolong the recovery time.[18] Before being discharged, the patient was asked to answer the questionnaire concerning the recovery.

Table 3.1 Steps and drugs used in halothane and isoflurane anesthesia

Phase of Anesthesia	Halothane	Isoflurane
Induction	Propofol 2 mg./ kg. I.V.	same
Intubation	S. choline 1.5 mg./ kg. I.V.	same
Muscle Relaxation	Vecuronium 0.08 mg./ kg. I.V. initially, then 1 mg. every 20 -30 min.	same
Maintenance	N_2O : O_2 = 2 : 1 L./ min. Halothane 0.5 - 0.75 % (end tidal)	same Isoflurane 0.75 - 1.2 % (end tidal)
Local infiltration	0.5 % Bupivacaine with Adrenaline 10 cc.	same
Reverse	Atropine 1.2 mg. and Prostigmine 2.5 mg.I.V.	same

Measurements

1. Demographic data : age, physical status, body weight,height, body mass index (BMI), and diagnosis.

2. Total dose of intravenous drug used

3. Duration of anesthesia : The time between intravenous propofol administration and the time the anesthetic agents discontinued.

4. Intraoperative complications:-

- Arrhythmia
- Hypotension
- Hypertension
- Awareness

5. Recovery times: Time from discontinuation of anesthetic agent to (Clinical assessment):-

- Response to verbal command to open eyes
- Extubation : criteria for extubation :-
  a. return of protective airway reflex
  b. normal respiration
- Orientation to : age
  name
  body parts (left vs right)
- Sit up,stand up and walk unaided

6. Ball Bearing Test: before anesthesia to get baseline performance (control) then every 30 min. after the end of anesthesia until patients can perform both BBT. and DSST. at the control level $\pm$ 10 %

7. Digit Symbol Substitution Test: (The same as BBT)

8. Postoperative complications:-

- Nausea
- Vomiting
- Headache
- Dizziness
- Sore throat
- Shivering
- Muscle pain
- Pain at injection site

9. Postoperative pain score (V.A.S.) and postoperative analgesic requirement.

10. Patients' acceptance and satisfaction

11. Number of the patients who can not perform the tests and their reasons such as nausea,vomiting and dizziness.

Measurement Review

The time course of recovery includes 3 distinct stages of recovery from anesthesia :-

1. Early recovery : the recovery of vital reflexes

2. Intermediate recovery : sufficient recovery of mental and physical health to return home (Home readiness)

3. Late recovery : the complete psychomotor recovery (to drive or to operate other complex procedures safely)

The tests used in this study are as follows

1. Clinical tests

- Response to verbal command to open eyes
- Extubation
- Orientation to age,name and body parts

- Sit up, stand up and walk unaided

2. Psychomotor and cognitive tests

- Ball Bearing Test
- Digit Symbol Substitution Test

All tests were chosen because they could be performed in daily clinical practice and did not need long training period before anesthesia. Moreover, they have been used successfully in many previous studies concerning the recovery from anesthesia.

They were proven to be valid and reliable in many studies :-

-H.Steinberg (1954)[14]

-F.Chung et al.(1990)[15]

-T.F.Boerner et al.(1990)[19]

-Ahmed F.Ghouri et al.(1991)[18]

-S.K.Tsai et al.(1992)[20]

etc.

Limitations

1. Maneuver Bias

Because of the different odour of these two anesthetic agents, it was possible to detect which agent had been used. Therefore, the bias might occur because the personnel who gave anesthesia might modify the anesthetic technique so that their preference would get satisfactory outcomes. To minimize this bias,the anesthetic techniques were standardized and the protocol was as rigid as possible.

2. Measuring Bias

Inter-observer variation

To reduce inter-observer variation, we used only one observer who was blinded to anesthetic agents which each patient received and he had trained in assessment and understood the protocol well. The way in which instructions about the tests given to patient was important and had to be as constant as possible.

Environmental distractions

The number of distractions such as noise, undue heat or cold to patients had to be minimized for optimal test performance. In this study we used the same recovery room for similar environmental factors and both preoperative tests (baseline tests) and postoperative tests were performed in similar conditions. In the Digit Symbol Substitution Test, to minimize training effect we used slightly different but equivalent sheets when the test was repeated.