CHAPTER 3
RESEARCH METHODOLOGY

POPULATION AND SAMPLE

Target population

Patients with abnormal uterine bleeding scheduled for fractional curettage.

Study population

The patients with abnormal uterine bleeding who attended the Obstetrics and Gynecology Outpatient Department, Faculty of Medicine Siriraj Hospital, and met all the eligibility criteria.

Eligibility criteria

Inclusion criteria

- Abnormal uterine bleeding
- Age > 18 y/o
- ASA physical status 1-2 (see APPENDIX III)
- Agree to participate in the study and sign consent form

Exclusion criteria

- Virgin
- Acute cervicitis
- Profuse uterine bleeding
- History of lidocaine hypersensitivity
- History of impaired liver function that may delay the metabolization of lidocaine
- Pregnancy
- Unable to understand how to score the visual analogue scale

Sample size

Sample size was calculated from the formula for comparing means of 2 independent populations as the following:

$$\text{n/group} = \frac{2[(z_\alpha + z_\beta)\sigma]^2}{\delta^2}$$

where

α = Probability of type I error = 0.05 (two-sided) $Z_{\alpha/2} = 1.96$

β = Probability of type II error = 0.2 $Z_\beta = 0.84$

δ = Meaningful difference in maximum pain score assessed by 10-cm VAS between control and treatment groups
= 2 cm[33]

σ = SD of 10-cm VAS pain score in Thai patients undergoing F/C under PCB
= 2.4 cm[18] (with the assumption of equal variance)

Therefore, n / group was 24, and to compensate for expected dropout of 10%, the n / group became 27.

INTERVENTION

Allocation of treatments

Patients were allocated to either treatment or control group by simple randomization. A computer-generating list of random numbers was chosen for this purpose. The third digit of each number was used to generate treatment code; even number was designated as treatment (PCB plus IUA) whereas odd number was control (PCB alone). Each code number was contained in a sealed opaque envelope, which was sequentially numbered. When a new patient was enrolled, an independent nurse

would open the next in a series of envelopes, and prepares the trial medications accordingly.

Trial medications

The trial medications, either placebo or treatment, were identical in physical appearance, i.e. clear colorless solution. They were contained in identical 10 ml disposable syringes, prepared by an independent nurse. Therefore the gynecologist who performs F/C and the patient were blinded from the treatment. The medications provided to each patient were as the following:

Control group

- PCB: 1% Lidocaine HCl with adrenaline (1:100,000) 10 ml
- IUA: 0.9% saline 5 ml (placebo)

Treatment group

- PCB: 1% Lidocaine HCl with adrenaline (1:100,000) 10 ml
- IUA: 2% Lidocaine HCl 5 ml (treatment)

SAFETY MEASURES

- The procedure was terminated immediately when serious adverse event occurs, or upon patient's request.
- The patient was observed in a recovery room for 60 minutes post operation.
- Postoperative pain relief medication was mefenamic acid 500 mg orally, provided by nurse upon patient's request. If the patient still had severe pain at 15 minute after mefenamic acid, fentanyl 0.05 mg is provided.
- Cardiopulmonary resuscitation instruments and medications were available.

EXPERIMENTAL PROCEDURE

Preoperative period

All F/C were performed on an outpatient basis. Before F/C was performed, each patient was informed about study procedure. The patient was

instructed to score the VAS, and then tested for her understanding by scoring on a test sheet containing 10-cm VAS with a question "How much pain you expect to have during curettage?" After checking for eligibility criteria, a signed consent was obtained. The patient was then interviewed for relevant demographic data, which was recorded in a case record form (CRF form A, see APPENDIX).

Intraoperative and immediate postoperative periods

The patient was placed in a modified lithotomy position at the end of operating table. Monitors including blood pressure and pulse oximeter were installed. Heparin lock using 20 g venous catheter was inserted into superficial vein at patient's wrist or hand of non-dominant side for drawing blood and for safety purpose. In order to reduce risk of PCB and to minimize variation from operators, all steps of the procedure were operated by the same gynecologist (investigator). The F/C was performed through the following steps:

1. Bimanual pelvic examination was performed. The external genitalia was painted with antiseptic solution (1:100 Chlorhexidine Gluconate solution) before draped with sterile clothes. Sterile Sims vaginal retractors or Graves vaginal speculum were introduced into the vagina for visualization of cervix. The cervix and upper vagina was painted with antiseptic solution.
2. PCB was performed.
3. IUA was performed.
4. F/C was performed.

When the F/C was completed, the tenaculum was removed. The cervix was cleaned with antiseptic solution. The vaginal retractors were removed. The patient was placed on supine position and was observed in a recovery room for 60 minutes before discharge. Patient's global satisfaction for the treatment was assessed before

discharge. Information during that period was recorded and CRF form B was completed by nurse.

DATA COLLECTION

Pain score

The primary outcome variable is pain score assessed by 10-cm VAS. Patients are instructed to indicate the intensity of their pain experience by marking an "___" in a 10-cm line anchored with terms describing the extremes of pain intensity. In this study, there are 2 descriptors, i.e. "no pain" at the lower end, and "intolerable pain" at the upper end (see CRF form C). The intensity of pain is assessed by measuring the line from the lower end to the marker "___", and reported in cm.

In this study, the pain score was measured immediately after insertion of retractor, after F/C, and at 15, 30 and 60 minutes after the procedure. In case that the patient had intolerable pain, the procedure was terminated immediately, and the pain score was recorded. If the endometrial tissue was not obtained at that step, the patient was then scheduled for further F/C under general anesthesia.

Immediate postoperative analgesic requirement

Immediately after operation, all patients were informed that they could request oral analgesic medication at any time during postoperative observation. Mefenamic acid 500 mg would be provided and the information was recorded in the CRF.

Patients' global satisfaction to the treatment

At the end of postoperative observation period, the patient was asked to rate her global satisfaction to the treatment which was a 4-categorical scale, i.e, very unsatisfied, unsatisfied, satisfied, very satisfied.

Safety monitoring

The patient was asked to report to the physician or nurse regarding any symptoms occurring during or after the operation.

Blood pressure, pulse, and oxygen saturation were continuously monitored, and recorded as following: (i) before the operation, after the patient was placed in a modified lithotomy position, (ii) after local anesthesia administration, (iii) after uterine curettage, and (iv) at 15, 30, and 60 minutes after operation.

Side effects of anesthesia (see CRF form B) were monitored by verbal communication with the patient during and after injection of the trial medication.

MEASUREMENT

All of the measured variables including administrative variables, baseline variables and covariates, efficacy variables, and safety variables are tabulated in table 3.1.

Table 3.1 Summary of measured variables

Variables	Scale	Descriptive Statistics
Administrative variables		
▪ Name		
▪ Identification no.		
▪ Address and telephone no.		
Baseline variables / Covariates		
▪ Age (yr)	Continuous numerical	Mean ± SD
▪ Education level	Ordinal categorical	N (%)
▪ Economic status	Ordinal categorical	N (%)
▪ Prior vaginal delivery	Dichotomous categorical	N (%)
▪ Prior curettage	Dichotomous categorical	N (%)
▪ Menopausal status	Dichotomous categorical	N (%)
▪ Body mass index (Kg/m^2)	Continuous numerical	Mean ± SD
▪ Dilatation of cervix	Dichotomous categorical	N (%)
▪ Uterine sound length (cm)	Continuous numerical	Mean ± SD
▪ Duration of operation > 10 min	Dichotomous categorical	N (%)
Efficacy variables		
▪ Maximum VAS pain score (cm)	Continuous numerical	Median (95%CV)
▪ Requirement of immediate PO analgesic medication	Dichotomous categorical	N (%)
▪ Patient's global satisfaction	Ordinal categorical	N (%)
▪ Success rate of F/C	Dichotomous categorical	N (%)
Safety variables		
▪ Adverse events	Nominal categorical	N (%)
▪ BP (mmHg), P (BPM) and oxygen saturation (%) at 6 different time points	Continuous numerical	Mean ± SD

Note: 95% CV = 95% central value; VAS = visual analogue scale; F/C = fractional curettage; BP = blood pressure; P = pulse