CHAPTER 3

RESEARCH METHODOLOGY

Target population

Female patients (20-45 years old) who have delivered the babies within 48 hours (immediate postpartum) and desired to have permanent birth control by transabdominal tubal sterilization (postpartum tubal ligation).

Population sampled

Postpartum patients at Siriraj Hospital who met the following criteria:

Inclusion criteria

1. Postpartum patients of ASA physical status 1 or 2 (Appendix A), within 48 hours after normal delivery.

2. Aged 20-45 years.

3. Desired to have postpartum tubal ligation under local anesthesia

4. Agreed to participate

5. Were admitted to the ordinary postpartum ward. (Private patients were excluded due to the variation of the surgeons.)

6. Could read and understand how to rate the of NRS score. (practice will be done during the visiting period)

Exclusion criteria

1. Patients with history of pelvic inflammatory disease in whom the surgeon might have difficulty in searching for the uterine tube due to adhesion. (If after randomization, an unexpected adhesion was found, she would not be excluded from the study unless the surgery could not be done, but would be in the failure group if ketamine or GA was needed).

2. Patients with history of hypersensitivity to local anesthetics.

3. Patients with history of liver disease which may interfere with lidocaine metabolism.

4. Patients who refused to be awake during the operation.

5. Patients with history of asthma or narcotic addiction

6. Patients with history of previous intraabdominal operation.

Sample size calculation

The main outcome of this study was the pain scores (NRS). Intraperitoneal lidocaine or morphine has its main effect on the scores and there may be interaction between these 2 drugs. If there was no interaction, the sample size could be calculated according to the factorial

design. For factorial design, we are interested in the effect of two main factors. We calculated the sample size from the formula :

For main effects, $k = 4$

$$f \quad = \quad \text{effect size} \quad = \frac{Sm}{S}$$

$$S \quad = \quad \text{common SD}$$

$$Sm \quad = \quad \text{SD of the k sample mean around the grand mean}$$

$$Sm \quad = \sqrt{\frac{\sum (\bar{X}_i - \bar{X}_G)^2}{k}}$$

$$(\bar{X}_i - \bar{X}_G) \quad = \quad \text{the deviation of individual mean } (\bar{X}_i) \text{ from}$$

the grand mean ($\bar{X}_G$)

From pilot study, NRS scores (0-10)

		Mean	SD
group	control	8.00	1.22
	morphine	7.80	1.78
	lidocaine	3.80	2.49
	mo.+ lido.	0.40	0.89
	Sm = 7.76	S = 3.58	f = 0.78

After f is known, by using Cohen's table[24] at $\alpha = 0.05$, $\beta = 0.2$, $k = 4$, n / group was found to be 8 .

Subgroup analysis:

The sample size estimated from the formula of the main effects might not have enough power for subgroup analysis if there is some interaction between the two factors. To answer the research questions, we should calculate the sample size for subgroup analysis so that the primary research question can be answered.

$$N/\text{group} = \frac{2[(Z_\alpha + Z_\beta)\, SD]^2}{(\bar{X}_c - \bar{X}_a)^2}$$

α error $=$ 0.05, β error $=$ 0.20

Z_α $=$ 1.96 (two tailed) ·

Z_β $=$ 1.645 (power = 95 %)

$\bar{X}_c$ $=$ 8.00

$\bar{X}_a$ $=$ 3.8

SD $=$ 3.58

N/gr. $=$ 18

To compensate for loss of patients,

$$N = N + (10 \% \text{ Of N})$$

$$= 18 + 1.8$$

Therefore, this study needed $=$ 20 patients per group.

Experimental maneuver

	Control. (Group I)	Morphine (Group II)	Lidocaine (Group III)	Lidocaine .+ morphine. (Group IV)
1. Preoperative visit.		same	same	same
1.1 consent signed				
1.2 practiced how to use NRS for intraoperative pain (verbal) and post operative pain (written) evaluation.				
2. (Intramuscular injection of 1 ml)	NSS.	Morphine 10 mg.	NSS	Morphine10 mg
3. Started IV.with LRS 1000 ml		same	same	same
4. At least 45 minutes post IM injection but not later than 2 hours,		same	same	same

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the patients were brought

into the operating room.

5. Monitor blood pressure,   same   same   same

   electrocardiogram (EKG),

   oxygen saturation

   (pulse oximetry)

6. Local infiltration for skin,   same   same   same

   subcutaneous tissue,

   rectus sheath overlying the

   uterine fundus with

   1% lidocaine 15 ml

7. Abdominal cavity was   same   same   same

   opened with one inch

   horizontal incision just

   below the umbilicus.

8. Intraperitoneal

   instillation (80 ml.)

     NSS   0.5% lidocaine   NSS   0.5%lidocaine

9. Waited three minutes

   before start searching

   for the uterine tubes

   (left side first).

10. As soon as the surgeon started searching for the left uterine tube, the patient was asked to rate the NRS pain score and to tell us if the score had changed from the previous one that she had told.

    10.1 If the NRS scores were 0- 3 , the patient was in mild pain and no rescue drug was given.

    10.2 If the scores were more than 3 (4 - 10), the patient was in moderate to severe pain and fentanyl 1-2 μgm/kg. was given.

    10.3 If after fentanyl, the scores were more than 6 (7 - 10), the patient was in severe pain and ketamine 0.5-2 mg/kg. was given. (If NRS score at any point had not been given before ketamine, the highest score before ketamine was used instead).

    10.4 General anesthesia (nitrous oxide, oxygen, halothane) might be needed for completion of the operation.

11. The blood samplings were taken from the antecubital area, contra lateral side to the IV line at 0,5,15,30,45,60,120 minutes after the abdominal instillation and were sent to the Division of Toxicology, Siriraj hospital for detection of plasma lidocaine level.

12. In the recovery room, vital signs were recorded every 15 min for 2 hours, NRS (written) were rated by the patients every 1 hr for 2 hr in the recovery room.

13. At ward:

    13.1 The patients rated NRS (written) every 3 hr for 24 hr

    13.2 The total number of paracetamol tablets consumed and side effects, e.g. nausea, vomiting, urinary retention, ileus, were observed and recorded for 24 hr

Measurement

Pain measurement has been attempted since the nineteenth century. Psychophysiological post-World War II studies by Kelle[26] have assisted in better understanding of the techniques of measuring pain.

Acute pain is easier to measure than chronic pain , as it generally is a unidimensional and short, time-limited event. Experimental pain is more similar to an acute-pain phenomenon. Measurement of acute pain has been reproducible and is not significantly affected by many other variables.

In contrast, chronic pain with numerous psychological, social, environmental, cultural, and economic factors that influence it , is much more of a complex phenomenon to measure.

The ideal pain measure should be sensitive, free of bias, valid, simple, accurate, reliable, and inexpensive. In addition, the measuring instruments should provide immediate information, with accuracy and reliability of the subjects. The ideal instrument would be useful in both clinical and experimental pain, allowing reliable comparison between these two types of pain. Finally, the ideal pain measure should provide absolute values that increase the validity of pain comparison between groups and within groups over time.

Subjective pain measurement is the most frequently used measure of pain. It is recognized that pain is a subjective experience, a very private sensation, and a complex phenomenon. Simple subjective pain measurement views pain as a unidimensional concept. The four frequently used, simple-pain measurement techniques in day to day clinical practice are the following:

Category scale. With this measurement, simple terminology is used to categorize pain into one of three or four qualities. The frequently used categories scale ranges from usually pleasant to quite ordinary to decidedly bad. This is highly simplistic and usually not useful in a clinical setting.

Descriptive pain scale (DPS) . Keele[26] described this scale in 1948. He also viewed pain in a unidimensional mode, e.g., absent/mild/moderate/severe. This method is frequently used in many pain studies in a clinical setting. However, it is nonspecific, not very sensitive, and not consistently reproducible. Using a similar technique, clinicians can use a descriptor pain relief scale (e.g., none/slight/moderate/good).

Numerical rating scale (NRS). In numerical pain scales, pain is viewed as a simple unidimensional concept and measured only in its

intensity. A scale of 0 to 5, 0 to 10, or 0 to 100 is used. This is helpful in clinical settings as a measurement tool in assessing response to selected treatment.

Visual analog scale (VAS). The VAS is the most commonly used measurement in many pain evaluation centers. It consists of a 10-cm line that represents the continuous severity of the pain experience. The line can be vertical or horizontal. It has "stops" at each end, at right angles to the line. The descriptors are used only at ends, being "no pain" on one end to "the worst possible pain" on the other, without any descriptor along the length of the line.

The VAS is a simple, robust, sensitive, and reproducible instrument. It has been validated and used in multiple settings and has been shown to be useful in reassessing pain in the same patient at different times.

For the practicing clinician, the VAS is probably the most effective instrument and can be compared for statistical significance.

VAS, while it is the most accepted and widely used method for measuring pain, needs some understanding for its use, (mechanical or writing). DPS is easy to understand but may be too crude to use in

research. NRS, even though it is not as sensitive as VAS is more suitable to measure acute intraoperative pain in this study.

In conclusion, the simple techniques view pain as a unitary phenomenon and measure only pain intensity. Of these, the most frequently used and practical in the clinical setting are the numerical scales of 0 to 10, 0 to 5, to 100% or the VAS.

In this study, the main outcome that needed to be measured is acute pain. Even though pain is a private, internal sensation and has multidimentional characters, acute pain is different from chronic pain because it depends more on the extent of injury (intensity) than the psychological factors such as fear, anxiety, cultural background etc., as in chronic pain. The method we used in this study to measure acute pain were numerical rating scale (NRS) and descriptive pain scale (DPS). (see appendix. A1, A2)

Methodological criteria of measuring instruments:

Before measuring, the instrument needs to be assessed for its reliability, validity, responsiveness, applicability and practicality.

Reliability : The extent to which repeated measurements of a relatively stable phenomenon fall closely to each other.

Assessment of instruments reliability:

Test-retest, for estimation of stability of the results.

Interater reliability, for estimation of the reproducibility of the results by different raters.

Intrarater reliability, for estimation of the reproducibility of the results by a single rater over repeated observations.

Internal consistency, for estimation of the relation of individual components of an instrument to each other and to overall content of the instrument.

Since acute pain is an unstable characteristic and NRS is the instrument which has only one component (intensity of pain), so the above assessments need not to be done.

Since it is possible to use two instruments at the same time to assess the outcome, so the reliability of the measurement of this study can be done by using parallel form method. If the two instruments have high correlation when measuring the same outcome, they both have high reliability. So DPS and NRS which are the only two instruments that can be used intraoperatively were used to test the reliability by using the intraclass correlation (ICC).

Validity: The degree to which results of the measurement correspond to the true state.

Assessment of the instrument's validity:

Content validity, to estimate whether the instrument represents the spectrum of content of the characteristic being measured, by inspection of the instrument.

Criterion validity, to compare the results of a new instrument with a criterion or gold standard.

Construct validity, to assess the meaning of the instrument in term of its hypothesized or theoretical basis by comparing with external variables related to the construct.

VAS, NRS and DPS have been widely accepted for evaluating intensity of pain, so they need no evaluation for content validity, and there is no gold standard in pain measurement, even though VAS seems to be recognized as the standard measurement for acute pain due to its validity, reliability and common usage.

Since DPS consists of the words that represent the degree of pain, by comparing with DPS, the NRS should be assessed for its validity. By using the SPSS program, the paired t-test was used to compare the differences between two scales.

Responsiveness: (The ability of an instrument to detect changes)

In theory, a valid and reliable measure should be sensitive enough to detect changes, but it is also related to the scaling system. Scale categories that are too crude may not detect changes while too sensitive scale categories cause patient's confusion. Recent study suggested that 10 and 21 point scales provide sufficient levels of discrimination of NRS.[27]

Applicability : The appropriateness of its use with a proposed study population.

Verbal NRS is appropriate for evaluating pain in the intraoperative period, while VAS which needs the patient's hand to be free can not be used.

Practicality : The instrument is practical in terms of patient compliance and professional burden.

From our pilot study, patients had good compliance in rating NRS, but had less compliance for DPS even though they could rate scores. In this study, NRS was used during the operation.

Data gathering technique

The pretest was done in 10 postpartum patients scheduled to have tubal sterilization under local anesthesia. During preoperative visit, each

patient was trained how to rate NRS and DPS using her labour pain which is usually the most severe pain as an example.

The formal DPS which was consisted of 4-5 levels of pain intensity (no pain to the worse possible pain) was modified in this pretest to 6 levels with plus and minus scores (appendix A2) so that it could be equally compared to the NRS. The modified DPS was evaluated by two anesthesiologists working in pain clinic who both agreed to this modified tool. One of them wondered if the scale was too fine, it might have the problem of confusion but suggested comparison with the NRS since they are the only two forms that can be rated verbally during intraoperative period.

Intraoperation, while the obstetrician pick up the uterine tube and pull it up for tying and cutting which is the most painful step, the patient was asked to rate the DPS as:-

1. pain or no pain?

2. very mild, mild, moderate, severe or very severe?

3. exactly or plus or minus?

(There was no problem in understanding the questions because all patients had been trained how to answer during preoperative period.)

4. from 0 to 10, what number represent your pain now?

After getting the DPS and NRS scores from each side of the tube, the maximum score was selected for comparison for all 10 patients.

Statistical test

Patient	DPS	NRS
1	8	8
2	5	5
3	6	8
4	6	8
5	8	8
6	7.5	5
7	7.5	8
8	5.5	8
9	10	10
10	0	1

Validity analysis :

By comparing with DPS which consists of the words that represent the degree of pain, NRS could be assessed for its validity, the ability to provide adequate prediction about a patient's pain behavior. By

using the SPSS program, the paired t-test was used to compare the difference between the 2 scales.

Paired sample t-test NRS

DPS

Variable	Number of cases	Mean	Standard Deviation	Standard error
NRS	10	6.7500	2.659	.841
DPS	10	6.0500	2.554	.808

(Difference) Standard Deviation	Standard Error	t value	Degree of Freedom	P	Mean
.7000	1.252	3.963	1.77	9	0.11

Interpretation:

Validity

The paired t-test comparing between DPS and NRS resulted in the P value of 0.111 which was not statistical significance. This meant the two scales were equivalent From the pretest, NRS which was the digital number (0 - 10) used to measure acute pain during the operation was proved to be valid as compared to DPS which represented the real feeling of the patient. NRS and DPS were the only two instruments that can be rated by mouth and feasible to do during the operation.

Reliability

In this pretest, the reliability of NRS was done using the parallel form method, and the intraclass correlation coefficient was equal to 0.9 which means high reliable of NRS. It means that if NRS is used repeatedly, the results will be stable and fall closely to each others. It was also proved from recent study[28] that mechanical visual analogue scale and simple numerical rating scale were both reliable.

NRS and DPS are commonly used for measuring pain and both were repeatedly compared to VAS[29,30] for their reliability. This pretest compared NRS (verbal) and DPS (verbal) which also shown high reliable (ICC = 0.9).

NRS (numerical rating scale), the instrument that was used to measure the main outcome of this study for intraoperative (verbal) and postoperative (writing) period had been proved to have its validity and reliability.