CHAPTER III

RESEARCH METHODOLOGY

RESEARCH DESIGN

The experimental study , randomized controlled trial , evaluator blind is performed in Thai enuretic patients aged above 6 years , seen in psychiatric department , Siriraj hospital and in school mental health program.

POPULATION AND SAMPLE SELECTION

Target population

All enuretic children aged above 6 years.

Sample population

1. All enuretic patients seen in psychiatric department , Siriraj hospital.
2. All enuretic children seen in school mental health program in which we weekly go to visit about 3 - 4 schools nearby Siriraj hospital.

Sample selection

Inclusion criteria

1. Children over the age of 6 years who have bed-wetting at least 2 nights weekly.
2. Children co - operate willingly in this study.

Exclusion criteria

1. Patients who have any contributing organic causes.
2. Patients who have any diagnostic mental disorders affecting the child 's ability to follow the instructions (MR , depression etc).
3. Patients who have any organic disorders affecting the child's ability to follow the instructions (can not communicate etc).
4. Patients who can not be followed-up for this study.

Sample size calculation

In sample size calculation for 2 independent groups , testing the difference of outcome variable in proportion , type I error of 0.05 , type II error of 0.1 (power of study = 90%) and magnituded of difference at 30%.

$$N / \text{group} = \frac{2 (Z_\alpha + Z_\beta)^2 \ \pi (1 - \pi)}{(\pi_t - \pi_c)^2}$$

$\pi = (\pi_c + \pi_t) / 2$

π_c = expected event rate in control group

π_t = expected event rate in treatment group

$\pi_t = 0.5$

$\pi_c = 0.2$

$Z_\beta (0.1) = 1.28$

$Z_\alpha (0.05) = 1.645$

$$\pi = (0.5 + 0.2)/2$$

$$= 0.35$$

$$N/\text{group} = 2 \times 0.35\,(1 - 0.35)(1.64 + 1.28)^2 / (0.5 - 0.2)^2$$

$$= 0.7 \times 0.65 \times 8.53 / 0.09$$

$$= 43.1238$$

if drop out rate expected about 10%

$$N_d = \frac{N}{(1-R)}$$

$$= \frac{44}{(1-0.1)}$$

$$= 48.89$$

Sampling technique

Stratified randomization with 2 potential prognostic factors

1. sex.
2. the case that the child can be waken up. Block randomization was used to prepare a randomization sheme.

OBSERVATION AND MEASUREMENT

Operational Definitions :

1. Remission : Absence of bed-wetting at least 14 consecutive nights.
2. Relapse : Having at least 2 wetnights in any 7 day period.
3. Much improved : Having less than two wetnights weekly.
4. Improved : Reduction of wetnights per week more than half of the beginning.

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5. Consciously waken : Child can recall correctly the wakening time which he was told last night.

6. Not consciously waken : Child can not recall the wakening time he was told last night.

7. Good compliance : The case that the child can follow the instructions properly more than half of the total treatment days (3 months).

8. No compliance : The case that the child can follow the instructions properly less than half of the total treatment days (3 months).

9. Social approval and disapproval : Approve the child socially for drynight and disapprove for wetnight.

10. Star chart : Calendar record, marking the star on the date of drynight.

11. Tangible reward : Give the child a reward such as some extra pocket money for dry night.

Measurement :

The outcome variables, we measured :

1. The proportion of the patients who meet the remission criterion (defined as having at least 14 consecutive drynights).

2. The proportion of the patients who relapses within 6 months after treatment ended (having at least 2 wetnights in any 7-day period).

3. Number of days taken to reach remission.

4. Number of wetnights before reaching remission.

5. Parent's satisfaction score for the method of treatment by using a visual analoque scale.

Interventions

There are two groups of treatment

	Treatment	Control
Pad and bell	X	
Fluid restriction		X
Night lifting		X
Social approval and disapproval	X	X
Star chart	X	X
Tangible reward	X	X

Manoeuvre

Both parents are asked to accompany the child to the clinic for the first appointment. Each child is first screened by the physician with history , physical examination , blood test for BUN and creatinine , and urinalysis to rule out any contributing organic problems.

Mental status examination and interview are performed by child psychiatrist.

Psychological test (Sentence completion test and Drawing test) are performed by psychologist.

Child psychiatrist and psychologist administer both programs of treatment.

Method is described and demonstrated clearly by child psychiatrist to the family.

The parent and child take the role - playing to test whether they understand the instructions or not.

A date is agreed upon for beginning the program.

A follow - up session of every 2 weeks both groups.

A weekly phone contact is kept with each family by the child psychiatrist to monitor the child's progress , to reinforce instructions and to ensure that the program is followed properly.

Even the child reaches the dryness criterion of 14 consecutive drynights , the treatment is still maintained until 3 months of treatment duration ended and following up every 2 weeks as well as the weekly phone contact are still kept.

We count as remission if continence can be maintained until 3 months of treatment ended.

After treatment ends , the every 2 week-following up is maintained to ensure a regular contact for 6 months. If the child has at least 2 wetnights in any 7-day period , we count as relapse and if the child is still continent until 6 months following up , we count as cure because it is very rare to relapse after 6 months.

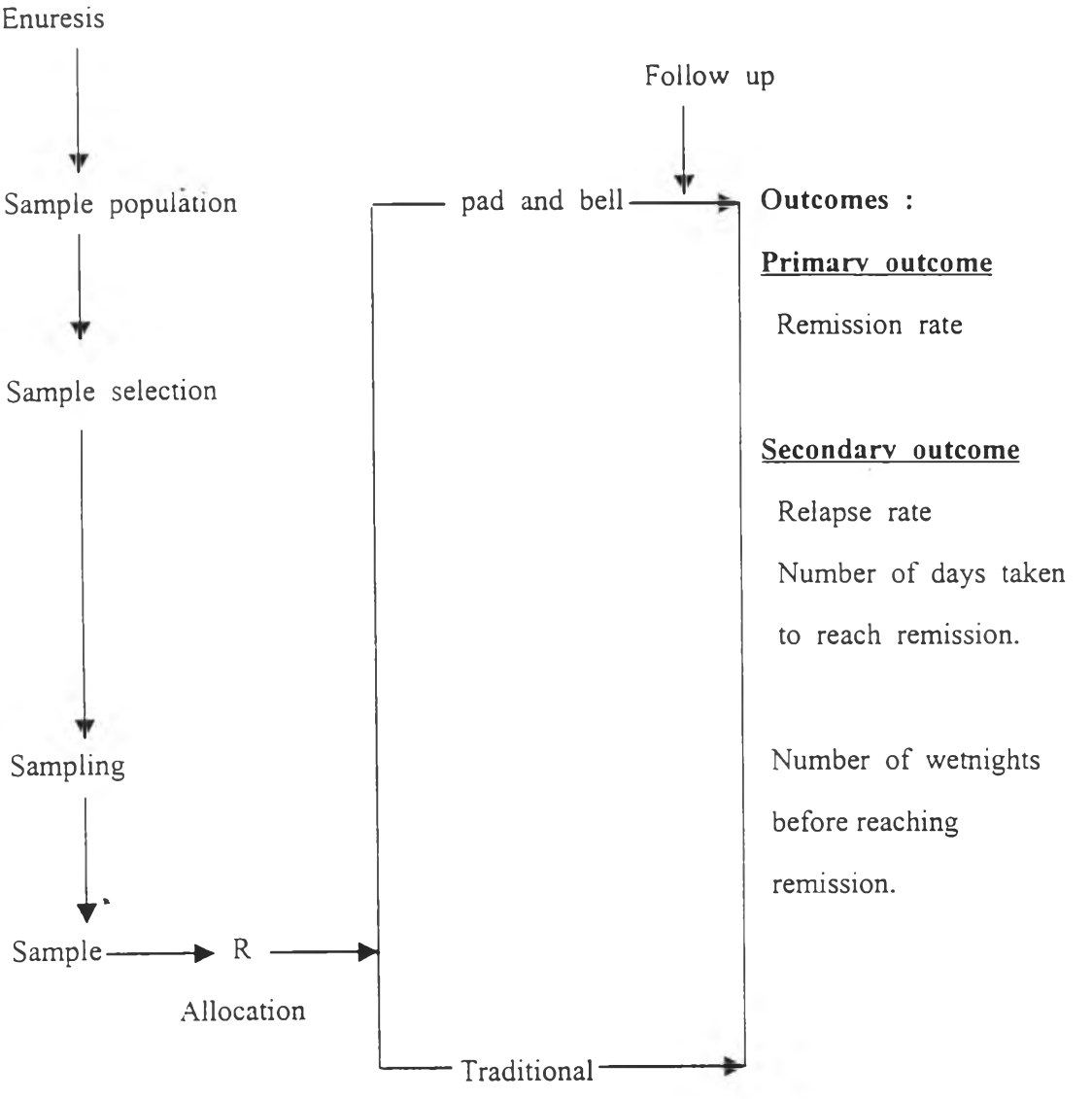
Both groups receive the pads for nightly use (marked with the date and number in order) to see whether the child has bed - wetting or not.

Home visits will be done by a child psychiatrist and or a social worker if there are any losses of regular contact with the patients.

During the treatment program , the child has to sleep with his parent so as to ensure that the child can follow the instructions properly , record the result in star chart and record the wakening time by a time - recorder correctly.

The parent and child have to be stated clearly about contamination and co-intervention that should be avoided.

Research framework



DATA COLLECTION

The child himself recorded the result by the surveillance of his parent , and the record forms were brought to the other physician who was the blind evaluator,(the evaluator never saw and contacted with the patient) checking the contaminated pads and time-recorder device to see whether they were corresponding to the record-forms.

The physician who gave the treatment to the patients had never known about the results of treatment and she had always a psychiatric nurse to join with during the treatment to ensure that she had not any bias to take more preference for any treatment methods.

The data which we collected were :

1. Administrative variables :

   1.1 name of patient and his/her parents

   1.2 address , telephone number

   1.3 school

   1.4 identification number

2. Zero - state variables :

   2.1 age , sex

   2.2 education of patient and his/her parents

   2.3 number of wetnights in the last 2 weeks before study (without any treatment)

   2.4 number of urination per wetnight

   2.5 profession of his/her parents

   2.6 type of wakening (the patient could be waken up consciously or not)

3. Outcome variables :

   3.1 the proportion of the patients who reached the remission criterion defined as having at least 14 consecutive drynights

   3.2 the proportion of the patients who relapsed within 6 months after treatment ended (having at least 2 wetnights in any 7 day period)

   3.3 number of days taken to reach remission

3.4 number of wetnights before reaching remission

3.5 satisfaction score of the parent for the treatment method by a visual analogue scale.

DATA ANALYSIS

Intention - to - treat analysis was applied in analyzing the outcome variables. Eventhough we tried very hard to a keep regular contact , closed following - up with the patients and home visitting , we still had two drop out patients (each one for each treatment method) and the reasons for drop out and outcomes of those patients were also reported.

STATISTIC USED IN DATA ANALYSIS

The baseline data were analysed as :

Variables	Descriptive statistics
1. Sex	proportion
2. Education of parent	proportion
3. Type of wakening up	proportion
4. Age	mean ± SD
5. Number of wetnights per week before treatment	mean ± SD

Analysis of outcome variables

Primary outcome

The proportion of patients who reached the remission criterion compared between two treatment programs were analysed by using Z-test because the sample size of each group was big enough ($np, nq > 5$) which we could assume that they were normal distributions and it was one - tailed hypothesis. A p-value of less than 0.05 was considered a significant difference.

Secondary outcome

1. The proportion of the patients who relapse during 6 months of following up compared between two treatment programs were also analysed statistically by using Z- test (one-tailed hypothesis). A p-value of less than 0.05 was considered a significant difference.

2. The mean of number of days taken to reach remission compared between two treatment programs were analysed statistically by using the unpaired t-test because we did not know the variance of two population. A p-value of less than 0.05 was considered a significant difference.

3. The mean of number of wetnights before reaching remission compared two treatments were analysed by using the unpaired t-test. A p-value of less than 0.05 was considered a significant difference.

Covariate analysis

Since in this study , there might be some potential prognostic factors affecting the outcomes such as sex and type of wakening. Therefore, the baseline differences were analysed by using Mantel-Haenszel method because sex and type of wakening are both discrete variables.

ETHICAL CONSIDERATION

Both treatment programs conducted in this study did not have any potential harm to the patients. However the ethical issue was presented to the ethic review committee of the hospital for consideration.

Every patient and his/her parents were explained about the details of the study and they were tested for the understanding of the general nature and purpose of this study.

Written informed consent was obtained from every patient 's parent . Patients and their parents had the right to withdraw from the study at any time.

LIMITATIONS

1. The patient ' s compliance was a crucial issue for this study because most part of the treatment depended on the patient and his/her parents and the treatment program might be new and somewhat difficult for Thai patients and their parents to follow the instructions.

2. The drop-out was another important issue that should be considered and planned.

3. The number of patients , eventhough enuresis is a very common problem in children but it is not a very serious disease so that the patient and his/her parents can tolerate. This study was hospital - based , tertiary care. Some exclusion criteria could limit the number of patients who could enroll in this study.

Strategies to solve the problems

Strategies to improve the patient ' s compliance include :

1. Include only the enuretic patients who were willingly treated without any enforcement.

2. Give the patient and his/her parents a very clear and simple instruction and a good demonstration.

3. Close following - up and regular contact with the patients.

4. Good doctor - patient relationship.

Strategies to deal with with drop - out patients include :

1. Exclude the patients who might have the problems with regular following-up according to the schedule (such as patient whose home was very far from the hospital).

2. Close following-up and regular contact.

3. Compensate for drop-out by using a drop-out rate from other studies to increase the sample size before study.

4. Analyse the data by intention-to-treat analysis for the drop-out patients.

Administration and schedule

Before the start of the research :

- Permission had been obtained from the Ethical Committee of Siriraj hospital , Mahidol University

- Research grant support had been received from China Medical Board

- Meetings were held for the research team to organize and plan about the process , technique , function of each research personnel , and all other things

- Pad and bell as well as the time recorder device had been invented for this research purpose through the co - operation from King Mongkut ' Institute of Technology North Bangkok

- Preparation of data record forms and written informed consent forms

This study took three months for preparation, eighteen months for data collection, one month for data analysis , one month for writing thesis and another month for correction and preparation for final presentation.

Time schedule