CHAPTER 3

RESEARCH DESIGN AND RESEARCH METHODOLOGY

3.1 Research Questions

3.1.1 Primary research question

Are there any differences in time to cord separation among 3 regimens of cord care: (1) daily triple dye, (2) daily triple dye while in hospital and alcohol at home and (3) daily triple dye while in hospital and no antiseptic used at home?

3.1.2 Secondary research question

Are there any differences in terms of parental satisfaction, bacterial colonization and complications compared between using triple dye and other regimens of cord care at home: alcohol or no antiseptic agent?

3.2 Research Objectives

3.2.1 Primary research objective

The purpose of this study was to determine the time to cord separation compared among three regimens of cord care: (1) daily triple dye, (2) daily triple dye while in hospital and alcohol at home and (3) daily triple dye while in hospital and no antiseptic used at home.

3.2.2 Secondary research objective

The secondary objectives of this study were to compare parental satisfaction, bacterial colonization on umbilicus stump and complications between using triple dye and other regimens of cord care at home: alcohol or no antiseptic agent.

3.3 Hypotheses

3.3.1 Research hypothesis

The regimens of cord care using triple dye only while in hospital and alcohol or no antiseptic agent while at home shorten time to cord separation compared to the regimen using daily triple dye until cord separation

3.3.2 Statistical hypothesis

Null hypothesis: No difference in population means of three groups

$$\mu_{TD} = \mu_{AI} = \mu_{N}$$

Alternative hypothesis: At least one population mean differs from the others

$$\mu_{TD} \neq \mu_{AI} \quad \text{or} \quad \mu_{TD} \neq \mu_{N} \quad \text{or} \quad \mu_{AI} \neq \mu_{N}$$

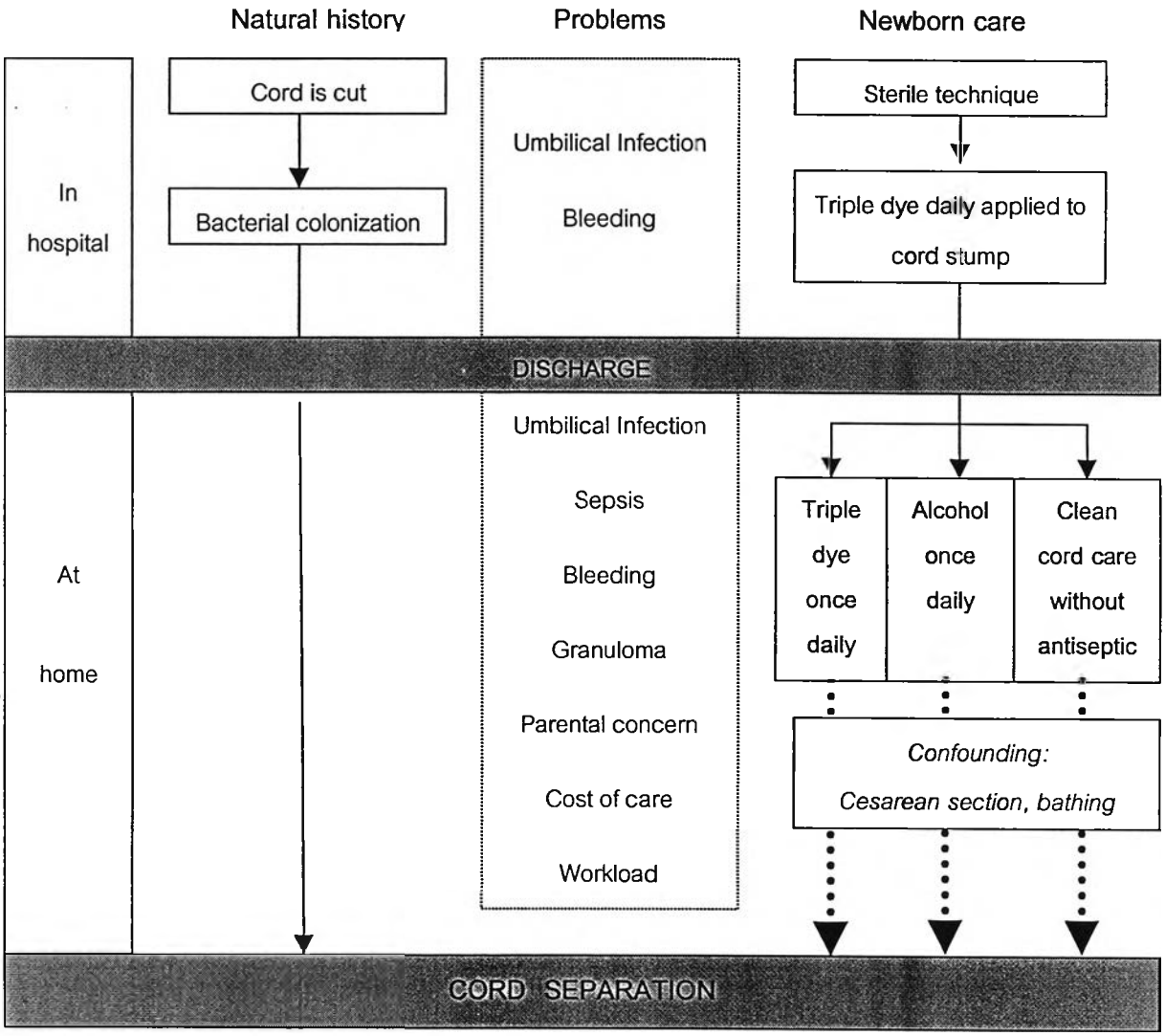
μ_{TD} = Mean time to cord separation in the infants using triple dye

μ_{AI} = Mean time to cord separation in the infants using alcohol

μ_{N} = Mean time to cord separation in the infants using no antiseptic treatment

3.4 Conceptual Framework

Figure 1 Conceptual framework



3.5 Keywords

Umbilical cord care

Time to umbilical cord separation

Triple dye

Alcohol

Clean cord care

3.6 Operational Definition

Definition for data analysis

Time origin: The time when the infant was born

End point for the primary outcome: The time when cord completely detached from the umbilical base

Time to cord separation: The duration from birth to the time when cord completely detached from the umbilical base

To determine time to cord separation, we counted the time at birth as time "0" and count the complete 24 hours after birth as one day and so on.

If parents were able to tell the exact time when cord detached, we counted the complete day after birth and then added the extra hours as a proportion of one-day (24 hours).

If parents were not able to tell exactly when cord detached, the ways to count time to cord separation was depended on the time at birth and approximate time when cord detached (daytime or nighttime). We referred the daytime to the time between 6.00AM and 6.00PM and the nighttime to the time between 6.00 PM and 6.00 AM).

Definition for diagnosis

Omphalitis:	The presence of erythema, swelling or serous or purulent discharge from the umbilical stump or the periumbilical tissue (30)
Granuloma:	The remaining grayish tissue of umbilical stump after cord separation

Sepsis: Having signs and symptoms such as fever, drowsiness, irritability, vomiting, diarrhea, tachypnea, apnea, tachycardia, jaundice, pallor with or without positive blood culture

3.7 Research Design

The study was a randomized controlled trial.

3.8 Target Population

Target population: Well-being, term newborn infants

Study population: Well-being, term infants born at Phramongkutklao Hospital

3.9 Sample Population

Infants who met the following criteria:

3.10 Eligible criteria

Inclusion criteria

1. Term infants (gestational age $\geq$ 37 weeks)
2. Infants born at Phramongkutklao Hospital
3. Parents agree to participate in the study and informed consent obtained

Exclusion criteria

1. Having high risk for infection
   - Maternal history of prolonged rupture of membrane (PROM $>$ 18 hours)
   - Maternal chorioamnionitis
   - Having meconium-stained amniotic fluid
   - Having Apgar score at 1 minutes lower than 8
   - Low-birth-weight infants (birth weight $<$ 2,500 grams)
   - Being admitted in the neonatal intensive care unit
   - Having procedures (e.g. intravenous fluid administration, blood transfusion)
   - Staying in hospital for longer than 4 days (96 hours)
2. Having difficulties to follow-up

- Having no telephone at home or no mobile phone
- Staying outside of Bangkok and boundary
- Maternal history of no or poor antenatal care (less than 4 times)

3.11 Sample Size

The main outcome of the study was the time to cord separation in days. The statistical analysis to detect a difference in mean cord separation time among three groups was one-way analysis of variance (ANOVA). We calculated the sample size from the formula

$f = \sigma_m / \sigma$

$\sigma_m = \sqrt{\sum (\bar{X}_i - \bar{X}_G) / K}$

σ_m = Standard deviation among groups

σ = Standard deviation within group (common standard deviation)

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

From Gladstone's study (8)

Treatment	n	Mean time to cord separation (day)	SE	SD
Triple dye once daily	14	17.4	1.8	6.73
Triple dye once and then daily	53	12.5	0.6	4.37
alcohol	48	12.9	0.6	4.16
Triple dye once				

$\sigma_m = 2.44$ $\sigma = 4.62$ $f = 0.53$

By using Cohen's table(31) at $\alpha = 0.05, \beta = 0.2, K = 3,$ n / group = 14

The sample size estimated had no enough power for subgroup analysis if there were some differences between groups. To answer the research questions, we calculated the sample size for multiple comparisons. Based on Gladstone' s study, we used the lowest difference of means between groups that have clinical significance $\bar{X}_{TD} - \bar{X}_{AI} = 3$

$$n = 2 \times [SD (Z_\alpha + Z_\beta)]^2 / (\bar{X}_1 - \bar{X}_2)^2$$

SD = Pooled SD = 4.62

For multiple comparison α was adjusted by $\alpha/3 = 0.05 / 3 = 0.017$

Z_α = 2.41

β = 0.20 Z_β = 0.84

$\bar{X}_1 - \bar{X}_2$ = Difference of mean time to cord separation = 3

$n = 2 \times [4.62 (2.41 + 0.84]^2 / (3)^2 = 50$

Compensation for 20% dropout

n / group = 60

3.12 Allocation Technique

Convenient sampling technique was used to recruit the infants who met the inclusion criteria and their mothers were willing to participate in the study.

Simple randomization was performed before discharging the infants from hospital (after 36 hours of age) using a randomization table.

Treatment allocation was concealed in separate well-sealed opaque envelopes.

3.13 Intervention

After obtaining written consent, infants were randomly assigned into one of the three groups before discharge.

Group 1 Triple dye

Mothers were instructed to applied triple dye to umbilical stump once daily after bathing and when the cord was soiled until cord separation.

Group 2 Alcohol

Mothers were instructed to applied alcohol to umbilical stump once daily after bathing and when the cord was soiled until cord separation.

Group 3 No antiseptic treatment

Mothers were instructed to keep the umbilical stump clean and dry. When the cord was soiled, the cord would be cleaned using clean water and wiping the area dry with a cotton swab or cloth.

Routine cord care in hospital

Umbilical cord was cut under sterile technique in a labor or operating room. Povidone-iodine was applied on the umbilical cord before and after cutting the cord.

On admission to the nursery, the baby's skin was cleaned using olive oil and triple dye was applied to the umbilical stump. Most infants stayed in nursery for at least 6 hours and then were transferred to maternal wards. Triple dye was applied to the umbilical stump once daily until discharge. No bathing in a washing tub was provided in nursery.

Maternal education

Instructions given to mothers before discharge included keeping the umbilical stump dry, folding napkin below stump and cleaning it with soap and water when soiled. Bathing in a washing tub once a day was also encouraged.

Mothers were educated to observe the infant's abnormal signs and symptoms including umbilical infection (erythema, swelling or discharge), impetigo and systemic infection (e.g. fever, drowsiness, irritability, poor feeding, vomiting, jaundice, etc). They were also suggested to bring the infant to the pediatric outpatient clinic when he/she had abnormal signs and symptoms. Telephone call to a pediatrician (a researcher) was allowed at any time if parents had questions regarding the infant's problem.

Mothers were instructed to record the cord separation date and time in a memo and also to answer the questionnaire on satisfaction (Appendix D)

Follow-up

The research nurses were mandated to contact mothers within 48 hours after hospital discharge. Home visits took place within 7 days post-discharge. On home visit, culture of umbilical base was performed. Information of cord separation time, problems of cord care and maternal concern were asked directly.

Infants were scheduled for follow-up at one month of age at the pediatric outpatient clinic. The assessments included infants' well being, problems of cord care (infection, bleeding or granuloma) and maternal concern. The memo of cord care and questionnaire on satisfaction were collected.

To obtain the information of cord separation, problems of cord care and maternal concern, mothers were contacted by telephone calls once or twice a week. If the call was not successful or an infant was lost to follow-up, mailing cards or letters were sent asking the mother to return the memo and questionnaire or contact the researcher.

Umbilical culture

The umbilical base was swabbed without applying any antiseptic agent. The swab was transported in Amies transport media, which was stable in room temperature. The specimens were inoculated on culture media including blood agar, MacConkey agar and Thioglycollate broth. The agars and broth were incubated overnight at 37°c. The definite organism was identified after 72-hour incubation. The sensitivity testing was performed using Agar disk diffusion technique as described by the National Committee for clinical laboratory standard (NCCLS)

Management of problems

If the infant had any problem associated with cord care, the management was guided as followings:

- For having umbilical infection, impetigo or clinically suspected sepsis, he / she was admitted and treated with broad-spectrum antibiotics.
- For umbilical granuloma, silver nitrate was applied on the granuloma. The infant was followed-up at continuing clinic every week until it resolved.
- For other minor problems such as bleeding or foul smell, appropriate suggestion and parental reassurance was given.

3.14 Outcome measurement

The outcome was analyzed by using "intention to treat "in purpose. The infant remained in the assigned group no matter what antiseptic or cord care practices were intentionally used at home.

The outcome variables measured were:

Primary outcome

Time to cord separation in days

Secondary outcome

1. Maternal satisfaction

   The questionnaire consisted of 5 items including stained-color, odor, dryness of umbilical stump, ease of application and timing of cord separation.

   The scores of each item were graded into 5 levels: strongly satisfactory (5 scores), satisfactory (4 scores), equivocal (3 scores), dissatisfactory (2 scores) and strongly dissatisfactory (1 score). The maximum total scores are 25. The total and average scores were calculated.

2. Bacterial colonization on umbilicus stump
3. Complications or adverse outcome

3.1 Infection (omphalitis, sepsis, conjunctivitis)

3.2 Granuloma

3.3 Exudate discharge and bleeding

3.15 Data Collection

The data recorded included:

1. Maternal data: age, gravida, mode of delivery level of education, perinatal complications and address and telephone number
2. Infant' s data: sex, gestational age, birth weight, mode of delivery, Apgar scores, length of hospital stay and age at home visit
3. Newborn care: caregiver, breast or formula feeding, bathing
4. Cord care: antiseptic used, frequency of cord care, timing of cord separation
5. Parental satisfaction scores
6. Result of bacterial culture of umbilical stump

7. Other problems: odor, exudative discharge and bleeding
8. Co-intervention

   Daily bathing was recorded because it was reported to delay the separation of umbilical stump. Factors affecting rate of umbilical cord infection such as breast or formula feeding, banding with clothes or bandages around abdomen and type of diaper used were recorded.
9. Contamination

   The use of other cord care regimens outside of the study assignment regarding type and frequency was recorded.

3.16 Data Analysis

Primary outcome

Descriptive statistics were used to present time to cord separation as mean $\pm$ standard deviation and 95% confidence interval.

Difference of mean time to cord separation among 3 groups was identified by using one-way analysis of variance (ANOVA). The data of time to cord separation in each group was normal in distribution but homogeneity of variances was not presented. Therefore, multiple comparisons to determine the differences between 3- pair means were performed using Dunnett T3' s procedure. Mean differences of time to cord separation and 95% confidence interval compared between groups were reported. The mean difference was significant at the 0.05 level.

The determine the effect of covariates such as cesarean section, birth weight, and bathing, multiple regression analysis was performed.

Secondary outcome

1. Parental satisfaction scores

   Since the satisfaction scores were ordinal scales, non-parametric test, Kruskal Wallis, was used to identify difference of rank scores among groups. The differences of satisfaction scores between triple dye and other regimens: alcohol or no antiseptic agents were performed by using Mann-Whitney test at the significant level of 0.025.

2. Bacterial colonization

The overall rate and distribution of bacterial colonization in study infants were analyzed using descriptive statistics.

Comparison of bacterial colonization on umbilical stump between groups was performed using Chi-square test.

3. Complications and adverse outcome

Prevalence of infection, omphalitis, conjunctivitis, exudative discharge and bleeding were performed using Fisher exact test

SPSS version 11.0 statistical software was used for statistical analysis

3.17 Ethical Consideration

Institutional Review Board of Phramongkutklao College of Medicine approved the study protocol. Parents were thoroughly explained about the detail of the study and possible adverse effects. Written informed consent was obtained from parents before enrollment. Parents were allowed to contact a physician (researcher) by telephone call at any time regarding the infant's problems or parental concerns. Parents were allowed to use other antiseptic agents if they concerned of the substance used.

Infants having infection and granuloma were treated according to the guideline.