DYSPNOEA SURVEY IN THE EMERGENCY DEPARTMENT HUSM 2014

DR GAN KIAT KEE

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF MASTER OF MEDICINE
(EMERGENCY MEDICINE)

UNIVERSITI SAINS MALAYSIA

2017

Patients and Methods: A total 120 babies less than 28 days old were randomized into bladder stimulation group and control group. The specific objective was to compare the successful rate of urine collection between bladder stimulation and conventional technique of urine collection in neonates. The success is defined as the collection of a sample within 300 seconds (5 minutes) of stimulation manouvres (Maria 2012). As for the subsidiary objectives were, to compare the adverse events between the two groups and to compare mean time taken to collect urine between the two groups

Results: A total 120 babies were included in the study. These babies were randomized to the intervention and control group. Fifty four babies were put in the intervention group and 56 in the control group. The result was considered statistically significant when compared between the success rate in collecting urine in the intervention group, compared to the control group. However we could not analyse intention to treat analyses as there did not pass urine during the manouvres were done.

Conclusion: The successful rate in urine collection is higher in the intervention group as compared to the control group. However, the rate of refusal by parents need to be addressed further.

ACKNOWLEDGEMENT

I would like to express my thanks and deepest gratitude to my research supervisors Associate Professor Dr Noorizan bt Abdul Majid, co- supervisor Dr Nor Rosidah bt Ibrahim for the advices, correcting and giving me the encouragement in the preparation of this dissertation. Without their help and support, this project would be impossible to carry out.

Special gratitude to Associate Professor Dr Ariffin bin Nasir, the co-researcher for his support and teaching me on efficient way of study design and the correct way to analyse data.
My special thanks to HUSM (Paediatric Clinic and Neonatal Ward) staff for their cooperation and contribution in making this study a success.

During the preparation of this project, many sleepless nights passed by and it was not possible without the support of my dear husband, Wan Zulhelmi Wan Ahmad Kamar, and my beloved family.

Finally, I would like to dedicate this dissertation to all the beautiful people who were involved directly or indirectly in this study. Last but not least, my special thanks to the parents and children who participated in this study in which without them, this project would never been possible.

TABLE OF CONTENTS

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRAK

Pengenalan

Pengambilan sampel urin dikalangan bayi yang berumur 28 hari adalah sangat penting sebagai alat saringan untuk jaundis yang melebihi dari 28 hari. Ini adalah kerana salah satu punca jaundis yang melebihi 28 hari adalah disebabkan oleh jangkitan ar kencing. Selain dari itu, sampel air kencin juga penting untuk bayi yang mengalami demam, tetapi punca demam tidak diketahui. Maka dengan itu, sampel air kencing perlu diambil untuk mengetahui samaada bayi tersebut menghadapi jangkitan air kencing atau tidak. Sekiranya bayi menghadapi jangkitan air kencing, ini merupakan keadaan yang serius kerana kebanyakan kes bayi yang mempunyai jangkitan air kencing, berkaitan dengan ketidaknormalann fungsi sistem perkumuhan. Banyak kajian telah dibuat tentang menentukan cara yang paling efisien dan cepat untuk mengumpul air kencing bayi. Namun tiada data yang membandingkan cara mana yang paling cepat untuk mengumpul urin.

Objektif

Untuk mengkaji kegunaan stimulasi pundi kencing dengan cara konvensional (tangkapan air kencing) untuk mengumpul urine dikalangan neonat (bayi berumur kurang dari 28 hari) di NICU, SCN dan Klinik Kanak HUSM, Kubang Kerian

Kaedah

Seramai 110 bayi yang berumur kurang dari 28 hari telah ditentukan secara rawak samada mereka tergolong dalam kumpulan yang air kencing ditadah setelah mereka selesai minum susu, atau kumpulan yang air kencing ditadah setelah selesai minum susu dan stimulasi dilakukan keatas mereka. Hasil utama adalah mengkaji kegunaan stimulasi pundi kencing untuk mengumpul air kencing. Disamping itu, juga

untuk membandingkan kadar kejayaan untuk mengumpul urin diantara stimulasi punci kencing dengan cara konvensional dan membandingkan kesan sampingan diantara kedua kumpulan

Keputusan

Seramai 120 bayi telah dipilih secara rawak. Seramai 54 orang bayi telah dilakukan stimulasi pundi kencing, dan seramai 56 bayi, tidak dilakukan stimulasi punci kencing. Perbezaan yang ketara dapat dilihat diantara kedua kumpulan ini dari segi kejayaan untuk mendapat air kencing. Didapati tiada perbezaan berat bayi diantara kedua-dua kumpulan.

Kesimpulan

Cara pengambilan air kencing di dalam kumpulan intervensi adalah lebih berjaya jika dibandingkan dengan kumpulan kontrol

Abstract

ENGLISH VERSION

Introduction

Urine collection in neonates (babies less than 28 days) is an important screening tool for prolonged jaundice. Urinary tract infection is a known cause of prolonged jaundice in neonates. Urine investigation is also indicated in febrile neonates with urinary tract infection as well as those with no apparent cause. Urinary tract infection in babies may be correlated with underlying congenital urinary tract abnormality. If urinary tract abnormality is diagnosed early, it will help to prevent renal scarring. In neonates, urine collection is very difficult and at present, no data is available as the best and fastest method to collect urine.

Objective

To investigate the usefulness of bladder stimulation versus conventional technique (clean catch midstream urine) to collect urine in neonates in NICU, SCN and Paediatric Clinic at Hospital USM, Kubang Kerian

Methods

A total 120 babies less than 28 days old were randomized into bladder stimulation group and control group. The specific objective was to compare the successful rate of urine collection between bladder stimulation and conventional technique of urine collection in neonates. The

success is defined as the collection of a sample within 300 seconds (5 minutes) of stimulation manouvres (Maria 2012). As for the subsidiary objectives were, to compare the adverse events between the two groups and to compare mean time taken to collect urine between the two groups

Result

A total 120 babies were included in the study. These babies were randomized to the intervention and control group. Fifty four babies were put in the intervention group and 56 in the control group. The result was considered statistically significant when compared between the success rate in collecting urine in the intervention group, compared to the control group. However we could not analyse intention to treat analyses as there did not pass urine during the manouvres were done.

Conclusion

The successful rate in urine collection is higher in the intervention group as compared to the control group. However, the rate of refusal by parents need to be addressed further.

1. INTRODUCTION

Urine collection in neonates is important in order to diagnose urinary tract infection and is useful as a screening tool for prolonged jaundice. However the process to get a clean and fast urine collection is difficult in this age group as they are unable to indicate when they want to pass urine. The tedious and long duration needed for urine sample collection can be a frustrating experience for parents.

A prospective feasibility study in Spain (n=80), using a new technique (suprapubic tapping and lumbosacral massage), showed that the mean time of obtaining urine sample was 57secs (SD 48.6secs), and the median time of 45secs (IQR 30) with success rate 86%. No statistically representative differences with regard to sex were found in success rate, time of sample collection or complications. There were no complications, but controlled crying occurred in 100% of infants (Maria 2012).

A randomised non-blinded study in pre-continent children using a vibrating bladder stimulator (n=97), showed significant improvement in time to pass urine (1 hour 4 minutes). Eighty percent (80%) pass urine in under 2 hours. The device group obtain the sample earlier in between 15-60minutes. Five (5) parents felt that their children are more upset and 2 commented on a transient red mark on the child's skin (P. Davis 2008)

As an idea of the size of the problem, at Hospital Universiti Sains Malaysia, the number of neonates requiring urine collection for various reasons in the clinic is about 400 per year (2013). There are a few RCT comparing existing and new techniques on this topic. To date, there is no study done comparing bladder stimulation technique and conventional technique in Malaysia. Thus, it is beneficial to do a study comparing these two groups.

2. LITERATURE REVIEW

2.1 Neonates

Neonates is a group of people whose age is less than 28 days of age. By being in this age group, they are prone to getting conditions that warrant urine collection Urine collection in this age group can be very frustrating and challenging to both parents and care takers, as the babies cannot dictate or let the elder persons know when they are about to pass urine. Thus it is very important for us to have a new technique that is easier and faster for urine collection in this age group. Urine sample in neonates is being taken for various reasons namely, for presumed sepsis, urine for electrolytes and diagnosing urinary tract infection.

2.2 Anatomic Development of the Bladder

Urinary tract development in human starts as early as week 3 gestational age (K.Kathleen 2015). In a Chapter 27, Pediatric Voiding Function and Dysfunction (S.A Zderic 2015) mention that, urorectal septum is the partitioned for urinary bladder and rectum that from the primitive hindgut. Sensory innervation from S2, S3, and S4 sacral segments is shared by the bladder and rectum substantially. In the mature child, the perception of fullness of the bladder involved cortex, whereas in the adult, pontine micturition center, regulates the exerts volitional control over. Barrington's nucleus is a cluster of neurons that involve in coordination of micturition. The afferent sensory nerves enter the posterolateral region of the sacral segments, when the bladder is filling. In a study done by (Prasad, 2011), in adult multiple sclerosis patients with bladder dysfunction, were randomized into abdominal pressure and percutaneous vibrator to aid bladder emptying in multiple sclerosis patient. It shows that the post void residual volume (PVR) decreased from 231 (SD 119) ml during no treatment to 191 (SD 132) ml with abdominal pressure ($p=0.242$). Using suprapubic vibration the PVR reduced further to 126 (SD 121) ml, which was highly significant ($p = 0.002$) compared with no treatment. (Maria et al, 2012) proposed that, the detrusor muscle

is innervated by the parasympathetic pelvic nerves S2–S4. (Sillen U, 2015) mentioned that the spinal micturition reflex is a simple arch reflex. The efferent fibres going to the medulla is stimulated by the distended bladder wall, in which S2-S4 produce the arch reflex. In which then stimulated the afferent fibres to stimulate the detrusor muscle which contract to pass urine. In newborns, this voluntary reflex does not occur. Newborns voiding pattern is characterized by small and frequent voids. In the toilet trained children, they voids 4-7 times per day, as compared to preterm and full term newborns, void onve an hour (20-24 times per day).

2.3 Usefulness Urine Collections in Neonates

2.3.1 Urine for Urinary Tract Infection as a Cause for Prolonged Jaundice

In the neonatal age group, urine is collected for various reasons. Urinary tract infection (UTI) is a common infection in children especially below 2 years of age, with a reported prevalence of 4.1- 7.5% in febrile children. Undiagnosed UTI can lead to life-threatening septicaemia. Delayed treatment was associated with increased risks of renal scarring. Recent researches have revealed that vesicoureteral reflux (VUR) is not the only predictor of renal parenchymal damage, and two distinct and sex-related patterns of 'refluxnephropathy' were recognized. The first pattern, likely a form of congenital renal dysplasia, involves high grade VUR and grossly contracted kidneys on DMSA scan

It is useful as a screening tool to diagnose urinary tract infection (UTI) as a cause of prolonged jaundice. The association between unexplained neonatal jaundice and UTI is well known .The incidence of UTI in asymptomatic, afebrile and jaundiced infants was 5.5% in 217 patients, 5.8% in 400 patients with a mean age of 10 days, 6% in 100 neonates between 2 to 4 weeks of age , 7.5% in 160 patients younger than eight weeks , 7.8% in 102 neonates younger than two weeks, 12.5% in 120 neonates younger than four weeks, 18% in 104 neonates between4 and 14 days of age,and 21% of 152 neonates younger than four weeks.

UTI was found in 6.5% of 462 jaundiced neonates, ages ranging from 3 to 25 days, 68% of whom were asymptomatic and afebrile .The only study with a control group among these studies was that performed by Shahian et al. In that study, incidence of UTI was 12.5% in 120 asymptomatic jaundiced neonates versus none in 122 healthy neonates younger than four weeks (Kasap et al 2014)

In a study done by (Puspapor et al 2007) mentioning that of 100 neonates who were evaluated, 43 were boys and 57 were girls in the study. They found out, six suffered from UTI (4 boys and 2 girls). Reflux was detected on voiding cystourethrography in 1 and cortical defect in the kidney on renal scan in 2 boys. In that study, they concluded that UTI remains as an important cause of prolonged jaundice. Despite the high rate of urogenital system abnormality accompanied by neonatal UTI, there was not a significant difference between the signs and symptoms of jaundice in patients with and without UTI. Performing urine cultures should be considered as a routine procedure in the evaluation. UTI may be the presenting manifestation that identifies a neonate with an underlying congenital anomaly of the kidney and urinary tract (CAKUT). Thus this shows that urine screening is very important in babies with prolonged jaundice as it can aid us in diagnosing of the underlying conditions or problem.

2.3.2 Urine for presumed sepsis

Apart from screening in prolonged jaundice, urine sample in neonates is also important in febrile or presumed sepsis neonates, as urinary tract infections (UTIs) are the most common cause of serious bacterial infections in febrile infants less than 90 days old (Bachur et al 2001). In that study of 5279 febrile infants studied, serious bacterial infection (SBI) was diagnosed in 373 patients (7%) in which 316 urinary tract infections (UTIs), 17 meningitis, and 59 bacteremia (8 with meningitis, 11 with UTIs). The model sequentially used 4 clinical parameters to define high-risk patients: positive UA, WBC count >/=20 000/mm(3) or </=4100/mm(3), temperature >/=39.6 degrees C, and age <13 days. The sensitivity of the

model for SBI is 82% (95% confidence interval [CI]: 78%-86%) and the negative predictive value is 98.3% (95% CI: 97.8%-98.7%). The negative predictive value for bacteremia or meningitis is 99.6% (95% CI: 99.4%-99.8%). The relative risk between high- and low-risk groups is 12.1 (95% CI: 9.3-15.6). Sixty-six SBI patients (18%) were misclassified into the lower risk group: 51 UTIs, 14 with bacteremia, and 1 with meningitis.

2.3.3 Urine for Group B Streptococcus in neonates

In patients presented with congenital pneumonia, as described by (MacIntosh et al, 1992), Of 188 neonates investigated, 17 (9%) had GBS sepsis. The urine antigen test had a sensitivity of 88% and specificity of 98%. The positive predictive value was 79% and the negative predictive value 99%. Blood culture was positive in only five neonates (29%). The annual incidence of GBS sepsis was 4.0 per 1000 and of blood culture positive GBS disease was 1.2 per 1000 live births.

2.4 Methods of Urine Collections in Neonates

There are various methods in obtaining urine in neonates. As neonates are classified in the non- toilet trained, collecting urine in this group can be frustrating. Urine collection in neonates is generally accomplished using one of four methods: urethral catheterization, supra-pubic aspiration, a urine bag or clean-catch technique (Shroeder et al 2005). Both catheterization and suprapubic aspiration are believed to be the most reliable methods because they minimize false-positive results; however, these methods are invasive and uncomfortable for children. The urine bag is noninvasive and is an easy alternative but has been criticized because of high false-positive rates, prompting the American Academy of Paediatrics to discourage its use for urine cultures in infants (AAP 2011)

2.4.1 Clean catch urine

Obtaining a clean-catch urine sample is the recommended method for urine collection in toilet-trained children. However, in children lacking sphincter control, urine catch is difficult and time consuming. Therefore, invasive methods are commonly used as decribed by (Verrier K et al 2007). The use of standardized stimulation techniques as described by (Maria et al 2015) can facilitate and shorten the time for sample collection. Data comparing the yield of cultures obtained using catheterization and clean-catch are limited (7). There is wide variability in false-positive and false-negative rates. One hundred twenty matched samples were obtained from the remaining 60 patients. Mean age was 44 days old and median age was 40 days old (range two to 90 days). Forty-two (70%) were male (all were uncircumcised). The culture results from clean-catch samples included 37 positive (62%), 20 negative (33%) and three contaminated (5%). The clean-catch technique resulted in two false-positive (10%) and one false-negative (7%) culture corresponding to a sensitivity of 97% (95% CI 82% to 100%); specificity was 89% (95% CI 65% to 98%). The prevalence of UTIs in this population was 63% (95% CI 49% to 76%). Positive likelihood ratio was 9.21 (95% CI 2.48 to 34.22) if the clean-catch urine culture was positive. Negative likelihood ratio was 0.03 (95% CI 0.00 to 0.23). The post-test probability of having a UTI was 94% (95% CI 81% to 98%) if the clean-catch urine culture was positive (Maria et al 2012)

Another study done by (Nada et al 2008) showed that, a total of 662 children were treated in ICU during the observed period. The urine sample for routine biochemical tests was obtained from all patients. In 107 patients (16.2 %) urine culture examination was indicated. In 48 (44.9%) patients urine sample was obtained by bag collection, in 41 (38.3%) by clean catch, and 18 (16.8%) by urethral catheterization. Out of 41 patients by clean catch, only one patient had urine contamination. Thus it shows that clean catch urine sample, if done with a proper technique, has a lesser or comparable rate of contamination with other methods

2.4.2 Suprapubic bladder tapping

Suprapubic tap for urine collection the gold standard for urine collection in neonates (Austin et al 1999). Any growth of pathogenic bacteria in an SPA specimen is felt to be significant. 'Blind' SPA (suprapubic aspiration) has an approximately 50% chance of obtaining urine. The use of ultrasound increases the chance of success to 80-90%. Ultrasound is a useful tool to determine when not to do an SPA. There are two types of ultrasound that can be utilized: Real time 2D ultrasound provides visualisation of the bladder and an estimation of its fullness. It is more accurate than the automated bladder ultrasound and should be used in preference to this if expertise in using a 2D ultrasound is available. Automated bladder ultrasound provides a urine volume in mls. It does not visualise the bladder. Its ability to detect volumes less than 20 mls is poor. It should be used only when 2D ultrasound equipment or expertise is not available (The Royal Children's Melbourne Hospital). Suprapubic bladder aspiration in neonates is a simple, safe, and useful technique for collection of sterile urine. The procedure can be performed in the hospital or office. Neither sedation nor local anesthetic is required. Suprapubic bladder aspiration of urine is the preferred method of collecting urine for culture in septic neonates. The technique is also indicated to verify urinary tract infection in neonates. Suprapubic bladder aspiration is contraindicated in the presence of abdominal distension or an empty bladder. Carefully and properly performed, the risk of complications should be negligible, and the success rate in obtaining urine is 90% (Akierman RA 1987)

A study done by (Pollack et al 1994) showing that suprapubic collection is widely used in neonates. But it has relatively low rates of collecting urine, between 25% to 60%. SPA success rate after one attempt was similar to other reports, 64% compared with 25-60%. With two attempts success rate increased to 82%. SPA success rate can be improved to 70-100% by doing ultrasound prior to the SPA (Tobiasky et al 1998). In another study, in 20 very low birth weight infants (502-1210g), the success rate for obtaining urine for culture was 95%, with 80% obtained on the first attempt. Sufficient urine for analysis was obtained in

40%. Issues of consent must be discussed with parents as suprapubic aspiration can carry a risk, although complications are very rare (Barkemeyer, 1993). The procedure can cause anxiety for parents and doctors (Ross, 2000). According to (King C et al 2000), Intestinal perforation can occur if a loop of bowel overlies the bladder, but the small puncture rarely leads to peritonitis. Intestinal (or other viscus) perforation can be avoided if the procedure is not performed in children who have abdominal distension, organomegaly, volume depletion, or congenital anomalies of the gastrointestinal or genitourinary tract. Study done by (Badiee et al 2014), SPA is more painful than urethral catheterization in premature male infants as assessed by PIPP (Premature Infant Pain Score).

2.4.3 Urethral catheterization

Urethral catheter for urine collection has been widely used in neonates. Urethral catheterization was approved as a method of urine sampling whenever sepsis was suspected. (Austin et al 1999). A study done in uncircumcized boys, both clean void urine (CVU) and catheter urine (CathU) were prone to contamination. Though the contaminating bacterial counts were lower in CathU culture, the false-positive rates were high with the lower cut off CFUs. Contrary to previous recommendations, CathU should be interpreted similar to CVU to avoid false positive diagnosis of UTI. (Lau et al 2007).

2.4.4 Urine bag

Bag urine collection involves taping a sterile plastic collection bag over the genitalia and waiting for the child to void into it. Although this method is noninvasive and is often the clinician's 'kindest' choice, it has the highest rate of contamination (up to 50%), commonly with periurethral flora (20-25). In many hospitals and outpatient settings, bag urine collection is the initial method of choice among nurses and doctors

because of its simplicity and noninvasiveness. As a result, there is often a reluctance to use other confirmatory sample collection methods (Davies et al 2004)

A 2009 study published in the Journal of Pediatrics found that bag-obtained specimens produced a significantly higher number of false-positive results (parents were told their child had a UTI, when in fact, he did not. In addition, there was a higher number of false-negatives (parents were told their child did not have a UTI, when he in fact did.

A study done by (Nada et al 2008), showed from urine sample taken 107 sample, 48 samples were collected via urine bag. From all 107 patients, sterile urine was in 80 patients (74.8%), 20 patients (18.7%) had positive urine culture with significant number of pathogens, and 7 patients (6.5%) had contaminated urine culture. Six out of seven contaminated urine cultures were collected by a sterile bag. Only one contaminated urine culture was collected by midstream. It shows that urine collection clean bags, yield more contamination rate.

3. OBJECTIVES OF THE STUDY

3.1 General Objective

The general objective was to investigate the usefulness of bladder stimulation versus conventional technique (clean catch midstream urine) as a method for collect urine collection in neonates

3.2 Specific Objective

The specific objective was to compare the successful rate of urine collection between bladder stimulation and conventional technique of urine collection in neonates. The success is defined as the collection of a sample within 300 seconds (5 minutes) of stimulation maneuvers (Maria 2012)

3.3 Subsidiary objectives

The subsidiary objectives :

1) To compare the adverse events between the two groups

2) To compare mean time taken to collect urine between the two groups

3.4 Null hypothesis

There is no significant difference between the intervention and the control group in terms of successful rate or urine collection in neonates

4.0 METHODOLOGY

4.1 Research Design

This was a non blinded, parallel, randomised control trial. This study was conducted in the month of November 2016.

4.2 Study Population

The reference population consisted of all neonates requiring urine collection in Kelantan. The source population consisted of all neonates in Paediatric Clinic, Neonatal and SCN Ward Hospital Universiti Sains Malaysia.

4.3 Inclusion criteria

The neonates who were less than 28 days old who had a diagnosis which requires a urine sample for investigation namely, prolonged jaundice, suspected urinary tract infection and presumed sepsis. Parental consent was required

4.4 Exclusion criteria

The exclusion criteria were neonates who required assisted ventilatory support

4.5 Withdrawal criteria- (intention-to treat analysis)

The withdrawal criteria included:

- Babies whose parents opted to withdraw while bladder stimulation was done to their babies
- Babies with uncontrollable and inconsolable cry

4.6 Ethical Approval

This study was approved by the Research and Ethics Committee, School of Medical Sciences, University Science Malaysia. Written informed consent was obtained from all parents of the neonates included in the study criteria

4.7 Sample size

In previous study , data from the preceding baseline study measuring time to void for children requiring Clean Catch Urine using standard urogenital cleaning alone, 12/57 (21%) of patients aged 1-12 months voided within 5 minutes . After discussions with a few experts (Paediatricians at consultant level) an increase in success rate of approximately 50% would suggest that this technique should be incorporated into our clinical practice (Kaufman J,2016)

At power 90%, we conducted a study of independent cases and controls with 1 control(s) per case. Prior data indicate that the success rate among controls is 0.21. If the success rate for experimental subjects is 0.5, we will need to study 55 experimental subjects and 55 control subjects to be able to reject the null hypothesis that the failure rates for experimental and control subjects are equal with probability (power) 0.9. The Type I error probability associated with this test of this null hypothesis is 0.05. We will use an uncorrected chi-squared statistic to evaluate this null hypothesis. With 10% dropped out, a sample size of 120 is needed to answer this objective

4.8 Randomization

A computer generated list of random numbers was used for allocation 0f participants using computer software “Research Randomizer’ (www.randomizer.org). All subjects were randomized into 2 groups that were: group 1- intervention and group 2-control, by block randomization with 1:1 allocation using random block size of 4 creating 2 sets of 60 unit number per set. The concealment of allocation from researcher’s enrolling participants was ensured using sealed and opaque envelope. Coding systems was used instead of real name to identify each baby. All subjects’s data was kept in a secured and separate locked file with the investigator. Once consent was obtained, a research assistant will alert the principal investigator and the research assistant will open the envelope and will know into which group the participant is allocated to. This research assistant will also be the person who will conduct the procedure. Because of the nature of the study, blinding is not possible as everyone will know in which group they are belong to.

4.9 Definition

The success is defined as the collection of a sample within 300seconds (5 minutes) of stimulation manouvres (Maria 2012)

Adverse events were defined as:

- Uncontrolled crying after the manouvre
- Parental complaint
- Urine contamination

The uncontrolled crying was defined as inconsolable crying for 10 minutes

Parental complain was defined as complained of redness of skin at the tapped area or any other complaint related to the manouvres done

Urine contamination was defined as cultures with more than 1 microorganism or reported as mixed growth present (R. Lewis 2012)

4.10 Intervention

Once patients identified eligible for the study based on inclusion criteria, they were given an opaque envelope that stated to which group of study they are belong to. For the neonates in the intervention group, the first step was to breast feed or give formula milk according to their normal requirement. Immediately after feeding completed, the neonates genital area were cleaned thoroughly with water and soap and dried with sterile gauze and a sterile collector is placed near the neonates. Before administering the technique, non pharmalogical analgesia was given to neonates : nutritive sucking, glucose 10%. Then care taker of the baby / staff nurse assisted by holding the babies under their armpits and keep their legs dangling. If patient developed uncontrollable crying, appropriate actions will be taken accordingly (i.e offer milk, give dextrose 10% as a analgesic)

Two designated trained staff started stimulation which consist of a gentle tapping at the suprapubic area for 30 seconds subsequently followed by stimulation of lumbar paravertebral zone in the lower back with circular motion of 30 seconds. Both stimulation manouvres were repeated until micturition started and a midstream sample can be caught in a sterile collector and time limit is 5 minutes. The manouvre was done within 5 minutes time limit. If no urine collected, we continued for another 5 minutes. Thus 10 minutes in total duration study. Time was recorded from the end of feeding until sample collected.

We were aware that patient might be having excessive cry or redness at the massaged area. If patient cried during manouvres, we stopped and determined the cause, either he/ she needed milk, passed stool or had discomfort secondary to the manouvre. If it is caused by the discomfort, we offered dextrose 10% 5-10ml as an analgesia.

As for the controlled group, they were also be given milk according to their needs, right after they completed their feeds, sterile collector is placed near the neonates and time will be recorded from the start of they finish their feeds and urine collection sample collected within 10 minutes as well.

During the study period, every babies only had to participate once and time needed were 10 minutes starting from the finished feeding until urine collected in 10 minutes. If no urine collected in 10 minutes, we concluded as no urine collected in the time frame.

Once urine was collected, sample was sent to lab for analysis. Result of the urine sample were reviewed via LIS system that was available in Hospital University Science Malaysia

4.11 Statistical Analysis

Data entry and analysis was performed using Statistical Package for Social Sciences (SPSS) Version 22 software. The outcomes were analyzed using both intention to treat and per-protocol analysis. Numerical data was expressed using mean (SD) or median (IQR) depending on the distribution. The distribution was checked using histogram with normal curve.

5. RESULTS

5.1 Demographic Data

A total of 120 participants were assessed for eligibility to participate in the study, in the month of November 2016 until 28 Nov 2016 in Ward NICU, SCN and Paediatric Clinic, Hospital USM. One hundred and ten babies were enrolled based on the preset inclusion and exclusion criteria. One group received bladder stimulation technique (intervention group) and the other group clean catch urine (control group) as illustrated in **Figure 5.1**

As per protocol, 10 babies were excluded from analysis, 4 from control group and 6 from intervention group due to various reasons as listed in **Figure 5.1**. Hence a total of 56 babies in the control group and 54 babies in intervention group were analyzed.

Table 5.1 is showing the baseline demographic data of the participants. The different mean age for both groups is statistically not significant. As for the gender, in intervention and control group, is also not statistically significant as the p-value is 0.09. In the intervention and control group, as for the birth weight and current weight, were also statistically not significant as the p- value is 0.22 with mean difference -0.12 (0.09, -0.32) and 0.26 with mean difference of -0.13 (-0.5,0.96) respectively. The p value for gestational age is 0.83, thus it is not statistically significant. In the indication for urine examination, the p-value (Fisher Exact Test) is 0.39. Thus, there were not statistically significant differences in the age of study infants, gestational age (weeks), birth weight, current weight, gender and indication for urine collection

Table 5.1 Demographic Data of Participants

	Intervention (n=54)	Control (n=56)	p-value
Age ,mean (SD)	15.3 (10.4)	15.1(9.8)	0.39[a]
Gender ,n(%)			
Male	29 (53.7)	39 (69.6)	0.09[b]
Female	25 (46.3)	17 (30.4)	
Birth weight,mean (SD)	2.9 (0.52)	2.9(0.48)	0.22[a]
Current weight,mean (SD)	3.3 (0.59)	3.5(0.59)	0.26[a]
Gestational age,mean (SD)	38.1(1.58)	38.1(1.72)	0.83[a]
Indication for urine collection			
Prolonged jaundice	29 (53.7)	32 (57.1)	
Presumed sepsis	20 (37)	23 (41.1)	0.39[c]
Mother Group B Streptococcus Carrier	3(5.6)	0(0)	
	2(3.7)	1(1.8)	

[a] Independent t Test [b] Chi-square [c] Fisher-Exact Test

Figure 5.1 Flow Chart for Experimental Design

Randomized Control Trial Comparing Bladder Stimulation versus Conventional Technique For Urine Collection in Neonates

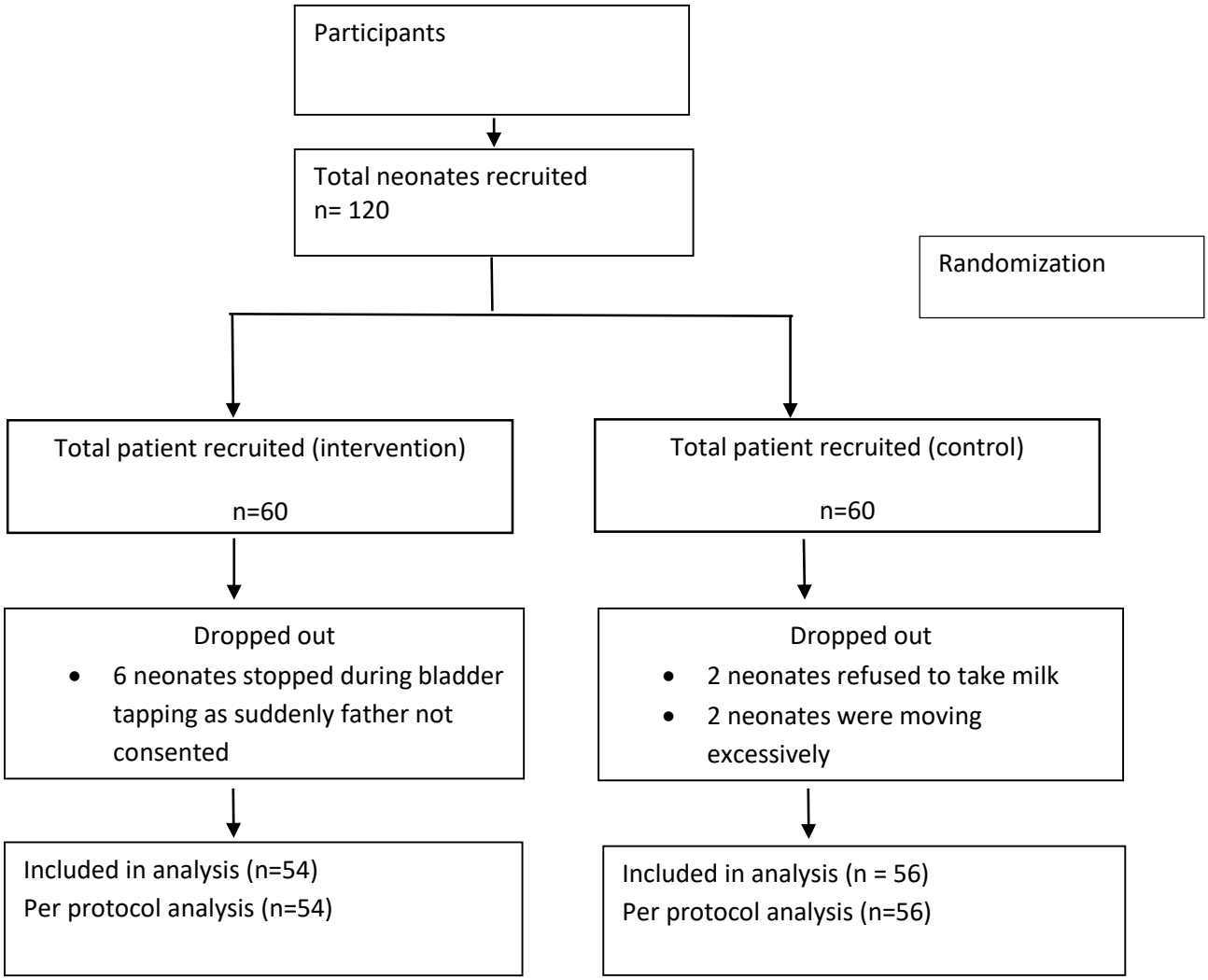


Figure 5.2 Time to Pass Urine in Overall Neonates

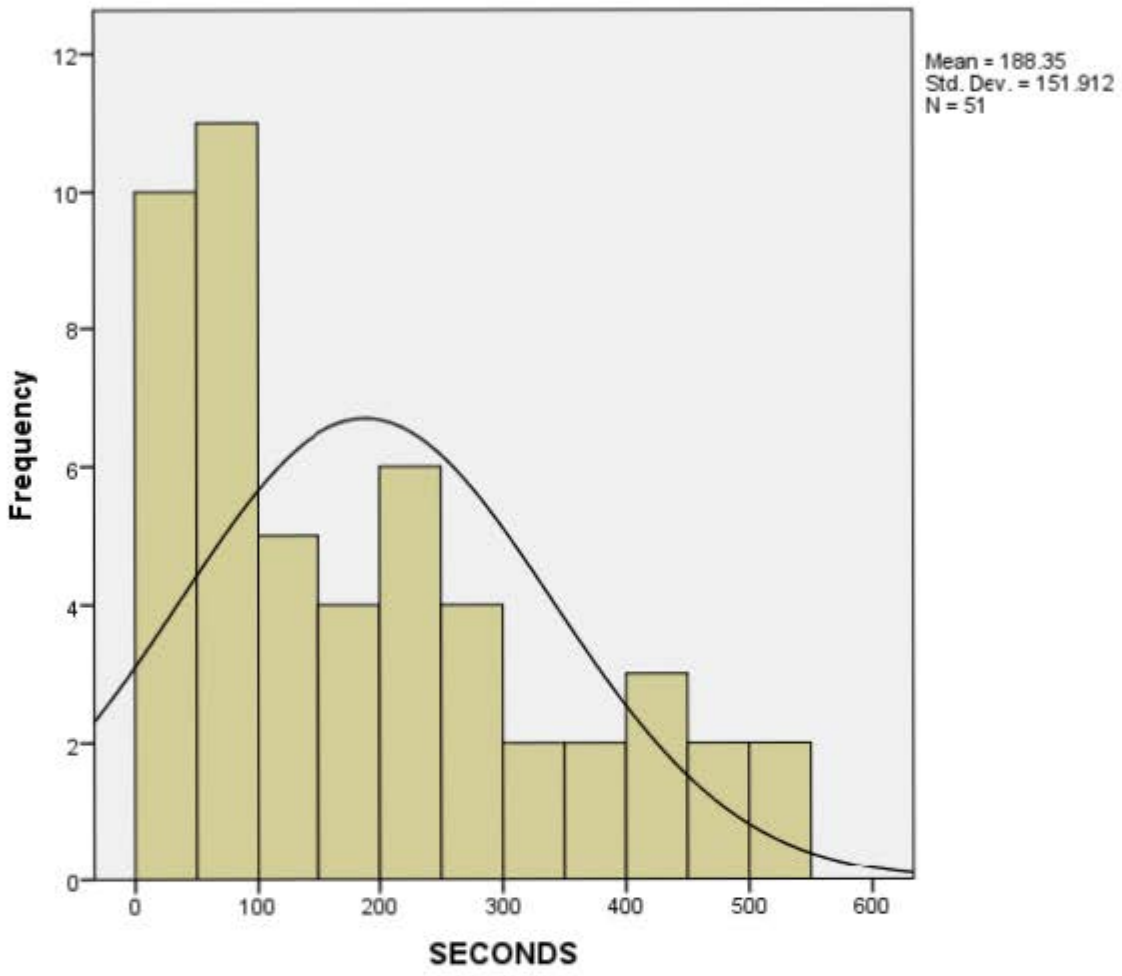


Figure 5.3 Time to Pass Urine in Neonates in Intervention Group

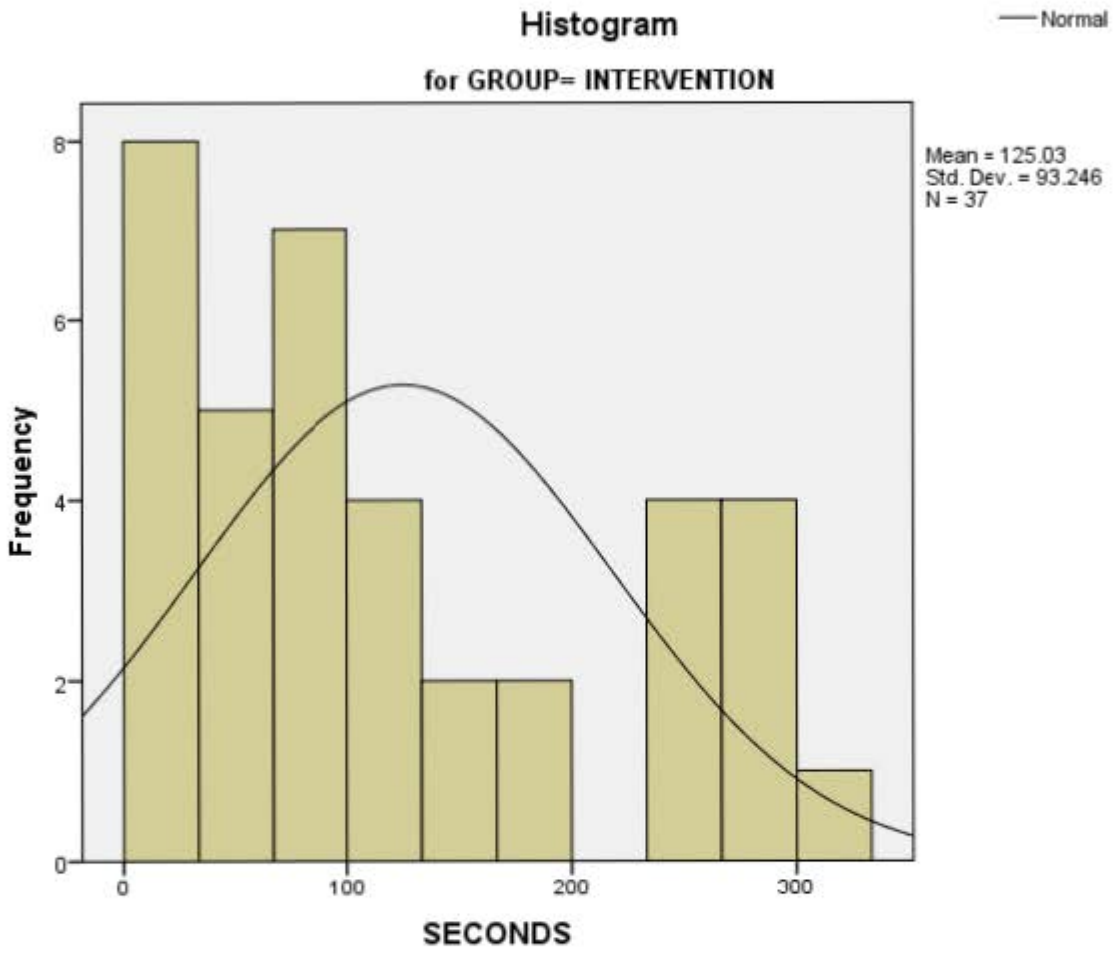
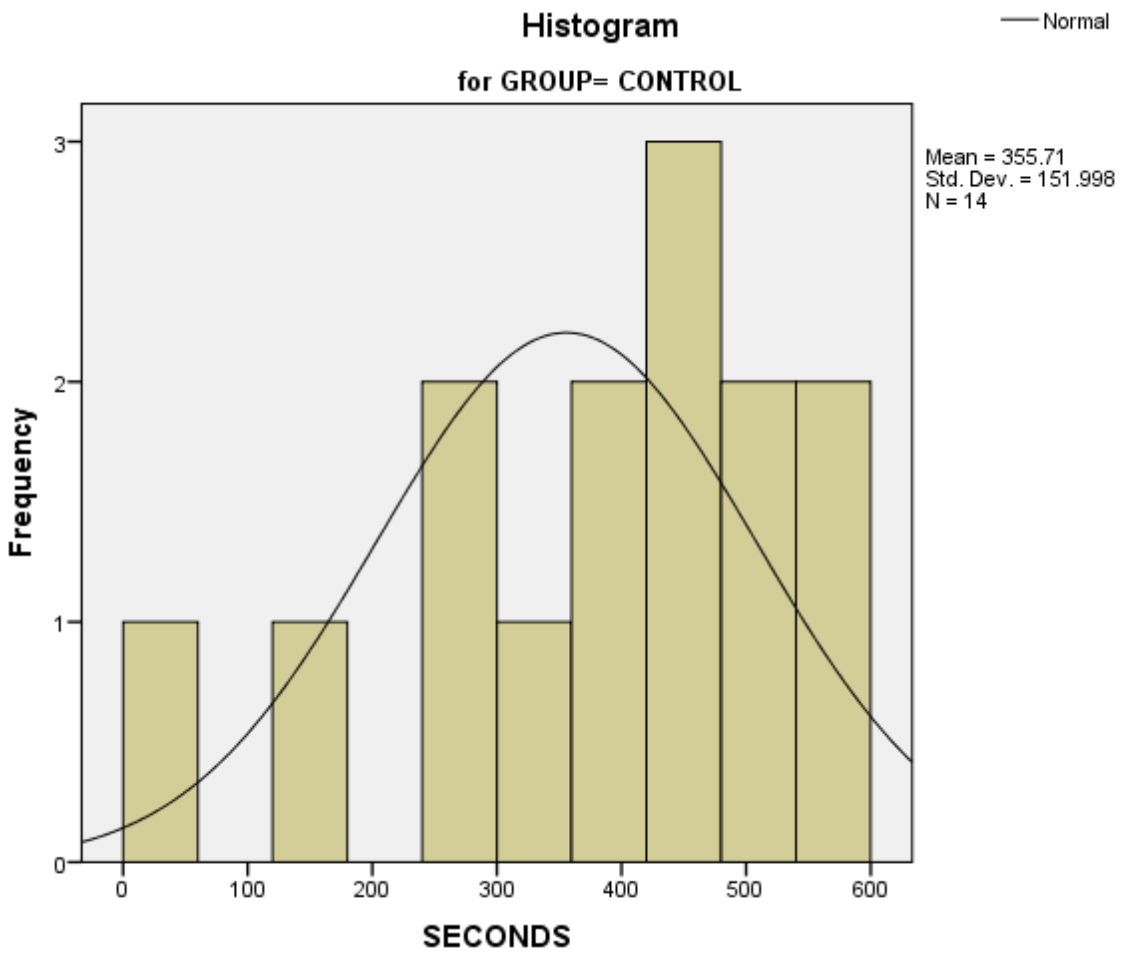


Figure 5.4 Time to Pass Urine in Neonates in Control Group



5.2 Specific Objective- Success Rate of Urine Collection in the Intervention and Control Group

The specific objective of this study was to compare the successful rate of urine collection in the intervention and control group. As we can see from the Figure 5.2, showing the overall time to pass urine in both groups. In **Figure 5.3,** is showing the time to pass urine in the intervention group. We can say that in the intervention group, there were more neonates pass urine in less than 300 seconds (5minutes). Whereas in the control group, **Figure 5.4**, less neonates pass urine less than 300 seconds (5 minutes)

5.4 Subsidiary objectives

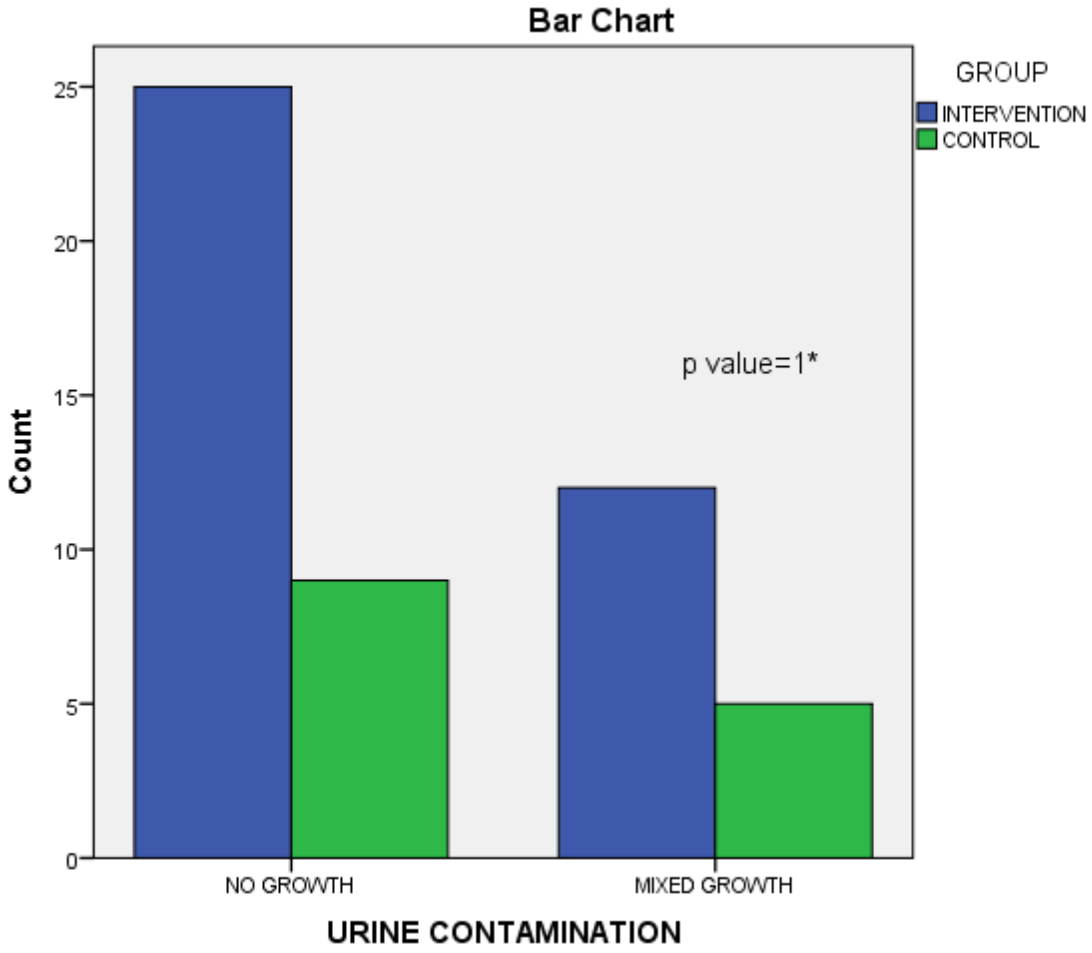
5.4.1 To compare the adverse Events in the Intervention and Control Group.

The first subsidiary objective was to compare the adverse events between the intervention and control group. There were not statistically significant different in the adverse events as we only encountered one neonate had uncontrolled crying in the intervention group. None of them, where the parents complaints of redness of the skin on any other parental complaints. Apart from the adverse event mentioned above, we also compare rate of urine contamination in the intervention and control group.

5.4.2 Rate of Urine Contamination in the Intervention and Control Groups

In our study, there were higher contamination rate in the intervention group as compared to the control group, as in **Figure 5.5.** The contamination rate in intervention group was 12 and in the control group was 5. However these were not statistically significant as the p value was 1.

5.5 Urine contamination in Intervention and Control Group (n=51)



***Fisher Exact Test**

5.4.3 To Compare the Mean Time to Collect Urine between Two Groups

The second subsidiary outcome was to compare the mean time to collect urine between two groups. Figure 5.6 is showing the mean time to collect urine in the intervention group is faster than in the control group with 125 seconds and 355 seconds respectively with p-value of <0.001

Figure 5.6 Mean Time to Collect Urine between Two Groups