


The efficacy of a homoeopathic complex (Cantharis vesicatoris 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Staphisagria 12CH, Uva ursi 12CH) in the treatment of nocturnal enuresis in children between the ages of five and eighteen years, residing in children's homes.

By

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Dissertation submitted in partial compliance with the requirements for the Master's Degree in Technology: Homoeopathy, in the Faculty of Health Sciences at the Durban Institute of Technology.

I, Heather Lockyear, declare that this dissertation is representative of my own work, both in conception and execution.


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DEDICATIONS

Ted and Denise Lockyear

I would like to thank my mom and dad for their financial and emotional support as well as their abundance of unconditional love, which is my strength. They have always encouraged and believed in me.

Jamie Lockyear

My brother for friendship, love, homoeopathic books and my entertainment budget!

E

My fairy gran, who is always there.

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ABSTRACT

The purpose of this randomised double blind study was to evaluate the efficacy of the homoeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH) in the treatment of nocturnal enuresis with regard to the number of wet nights per week. It focused on children between the ages of five and eighteen, residing at children's homes in the greater Durban area. It was hypothesised that the homoeopathic medication would reduce the weekly incidences of bedwetting and thus provide a, safe, viable and effective alternative to existing treatment options.

The motivation for this trial was based on the high incidence of enuresis in children's homes. A literary search yielded a paucity of placebo controlled homoeopathic trials on this subject despite anecdotal and clinical evidence suggesting its efficacy in treating enuresis. In order to participate in the trial the children, together with their guardians, were required to sign assent and consent forms respectively after which the children could undergo a homoeopathic interview, physical examination and urinalysis, ensuring that inclusion and exclusion criteria were met.

Thirty-one children participated in the trial. They were randomly divided into two groups: fifteen children received the homoeopathic complex and sixteen received placebo. The trial was conducted over an eight week period. The first two weeks served as an observation period and baseline for statistical analysis, followed by two weeks of

treatment during which the treatment group received lactose powders impregnated with the homoeopathic complex in 73% alcohol whereas the placebo group received lactose powders identical in appearance but impregnated with 73% alcohol alone. The last four weeks of the trial were for observation purposes to record any changes in the incidences of wet nights. Upon completion of the study, the placebo group was offered treatment free of charge.

The results were analysed at a 95% confidence level as follows:

- Demographic data looked at age and gender distributions amongst subjects.
- The average number of wet nights per group was represented graphically.
- Comparisons based on percentage differences between the placebo and control groups were made.
- Wilcoxon's Signed rank test was used to evaluate improvement within each group i.e. intra group analysis.
- The Mann-Whitney U test was used to compare the groups i.e. inter group analysis.

Statistical analysis of the results revealed that the homoeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH) did not reduce the weekly incidences of bedwetting in a statistically significant way. Improvement in both groups over the duration of the trial was inconsistent and thus unlikely due to homoeopathic treatment. The improvement may be explained in terms of a placebo effect i.e. improvement not due to the medicinal effect of the substance but due to other factors.

One explanation for the limited success observed in this study could be that the complex was inappropriate for treating enuresis in the context of children’s homes. The complex in this study focused on the urogenital system and enuresis as apposed to mental emotional symptoms. In retrospect, enuresis in children’s homes has a significant psychological component and thus more significant results may have been observed had the complex placed greater emphasis on addressing the mental emotional nature of the condition.

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DEFINITION OF TERMS

Antidiuretic hormone (ADH)

Hormone secreted by the posterior pituitary gland that increases the permeability of the collecting tubules and collecting ducts in the kidney allowing greater reabsorption and hence less excretion of water from the body (Guyton, 1992).

Complex remedies

Combinations of two or more homoeopathic medicines, which are prepared from more than one stock and incorporated into one dosage form. These medicines are generally complementary remedies. Also referred to as combination remedies (Swayne, 2000: 46).

Enuresis

Ullom-Minnich defines enuresis as the involuntary discharge of urine after the age by which bladder control should have been established, usually considered to be the age of five years.

Primary nocturnal enuresis is the failure to achieve dryness at night consistently. It accounts for more than 90% of enuresis.

Secondary enuresis refers to the return of incontinence after an extended period of dryness (1996: 2259).

Homoeopathy

A therapeutic method using preparations of substances whose effects when administered to healthy subjects correspond to the manifestations of the disorder (symptoms, clinical signs, pathological states) in the individual patient... known as the similia principle. The method was developed by Samuel Hahnemann (1755-1843).

Homoeopathic materia medica

The description of the nature and therapeutic repertoire of homoeopathic medicines; of the pathology, the symptoms and signs and their modifying factors (modalities), and the general characteristics of the patient associated with them, derived from their toxicology, homoeopathic pathogenetic trials (provings) and clinical experience of their use (Swayne, 2000: 133).

Hydroureteronephrosis

Distension of the ureter and kidney with urine or fluid (Dorland, 1995: 390).

Parasympathetic nervous system

The cranial sacral portion of the autonomic nervous system, its preganglionic fibers traveling with cranial nerves III, VII, IX, X, and XI, and with the second to fourth sacral

ventral routes. It innervates the heart, smooth muscle and glands of the head and neck, and thoracic, abdominal, and pelvic viscera (Guyton, 1992).

Placebo

Swayne (2000: 162) defines placebo as an inactive agent used for comparison with the substance or method to be tested in a controlled trial, and indistinguishable from it.

Placebo group

The group of subjects in a trial receiving placebo, usually as a measure against which treatment is compared.

Potency

The power, vitality, strength, or dynamis, which a homoeopathic remedy possesses, often represented as a number attached to the remedy name, either immediately before or after.

The potency of the remedy comes as a result of the succussion step in the remedy preparation process (Yasgur, 1998: 193).

Potentisation

The process of preparing a homoeopathic potency through serial dilution and succussion or trituration.

Proving

The process of determining the medicinal properties of a substance; testing substances in material dose, mother tincture or potency, by administration to healthy volunteers, to elicit effects from which the therapeutic potential or materia medica of the substance may be derived.

The effects of a homoeopathic medicine used in treatment that are characteristic of the materia medica of the medicine itself and not of the patient or the illness (Swayne, 2000; 174).

Remedy

For the purpose of this study, a remedy refers specifically to a medicine made up according to homoeopathic principles.

Repertory

Systemic cross reference of symptoms and disorders to the homoeopathic medicines in whose therapeutic repertoire (materia medica) they occur... used in case analysis to identify the medicine indicated for the patient. This process is called repertorisation (Swayne, 2000: 183).

Simillimum

The simillimum is the drug picture that is most like the clinical picture in the patient (Swayne, 2000: 194).

Success

Success in this study is defined by a 50% improvement i.e. a 50% reduction in the weekly incidences of bedwetting in subjects.

Succussion

Vigorous shaking, with impact or 'elastic collision', carried out at each stage of dilution in the preparation of a homoeopathic potency (Swayne, 2000: 165).

Sympathetic nervous system

The thoracolumbar part of the autonomic nervous system, the preganglionic fibers of which arise from cell bodies in the thoracic and first three lumbar segments of the spinal cord. Postganglionic fibers are distributed to the heart, smooth muscle, and glands of the entire body (Guyton, 1992).

Treatment group

The group of subjects in a trial receiving treatment that is hypothesized to be specific for a given condition.

Urinalysis

Analysis of the urine using urine dipsticks, which indicate the chemical constituents and status of the urine.

CHAPTER 1

INTRODUCTION

Enuresis can be defined as the involuntary discharge of urine after an age, usually five years, by which time bladder control should have been established (Ullom-Minnich, 1996: 2259). More specifically, nocturnal enuresis is the voiding of urine at night without the child noticing it (Norgaard et al., 1998: 1).

Traditionally nocturnal enuresis is divided into primary and secondary enuresis. Primary enuresis refers to the failure to achieve dryness and accounts for more than 90% of cases whereas secondary enuresis refers to the return of incontinence after a period of dryness (Ullom- Minnich, 1996: 2259).

The incidence of nocturnal enuresis appears to be high in the United States (Ullom-Minnich, 1996: 2259). There are no epidemiological studies in South Africa on the subject, although it was recognized to be a significant problem in children's homes in Durban (Govender, 2001).

Despite the prevalence of nocturnal enuresis, the aetiology, understanding and hence treatment of the condition remains unclear and controversial. The condition seems to be

multifactorial (Cendron, 1999: 2). Possible aetiologies of primary nocturnal enuresis include developmental delay, genetics, sleep disorders, behaviour and psychogenic disorders, constipation and increased diuresis at night due to low levels of antidiuretic hormone (Cendron, 1992: 2). Causes of secondary enuresis include neurogenic bladder and associated spinal cord abnormalities, urinary tract infections and urethral disorders (Cendron, 1999: 4).

Pharmacological and non-pharmacological treatment options exist for dealing with the condition. The main drugs of choice are Imipramine hydrochloride (Tofranil), an antidepressant; Oxybutynin chloride (Ditropan), an antispasmodic agent; and Desmopressin acetate (DDAVP), a synthetic antidiuretic hormone. None of these medications offer a cure, but are a stopgap measure until the children are able to wake on their own to void urine (Cendron, 1999: 5-8). These drugs are also known to have side effects (Appendix 7) and can be costly. Non-pharmacological treatments include the alarm system, bladder stretching, dry bed training, hypnosis and chiropractics (Ullom-Minnich, 1996: 2264; Grobler, 1996).

Clinical experience and success in the treatment of nocturnal enuresis with homeopathy are recorded in several reputable homeopathic materia medicas e.g. Farrington (1950), Herscu (1991), Nash (1997) and Vermeulen (1994). Journal articles also discuss cured cases with the use of homeopathic remedies (Sharma, 1995; Popescu, 1988; Jaiswal, 1989). No double blind clinical trials have been conducted on the use of a homeopathic complex in the treatment of nocturnal enuresis.

1.1 Objectives

This study proposed to evaluate the efficacy of the homeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH) in the treatment of nocturnal enuresis with regard to the number of wet nights per week. It focused on children between the ages of five and eighteen, residing at children's homes in the greater Durban area. It was hypothesised that the study would demonstrate the complex to be a viable, safe and effective alternative to existing treatment options.

In order to statistically evaluate the effect of the homeopathic complex by means of hypothesis testing, three objectives were identified:

Objective one proposed to evaluate the response of the placebo group to the placebo treatment, in order to evaluate the role placebo played in the management of nocturnal enuresis. Wilcoxon's Signed Rank test was used to compare the intra-group data from this group (Statistical procedure 1).

Objective two proposed to evaluate the response of the treatment group to the homeopathic complex, in order to evaluate the role this played in the management of nocturnal enuresis. Wilcoxon's Signed Rank test was used to compare the intra-group data from this group (Statistical procedure 2).

The third objective proposed to compare the responses of the treatment and placebo groups in order to evaluate the efficacy of the homoeopathic complex in the treatment of nocturnal enuresis. The Mann-Whitney U test was used to perform the inter-group comparisons (Statistical procedure 3).

CHAPTER 2

REVIEW OF THE RELATED LITERATURE

2.1 Introduction

The following discussion will review literature concerning functional nocturnal enuresis. The focus will be on understanding what constitutes nocturnal enuresis, the physiology of this condition as pertains to this study, and the current treatment modalities employed to manage this condition.

2.2 Definition

Enuresis can be defined as “involuntary discharge of urine after the age by which bladder control should have been established... usually five years” (Ullom-Minnich, 1996: 2259).

Norgaard *et al.* (1998:1), describes nocturnal enuresis as the voiding of urine in bed at night without the child noticing it. Most authors further subdivide enuresis into primary and secondary types. “Primary enuresis is the failure to achieve dryness consistently and accounts for more than ninety percent” whereas “secondary enuresis refers to the return of incontinence after an extended period of dryness” (Ullom-Minnich, 1996:2259).

Norgaard *et al.* (1998:2) suggest that secondary enuresis should include an extended period of dryness of six months or more. According to Medel *et al.* (1998:50) nocturnal enuresis should be classified into mono-symptomatic and complicated types depending

on whether bedwetting is the only symptom or is associated with urinary tract infections, diurnal incontinence or urgency. Thus for the purposes of this research mono-symptomatic primary and secondary enuresis will be considered thereby separating children with a definable aetiology from those without.

2.3 Physiological anatomy of the bladder

The bladder is a hollow muscular viscus found in the pelvic cavity for the purpose of storing urine. Its shape, size, position, and relations vary with the amount of urine it contains and with the age of the person. An empty adult bladder lies in the pelvis minor. As it fills it extends into the pelvis major and can reach the level of the umbilicus in a very full bladder. An infant's bladder rests in the abdominal cavity until age six when it shifts down into the pelvis major, only residing completely in the pelvis minor after puberty (Moore, 1985: 275).

The bladder consists principally of two parts: (1) the body, which is the major part, storing and receiving urine via the two ureters, and (2) the neck, which is a funnel shaped extension of the body, passing inferiorly to the urethra. The smooth muscle of the bladder is known as the detrusor muscle. The bladder has two sphincters: (1) the internal sphincter, which consists of smooth muscle and makes up the neck of the bladder and is under involuntary control and (2) the external sphincter, which is a layer of voluntary skeletal muscle making up the urogenital diaphragm through which the urethra passes.

The natural tone of the internal sphincter keeps the bladder neck and posterior urethra empty of urine and therefore prevents emptying of the bladder until the pressure in the body of the bladder rises above a critical threshold. The external sphincter, being under voluntary control, can be used to prevent urination even when the involuntary controls are attempting to empty the bladder.

2.3.1 Innervation of the bladder

The bladder has both a parasympathetic and a sympathetic nerve supply. The principal innervation of the bladder is via the parasympathetic pelvic splanchnic nerves (S2, S3 and S4). The detrusor muscle is governed by the motor component of this plexus, which causes the bladder to contract in response to being stretched. The sensory component is inhibitory to the internal sphincter causing it to relax as the bladder contracts, allowing the urine to flow into the urethra. The parasympathetic nerves are thus exclusively responsible for emptying the bladder. The sympathetic fibres are derived from T11, T12, L1, and L2 nerves and are probably inhibitory to the bladder.

The external sphincter of the bladder is innervated by the motor fibres from the pelvic and pudendal nerves, which are somatic to the voluntary skeletal muscle of the sphincter. (Guyton, 992: 244; Moore, 985: 277).

2.3.2 Micturition and the micturition reflex

The process whereby the bladder empties when it becomes filled is called micturition.

There are basically two components to the process: (1) the bladder fills until the tension in its walls rises above a threshold level which results in (2) a nervous reflex called the micturition reflex that either causes micturition or at least causes a conscious desire to urinate. Thus micturition contractions are a result of a stretch reflex initiated by stretch receptors in the bladder wall. Sensory signals are conducted to the sacral segment of the cord through the pelvic nerves and then back again to the bladder through the parasympathetic fibres in these same nerves. A micturition reflex is self-regenerative once it begins. That is, an initial contraction of the bladder activates the receptors to cause still further increase in sensory impulses from the bladder and posterior urethra, which causes further increase in reflex contraction of the bladder. This cycle repeats itself again and again until the bladder has reached a strong degree of contraction. The reflex begins to fatigue after anything from a few seconds to over a minute, leading to a cease in the regenerative cycle of micturition reflex and a rapid reduction in bladder contraction. Once a micturition reflex has occurred but has been unsuccessful in emptying the bladder, the nervous elements of this reflex remain inhibited for at least a few minutes to an hour or more until the next reflex occurs. However as the bladder becomes more and more filled, the micturition reflexes occur more often and more powerfully until eventually another reflex via the pudendal nerves leads to the inhibition of the external sphincter. If this inhibition is more powerful than the voluntary constrictor signals from the brain to the external sphincter, urination will occur. If not, urination will not occur

until the bladder fills sufficiently to result in a strong enough micturition reflex to override the voluntary control over the external sphincter. (Guyton, 1992: 244-245).

2.3.3 Control of micturition by the brain

Despite the micturition reflex being an automatic cord reflex, the brain is able to override it through: (1) strong facilitatory and inhibitory centers in the brain stem and, (2) mainly inhibitory but at times excitatory centers in the cerebral cortex.

Thus, the brain exerts final control over micturition in the following way:

- the higher centers keep the micturition reflex partially inhibited all the time except when micturition is desired.
- even if a micturition reflex occurs, the higher centers prevent micturition by continued tonic contraction of the external sphincter until a convenient time.
- when the time to urinate arrives, the cortical centers can (a) facilitate the sacral micturition centers to help initiate a micturition reflex and (b) inhibit the external sphincter so that urination can occur. (Guyton, 1992: 244-245).

2.4 Aetiology

The aetiology of primary nocturnal enuresis has been widely debated but is not yet completely understood. Primary nocturnal enuresis is a diagnosis of exclusion and all other causes of bedwetting must be ruled out (Cendron, 1999:2). Causes of secondary

enuresis include neurogenic bladder and associated spinal cord abnormalities, urinary tract infections, and the presence of posterior urethral valves in boys or an ectopic ureter in girls. Posterior urethral valves cause significant voiding symptoms, such as straining to void and diminished urinary stream. An ectopic ureter causes constant wetting (Cendron, 1999).

The aetiology of primary nocturnal enuresis remains somewhat controversial, and the condition appears to be multifactorial (Cendron, 1999: 2). In addition, the well-recognised spontaneous resolution rate clouds the search for causative mechanisms. Possible aetiologies of primary nocturnal enuresis include developmental delay, genetics, sleep disorders, behavior and psychogenic disorders (Cendron, 1999: 2), constipation and increased diuresis at night due to low levels of antidiuretic hormone (Ullom-Minnich, 1996: 2259).

Maturational delay of the central nervous system is the most common form of nocturnal enuresis. The bladder fills, but the sensory information from the stretching of the bladder is not perceived or not sent to the brain thus central cortical control over the urinary sphincter contraction does not occur. Failure of the arousal mechanism may also contribute to the inability to inhibit micturition leading to incontinence during sleep (Cendron, 1999).

Genetics appears to play a strong role in nocturnal enuresis. One study found that only 15 % of children with enuresis had no family history of enuresis; 44% of children had one parent with enuresis, while 77% had a history of enuresis in both parents (Cendron, 1999).

There is varied information regarding the role sleep patterns play in enuretic subjects. Recent studies however have shown that bed-wetting may occur in any stage and is randomly distributed throughout the different sleep stages. One study indicates that enuretic children have difficulty in waking. This could be due to a neurological developmental delay (Cendron, 1999).

Psychological factors are thought to be an unlikely cause of primary enuresis. However a Danish study showed that patients with primary nocturnal enuresis seem to have a poorer sense of belonging to society and clearly have lowered self-esteem (Cendron, 1999). Stress during critical times of learning and development may affect normal development of bowel and bladder control. There appears to be an increased incidence of bed wetting in children from broken homes or in those who have experienced traumatic separations from their families. Although stress may not be the cause in the majority of cases, it should be considered as a contributing factor when a child reverts to bedwetting after attaining normal bladder control both by day and by night. In children with severe psychological or psychiatric problems, bedwetting can be part of a symptom complex. However, it is usually obvious that the enuresis is only part of an overall problem (Rosenfeld, as cited by Grobler, 1996: 16).

A more recent hypothesis is that children tend to diurese at night. Diurnal analysis of antidiuretic hormone (ADH) levels showed that the serum levels were constant in children with enuresis, while control subjects showed a diurnal antidiuretic hormone variation with a nighttime increase. ADH is a hormone secreted by the posterior pituitary gland that increases the permeability of the collecting tubules and collecting ducts in the kidney allowing greater reabsorption and hence less excretion of water from the body (Guyton, 1992). These findings suggest that children with enuresis have a normal bladder capacity that is exceeded by a high urine output at night. This high urine output results from the lack of an increase in antidiuretic hormone secretion at night. This hypothesis is the basis for desmopressin (DDAVP) therapy (Ullom-Minnich, 1996: 2261).

Excessive investigations should be discouraged, as most children with nocturnal enuresis have neither a psychiatric nor organic cause. However, urinary tract infections, Diabetes mellitus and an active urinary sedimentation rate suggesting the presence of underlying kidney disease, must be ruled out by performing a urinalysis on enuretic children. Only when abnormal findings are noted from the physical examination and/or urinalysis, should imaging studies and a urodynamic evaluation be considered to exclude vesicourethral reflux, bladder outlet obstruction, and hydroureteronephrosis associated with a thickened unstable bladder (Rushton and Warady et al., as cited by Grobler, 1996).

2.5 Prevalence

There are no epidemiological studies in South Africa on the subject. Authors from various texts concur with Marla et al. (1996:2259) that 10-20% of 5 year olds, 5-7% of 10 year olds and 2-4% of 12 to 14 year old children are affected. Cendron and Klauber (1998:26) report a spontaneous resolution rate of 15%, which is supported by other authors. Cendron (1999:2) further states that an estimated 5 to 7 million children are affected in the United States. The above figures suggest a notable prevalence despite the lack of local verification.

2.6 Treatment

2.6.1 Introduction

The treatment of and therapeutic approach to nocturnal enuresis is complicated by the multifactoral nature of the condition, lack of clear aetiology and pathophysiological understanding of the condition (Cendron, 1999: 2). The treatment can be divided into two broad categories, pharmacological and non-pharmacological.

2.6.2 Pharmacological treatment

2.6.2.1 Anticholinergic treatment

Studies done on the effectiveness of Oxybutynin chloride and Hyoscyamine are limited. They appear to act on smooth muscle, decreasing the bladders capacity to contract (Ullom-Minnich, 1996: 2259). Hyoscyamine is available in time release capsules, 0.375mg at bedtime, and is reported to be effective for at least eight to ten hours. Oxybutynin is administered in dosages of 5mg at bedtime in children over five years of age, increasing to 10mg in older children. A prospective study of thirty children with enuresis showed no difference in the response of children who were given 10mg of oxybutynin compared with children given placebo. The most common reported side effects (appendix 7) of anticholinergics in children are dry mouth, facial flushing, drowsiness, constipation, dizziness and occasional tremulousness (Cendron, 1999: 8). Cendron and Klauber (1998) demonstrated a 60% success rate in a study using Hyoscyamine and Desmopressin combined. The relapse rate however was high, pointing to palliation rather than cure.

2.6.2.2 Imipramine hydrochloride

This drug, a tricyclic antidepressant, has been used for approximately 25 years. It is hypothesized to either alter the sleep and arousal mechanism, affect sympathetic innervation of the bladder, increase the secretion of anti diuretic hormone or a

combination of these. The initial dosage of imipramine is 25 mg taken one hour before bed. If response is not satisfactory after two weeks the dosage can be increased to 50mg and in older children up to 75mg (Cendron, 1999: 9). Success rates range from 25%-50% with a relapse rate of 30% (Ullom-Minnich, 1996: 2259). Side effects (appendix 7) are common including anxiety, insomnia, dry mouth, nausea, personality changes, sleep disorders, tiredness and nervousness. Imipramine has also been associated with severe accidental overdose in both patients and their siblings (Cendron, 1999: 9).

2.6.2.3 Desmopressin Acetate

Desmopressin Acetate (DDAVP) is an anti diuretic, decreasing urine production at night by raising ADH levels. In patients without enuresis, the production of antidiuretic hormone increases at night, reducing the amount of urine produced. Enuretic subjects have been found to lack the normal diurnal rhythm of antidiuretic hormone and thus produce more urine a night. The success rate varies between studies from 10 to 70%, but all confirm limited if any side effects (appendix 7). Desmopressin is administered through nasal insufflation. It has a relatively long half-life of four to six hours and an extended duration of action. Patients should receive desmopressin for at least three to six months after which they should gradually be tapered off it. Desmopressin can be used intermittently by patients who have responded well to it in the past and thus can be used on an as needed basis (Cendron, 1999: 9). It is presently the drug of choice (Lackgren et al., 1988).

2.6.3 Non pharmacological treatment

According to Ullom-Minnich (1996), non- pharmacological treatments are usually used in combination with one another or in conjunction with pharmacological treatments. The alarm system is approximately 70% effective with a relapse rate of 30%. Bladder stretching, in which the child has to withhold urination for increasing amounts of time has an improvement rate of 60% but is time consuming and requires motivation. Dry bed training, which includes night waking, cleanliness training, positive practice and the alarm has an 85%-100% success rate and is considered a good treatment option. Hypnosis has a 40%-70% success rate but is expensive. Under hypnosis, the child is given suggestions to hold urine, to refrain from wetting and to use the toilet when necessary (Ullom- Minnich, 1996). One study has demonstrated a 40% success rate in the treatment of functional nocturnal enuresis with chiropractic manipulation therapy (Grobler, 1996).

2.7 Homeopathy

2.7.1 What is Homeopathy?

Boyd (1989: 1) defines homeopathy as a system of therapeutics for treating people and animals on the basis of the simile principle i.e. “Similia similibus curenter” or “Let like be treated by like”. The word homeopathy is derived from the Greek words “homoios”, meaning like or similar, and “ pathos”, meaning suffering. Thus the most appropriate

remedy is the one with a symptomatology i.e. symptoms that it is able to produce in a healthy person that most closely resembles the symptom-complex of the sick person.

Hahnemann, the founder of homeopathy, considered the action of the remedy to be due to its production of an artificial disease similar to the patients' illness. This artificial disease elicits a reaction from the body, which in turn cures the illness. The aim of homeopathy is not to remove or suppress symptoms but to restore the total balance of the organism. The 'totality of symptoms' and their relationship to each other guide the practitioner to the selection of a remedy, which will provide the stimulus to recovery (Boyd, 1989: 2-5).

Another principle in homeopathy is the use of remedies in extremely small quantities. The use of what are called 'potentised' remedies, is an extension of the method evolved by Hahnemann from experiment, and is not in itself homeopathy (Boyd, 1989: 4). The process of potentisation has two components: 1) serial dilution, in which the substance becomes less and less concentrated through dilution and therefore further removed from its toxicological effect and 2) succussion, which involves vigorous shaking of the remedy at each stage of dilution, which is thought to raise the efficacy and power of the remedy (Boyd, 1989: 53-54).

The concept of individuality is also an important principle in homeopathy. Homeopathy does not treat disease, but individuals. In other words an accurate prescription depends upon the correct match between the specific characteristics of the medicine and the individual characteristics of the illness as seen in the patient (Swayne, 1998: 23). Swayne uses asthma as an example stating that many people may suffer from asthma but they

present with distinctly different clinical pictures. It is these differences that are individualizing and thus most important to the homeopathic prescriber. The concept of individualization includes those characteristics that are not pathognomonic of the illness itself e.g. thirst or thirstlessness, irritability or weepiness, but reflect the individual's response to the diseased state. Other personal characteristics, known in homeopathy as constitutional characteristics e.g. temperament, food tastes, weather preferences etc., which are part of the person's healthy state, are also used to individualise the patient and the prescription (Swayne, 1998: 23). Prescribing the simillimum i.e. the remedy that most closely mirrors the individual, involves only giving the patient one remedy at a time. This is referred to as simplex prescribing. Combination prescribing, otherwise known as polypharmacy, differs in that it involves giving more than one remedy at a time.

2.7.2 Advantages of homeopathic treatment

Dana Ullman, discusses the various merits of homeopathy, 'Homeopathy is a sophisticated medical science that individualizes a substance based on the totality of a person's symptoms. No matter what the individual symptoms are, they are recognized as primarily an intrinsic effort of the organism to adapt to and deal with various internal and external stresses. Methods that simply suppress, control, or manage symptoms should be avoided, since such therapies compromise the innate tendency of the organism to defend and heal itself.' (1991: 28). Cendron states that none of the orthodox medications cure enuresis, instead they provide a stopgap measure until children are able to wake on their own to void (1999: 7). 'The side effects that these suppressive treatments cause are

actually direct effects of the treatment. Homeopathic medicines, on the other hand, are prescribed to aid the organism in its highly sophisticated efforts to heal itself. Inherent in the homeopathic approach is a basic respect for the body's wisdom; it is no wonder that it is a safer medicine.'(Ullman, 1991: 27-29).

In the light of the above, homeopathy would appear to be an appropriate treatment option for enuresis. The aetiology of primary nocturnal enuresis is controversial and appears to be multifactorial (Cendron, 1999: 2). Cortina (1994: 222) concluded from his study on subjects with enuresis, that nocturnal enuresis in the child appears to be an unconscious protest against the family or society due to repression or disciplinary excesses. He suggested that additional factors include attention-seeking behavior on the part of the child as well as parental separation or divorce. Homeopathy is able to embrace this complexity by treating the individual within his or her psychosocial context, restoring balance and health, as opposed to merely removing the symptom and not addressing the underlying cause. Dana Ullmann quotes Yehudi Menuhin: "Homeopathy is one of the few medical specialties which carries no penalties-only benefits."(1991: 51).

2.7.3 Combination remedies/Polypharmacy

This type of prescribing is also known as complex prescribing or polypharmacy as it involves prescribing combinations of as many as ten but generally between five and seven remedies, often in different but usually low potencies (Cook, 1989: 73). Complex prescribing is strongly criticized by some homeopaths, who assert that it is contrary to

Hahnemannian principles (Cook, 1989: 73). Complex remedies have never been subject to provings (although their constituents may have been proven individually), so they cannot be administered according to the *simillimum*, as it is not known what they can cause when given to a healthy person (Kayne, 1997: 41). Some describe the use of complex remedies as the “blunderbuss” approach, as opposed to the accurate “rifle” of the single remedy (Cook, 1989: 73). Opponents also argue that if the complex works, the prescriber will not know which of the constituents in the complex the patient responded to. In addition because the complexes are not proven, we do not know how the remedies are going to relate to each other when administered together. Some remedies are complimentary to each other while others are antagonistic (Kayne, 1997: 106).

Despite these valid criticisms of complex prescribing, clinical experience suggests that some homeopathic remedies can be mixed together and administered successfully as a complex (Kayne, 1997: 104). This method of treatment has become very popular in some countries. Kayne (1997: 105) discusses some of the companies that manufacture complexes, these include: Weleda in the UK, Naturo Pharm of Rotura and Miers Laboratories of Wellington in New Zealand, Brauer in South Australia and the Dr Reckeweg Company in Germany. Their survival as companies is perhaps testimony to the efficacy of complexes.

Kayne (1997: 105) suggests three reasons for using a complex instead of a single remedy: 1) the prescriber is uncertain as to which remedy is most appropriate, thus a complex is given to increase the chance of a correct prescription, 2) to treat more than

one symptom at a time e.g. flu with a headache, nausea and sore muscles, which implies complex prescribing deviates from the principal of individuality in that everyone with flu gets the same complex regardless of their individual manifestation of the flu and 3) for convenience i.e. it saves time and trouble.

Complex prescribing pays attention to the physical complaint as apposed to simplex prescribing, which treats the individual rather than the disease (Clover, 1991: 71).

Therefore the constituents of a complex are usually made up in middle range potencies (9-12CH), as these potencies are more effective in influencing tissue and organ function (Gaier, 1991: 433). The constituents of a complex are not always made up in the same potency. Furthermore, the dosage of complexes tends to be more frequent than that of single remedies and higher potencies. Complexes are often repeated daily and for protracted periods of time.

2.7.4 Constituents of the homeopathic complex

The complex employed in this study consisted of the following medicines with their relevant materia medica indications. The remedies chosen for the complex are not known to antidote or antagonize each other.

Cantharis vesicatoria: This medicine is characterized by a violent and aggressive action on the tissues. It is used mainly in disorders involving the mucous membranes, especially in the urinary tract. It can be indicated for involuntary urination or dribbling after

urination, worse during cystitis, worse during menses (Morrison, 1993: 97-98). Cantharis has characteristically small amounts of urine but voided often (Nash, 1997: 422).

Equisetum hyemale: The chief effects of *Equisetum* are found in the urinary organs (Clark, 1999: 707). Sometimes successful in cases which are not relieved by *Cantharis*. There is much inclination to urinate as with *Cantharis*, and there is pain in the bladder, as if it is too full of urine, which must be voided in order to get relief from both pain and pressure, but urination does not satisfy and he must go again soon. *Equisetum* is very useful in enuresis (Nash, 1997: 422). Clark (1999: 707) reaffirms this and adds that it is also useful for night time wetting.

Sarsaparilla: The main action is on the genito-urinary organs. Urine may be scanty, slimy, flaky, sandy or bloody. During the day, urine can only be passed while standing, but at night urine flows freely in bed. There can be crusty sediment in the urine (Vermeulen, 1994: 858). Skin and urinary symptoms may be combined. Indicated for enuresis (Morrison, 1993: 338).

Delphinium staphysagria: This person is very sensitive and may have a lot of suppressed anger. Nervous affections and marked irritability, diseases of the genito-urinary tract and skin, most frequently give symptoms calling for this drug. Sensation as if a drop of urine is rolling continuously along the urethra. There can be frequent urging to urinate with scanty or profuse discharge of watery urine. Involuntary and copious micturition,

especially on coughing (Vermeulen, 1994: 903-904). Morrison specifically lists its efficacy in the treatment of enuresis (1992, 360).

Uva Ursi: Vermeulen (1994: 982) states that the urinary symptoms are most important in this remedy. He goes on to mention that there can be frequent urging and severe spasms of the bladder as well as involuntary urination.

2.7.5 Potency selection

Each constituent in the complex was made up in the 12 CH potency. The rationale for selecting the 12CH potency rests on three tenets. Firstly, the 12CH potency (having a deconcentration of 1×10^{-24}) is the first dilution in which mathematically no molecules of the base substance are understood to exist (Avogadro's constant = 6.023×10^{23}). Thus, the 12CH potency was selected as no pharmacological effects nor harmful side effects were desired.

Secondly, it is generally accepted that the higher potencies (30CH or higher) are more indicated and more effective, the greater the simillimum between the symptom picture and the remedy picture (Jouanny, 1993: 91). In this case there is a relatively low similitude between the symptoms associated with enuresis and the clinical picture seen in the pathogenesis of the various remedy provings. This led the researcher to select the 12CH potency for the complex.

Thirdly, middle range potencies (9CH-12CH) are more effective in influencing tissue and organ function to return to a normal state of physiology (Gaier, 1991: 433).

2.8 Placebo and placebo effect

When approaching the topic of placebos, one is first confronted with a wide variety of usages of the terms 'placebo' and 'placebo effect'. Beecher (1995) defined placebos as 'pharmacologically inert substances'. Still today, a similar description is given: 'A placebo is a pharmacologically inactive substance that can have a therapeutic effect if administered to a patient who believes that he or she is receiving an effective treatment' (Iacono et al 1992). (Peters, 2001: 34). Homung (1994) defined a placebo as an inert preparation that looks like an active medication. Regardless of the uncertainties of the placebo concept, the placebo effect can be defined as the therapeutic effect of a placebo administration (Peters, 2001: 36).

Controversy exists as to what is a 'true' placebo effect as opposed to a 'perceived' placebo effect. The 'perceived' placebo effect, as seen in placebo-controlled trials, is a function of several factors. In order to arrive at the 'true' placebo effect one would need to run clinical trials with three groups: a treatment group, placebo group and untreated group. The 'true' placebo effect could thus be identified by subtracting the effects observed in the untreated control group from those in the placebo group. Such 'three armed' studies are the most unbiased way to investigate placebo effects in the setting of a clinical trial (Peters, 1992: 20).

Many factors are speculated to determine the size of the placebo effect, namely: the nature of the intervention, the therapist, the time factor, the patient, the nature of the complaint and the therapeutic setting. (Peters, 2001:25-26). If we are to optimize the

placebo effect, we need to understand it better than we do today. To reach this aim we should discard several persistent myths and investigate in detail the determinants of its power (Peters, 2001: 27).

2.9 Conclusion

Nocturnal enuresis is a prevalent and perplexing disorder (Butler et al., 1998: 29). The aetiology is unclear and although there are treatment options, few are without side effects and none seem to offer permanent cure. Nocturnal enuresis was found to be of significant concern to children's homes in Durban (Govender, 2001). Finding the simillimum i.e. the single most appropriate remedy is possible but extremely difficult because of language barriers as well as a paucity of information regarding medical and social history i.e. the child's behavior, likes and dislikes. A homeopathic complex bypasses the need for this type of information. There have been no clinical trials on the use of a homeopathic complex in the treatment of nocturnal enuresis.

CHAPTER 3

MATERIALS AND METHODS

3.1 The Data

This study made use of primary and secondary data. The primary data is represented by the number of wet nights the subjects presented with over an eight week period, as well as the medical records of each subject. Secondary data was obtained from the available literature on enuresis, as well as information sourced from the Internet.

3.2 Study design

3.2.1 Introduction

This research is part of a larger group project. It consists of three components, each applying a different approach to the same problem, i.e. the treatment of nocturnal enuresis. This research concerns itself with the use of a homeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH). The other components made use of homeopathic simillimum and Ilex paraguayensis 6x respectively. The clinical trials for the above three approaches were simultaneously run and share a collective placebo group. The results for each component are documented independently.

3.2.2 Subjects

Various children's homes in the Durban area were contacted and asked if they were interested in participating in the study. If interested, they were asked to provide an estimate of the number of children who bed wet as well as the number of incidences per child. A meeting was then set up with the social workers and caregivers of the various homes. At the meeting, the study was explained to them in detail, including homeopathic consultation, treatment and physical examination. Once they understood and agreed to participate in the study, the guardian was required to sign a consent form for each child (Appendix 1), implying that the guardian understood the terms and conditions of the study and agreed to let the child participate on those terms. Each child was also required to sign an assent form (Appendix 2). The assent form is the equivalent of a consent form but worded slightly differently so as to make it child friendly.

All subjects had to meet the inclusion criteria (section 3.2.3.), and were thus all between the ages of five and eighteen. Twenty-one children participated in this trial; 15 received the homeopathic complex and 6 received placebo. As stated above, this was part of a larger group project consisting of three components each applying a different approach to the same problem and sharing a collective placebo. Thus the larger group project comprised of 68 children divided into three groups, with the minimum objective being to have three treatment groups of 15 and a collective placebo group of 15. The final collective placebo for this study was 16. All 15 children who received the homeopathic complex (*Cantharis vesicatoria* 12CH, *Equisetum hyemale* 12CH, *Sarsaparilla* 12CH, *Delphinium staphysagria* 12CH, *Uva ursi* 12CH) completed the trial.

3.2.3 Inclusion criteria

- Subjects had to be between the ages of five and eighteen years.
- Subjects were considered for the study if they met the DSM 4-R (307.6) criteria:
 - A. Repeated voiding of urine into bed or clothes, (whether intentional or involuntary).
 - B. The behaviour is significant as manifest by either a frequency of twice a week for at least three consecutive months or the presence of clinically significant distress or impairment in social, academic (occupational), or other important areas of functioning.
 - C. Chronological age is at least 5 years (or equivalent developmental level).
 - D. The behaviour is not due exclusively to the direct physiological effect of a substance (e.g., a diuretic) or a general medical condition (e.g. spina bifida, a seizure disorder, diabetes) (DSM-4, 1995: 109).
- Subjects were included in the study once they and their guardians had signed an assent form (Appendix 2) and a consent form (Appendix 1) respectively.
- Subjects had to reside at the various homes.

3.2.4 Exclusion criteria

- Subjects on enuresis related treatments were excluded.
- Subjects with relevant anatomical abnormalities; neurological or otherwise were excluded.
- Subjects presenting with any other illness that could clinically contribute to their condition were excluded.
- Subjects with lactose intolerance were excluded.

3.3 Study procedure

3.3.1 Interview and case taking

Once the sample was obtained, each subject underwent a homeopathic interview. The interview began with a full explanation of the study, including what was to be done during the homeopathic consultation, the physical examination and the treatment. A translator was used if necessary to ensure that the subject understood the procedure. Having understood the nature of the study and what it involved, each subject was required to sign an assent form agreeing to partake in the study (Appendix 2). The researcher then performed a physical examination (Appendix 5), and homeopathic enquiry (Appendix 4), which included a medical history to rule out any known causes of enuresis. The subjects were screened for (Appendices 4 and 5):

- Infrequent or day time wetting
- Recurrent urinary tract infections
- Anatomical and neurological abnormalities that might complicate or result in nocturnal enuresis
- Systemic or metabolic causes e.g. hyperglycaemia
- Worm infection
- Urinary tract infections and hyperglycosuria (urine dipstick).

Subjects with any of the above were excluded from the study.

3.3.2 The Process of Randomisation

After the sample group of 68 subjects was established, they were divided into three sub-groups /projects (homeopathic simillimum, homeopathic complex and *Ilex paraguensis*); in addition each subgroup was randomly subdivided into a placebo and treatment group. The various subjects were allocated into three age categories (5-8, 9-12, 13-18) and divided along gender lines to ensure age and gender uniformity amongst the three sub-groups/projects. The supervisor then randomly selected a placebo group from the above three sub-groups/ projects. The placebo group had a similar age and gender distribution as the treatment groups. The randomisation was carried out to ensure the double blind nature of the trial. Each researcher knew the identities of their group members, but did not know whether they were part of the placebo or treatment group. Similarly the trial participants were aware that a placebo group existed but were unaware of its members. (see figure 1)

3.3.3 Medicine preparation

The researcher made up the homeopathic complex (*Cantharis vesicatoria* 12CH, *Equisetum hyemale* 12CH, *Sarsaparilla* 12CH, *Delphinium staphysagria* 12CH, *Uva ursi* 12CH) in the laboratory at the homeopathic day clinic at the Durban Institute of Technology. The complex was made up according to the standards and procedures outlined in the German pharmacopoeia. Constituents of the complex were individually potentised up to an 11CH from their respective mother tinctures. The mother tinctures were obtained from the stock at the day clinic at the Durban Institute of Technology and are manufactured by Parceval.

The constituents, in 11CH, were then combined and succussed up to a 12CH potency. A volume of 25ml of the homeopathic complex was prepared in 73% alcohol. This preparation was used to impregnate 100ml of lactose granules at 1% v/v, by means of triple impregnation. The lactose granules were then dispensed into lactose powders. Each powder received one layer of granules from the cap of the 100ml bottle to ensure an equal distribution of granules in the powders. The treatment group received lactose powders containing medicated granules whereas the placebo group received lactose powders containing unmedicated granules, impregnated with 73% alcohol alone. Each subject received fourteen numbered powders in two packs of seven. All fourteen powders received by each member in the treatment group were medicated. The appearance, presentation and administration of the powders were identical for both placebo and treatment groups, as well as for all three research projects.

3.3.4 The Trial

The trial took eight weeks in total. It was divided into a baseline period of two weeks, a two-week treatment period and finally a four-week observation period. The baseline period of two weeks was used to establish a baseline number of wet nights per week. To facilitate this process each subject was provided with a weekly diary (Appendix 6), that was marked with either a 'W' or a 'D' (wet or dry) each morning by the resident caregiver. The diary was collected at the end of each week by the researcher, and a new one provided. This enabled the caregivers to communicate any problems or queries regarding diary keeping to the researchers.

The baseline period was followed by a 2- week treatment period. Each subject received 7 powders numbered 1 to 7 as well as a one- week diary at the beginning of each week. The caregivers administered these powders to each subject before bed each night. At the end of the week, the diaries were collected and the following week's remedies and diaries provided.

The subjects were then observed for four weeks with diaries, but without treatment. This period was used to statistically evaluate the impact of the treatment i.e. was there any change in the frequency of bedwetting in comparison to the baseline period. There was a final consultation with each subject at the end of the trial. Subjects who showed improvement were referred to the homeopathic day clinic. All subjects who received placebo treatment were offered free follow up treatment. All examinations, special tests and treatment administered to the subjects during this study were free of charge.

3.4 Double blind

This was a placebo controlled, double blind and randomised study. Enuresis is not a life threatening condition. The children in the homes were not receiving any other form of treatment, thus participation in the trial did not necessitate the cessation of any other existing treatment modalities. In addition, the children participating in this study were informed before the trial began that they may receive placebo. With this in mind the researchers considered it ethically acceptable to use a placebo group as a measure against which treatment could be compared. At the completion of the study those that received placebo were informed and offered free treatment.

The 68 subjects involved were randomly divided into three groups. All groups underwent the same consultation and examination procedures and received their treatment in the same form and the same time intervals. Each subject in the treatment group received the homeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH), while those in the placebo group received placebo treatment. The researchers knew which subjects were in their group but were unaware which received the complex and which the placebo. The powders were administered before bed each night. The treatment and placebo powders were identical in appearance, taste and smell. The use of a collective placebo was motivated on the grounds that all interviews, consultations and posology were uniform amongst the three projects. In addition the trials were simultaneously run and comprised children from the same homes.

3.5 Statistical treatment of the data

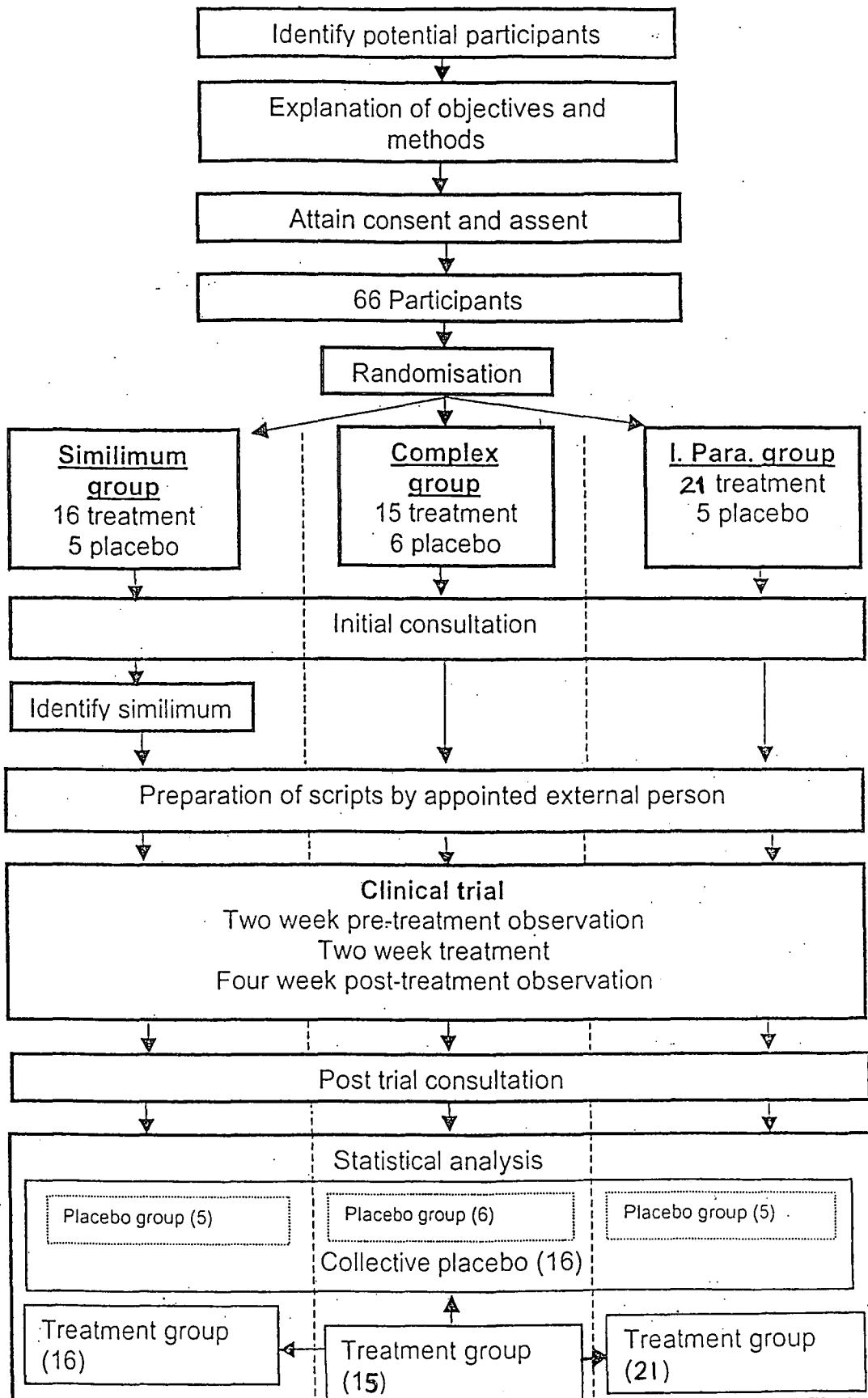
The data employed for statistical analysis was extracted from the case histories of each child and their diaries, which indicated the number of wet nights per week. Upon completion of the study, the data as an entirety was collated, analysed and interpreted by means of the following statistical methods:

- 1) Demographic data was used to look at age and gender distributions amongst subjects. Data was obtained from the case histories of subjects (section 4.5).
- 2) The next set of data presents the average median number of wet nights per week obtained for both the treatment and placebo groups (section 4.6).
- 3) The third set of data looks at the comparisons of improvement between the control and treatment groups based on percentage differences (section 4.7).

4) The final analysis applied non-parametric hypothesis testing to the data. Two tests were used:

- Wilcoxon's Signed Rank test was used in procedures one and two and analysed data from the treatment and placebo group independently of each other (Table 4.5-4.8) i.e. the test was used to make intra-group comparisons.
- The Mann Whitney U test was used in procedure three and sought to determine the statistical relevance of the results by comparing the treatment group and the placebo group (Table 4.9-4.12) i.e. inter-group analysis.

Fig 1 Summary of research design



CHAPTER 4

RESULTS

4.1 Introduction

This chapter presents the results of the trial. The results were derived from the data received from the wet night diaries of each subject. The lay out of the results is as follows:

Demographic data looks at age and gender distributions amongst subjects. Data was obtained from the case histories of subjects (section 4.4).

The second set of data presents the average median number of wet nights per week obtained for both the treatment and placebo groups (section 4.5).

The third set of data looks at comparisons of improvement between the placebo and treatment groups based on percentage differences (section 4.6).

The last set of results (section 4.7), applies non-parametric hypothesis testing to the data to determine the efficacy of the homeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH) in the treatment of nocturnal enuresis in terms of the number of wet nights

experienced by each subject weekly. The study focused on subjects between the ages of five and eighteen residing in children's homes in the greater Durban area.

4.2 Abbreviations

The following terms and abbreviations were used:

p= probability of equalling or exceeding $z/2$

n/s = no significant difference in the medians

s = significant difference in the medians

Improvement=a reduction in the average number of wet nights per week.

Success= a 50% or greater reduction in the average number of wet nights per week.

Treatment group= the group of subjects receiving the homoeopathic complex.

Placebo group= the group of subjects receiving placebo.

H₀= Null hypothesis

H₁ = Alternative hypothesis

Wk = week

If **P < 0.05** then no significant difference was concluded (5% level of significance)

If **P >= 0.05** then no significant difference was concluded (5% level of significance)

The following time frames were referred to in the course of the study:

Baseline period= the 2 week period of observation prior to treatment.

Trial period= the 2 week period during which the subjects received treatment.

Post-trial/ observation period= the 4 week period following the treatment period.

Table 4.1 Illustration of the different periods during the study.

Week 1	Baseline Period
Week 2	
Week3	Trial Period
Week 4	
Week 5	Post-trial/Observation Period
Week 6	
Week 7	
Week 8	

4.3 Criteria for Admissibility of Data

- Data was accepted only from subjects complying with inclusion and exclusion criteria. (section 3.2.3 and 3.2.4).
- Informed consent from the subjects as well as the legal guardian was required.
- Only data collected from the Wet Night Diaries of each subject was used.
- The data was accepted only if the diaries were correctly completed.

4.4 Demographic data

Figure 2 Gender distribution of the subjects.

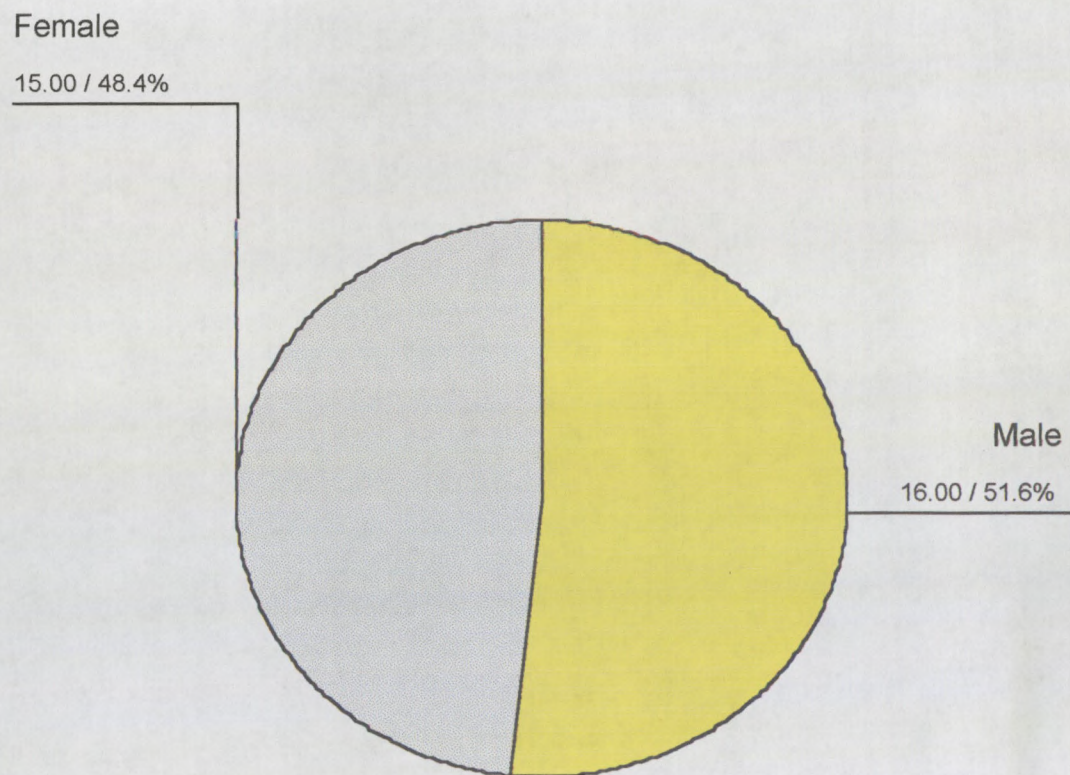
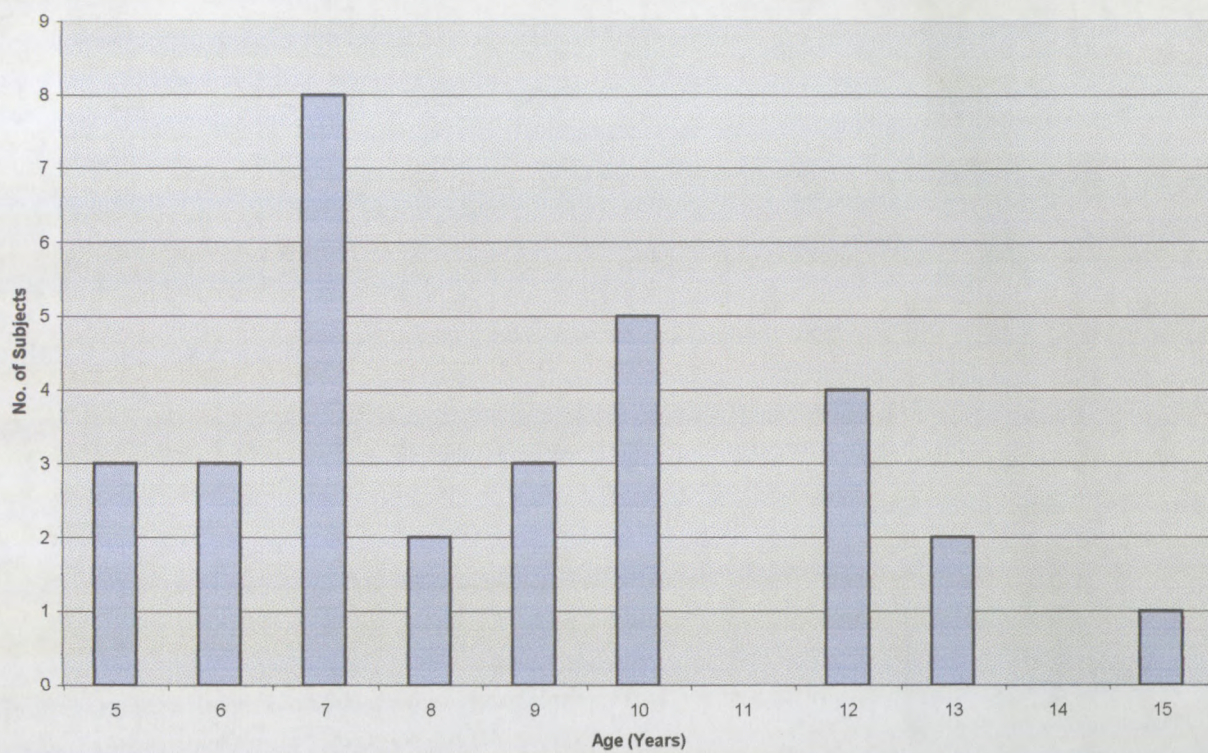
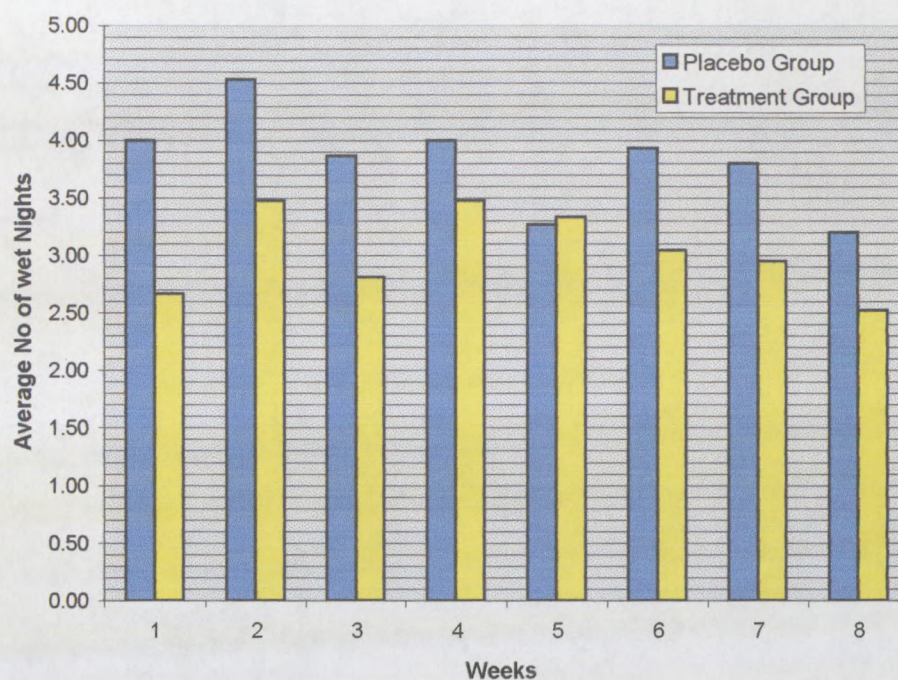


Figure 3 Age Distribution of the subjects



4.5 Comparison of the average number of wet nights per week obtained for both the treatment and placebo groups

Figure 4 Comparison of the average number of wet nights in the placebo and the treatment group.



In Fig 4.3 it was seen that the placebo group experienced decreasing numbers of average wet nights in weeks 3, 5 and 8. This could have been attributable to the ‘placebo effect’ – an improvement in symptoms not due to the medicinal effect of the substance. The figure does not show any consistent trends in the treatment group. The slight drop in the number of wet nights in the first week of the trial period (wk 3), could have been due to a placebo effect or an initial effect of the complex.

The increase in the average number of wet nights in the treatment group in week 4 could have been attributable to either: a random fluctuation in the wet nights, or a 'proving' type effect. A proving effect refers to the phenomenon by which a person develops symptoms that the medicine is supposed to cure. This is possible because the administration of the medicine is based on the law of similars, i.e. what it is able to cure, it is able to cause. Thus if a medicine is repeated too frequently it can cause the symptoms it is supposed to alleviate. The proving symptoms are not permanent as they are a result of an 'artificial' disease, energistic in nature, which is engrafted by the medicine. In this case the subjects exposed daily to homoeopathic medication, initially evidence a slight decrease in number of wet nights (wk 3) after which they start to develop symptoms of the remedy complex they are taking i.e. a proving (wk 4). This is supported by the consistent decrease in the average number of wet nights following the end of the trial period. As the proving effect wore off, the symptoms of the proving i.e. increased enuresis, started to decrease over the next few weeks.

Table 4.2 Comparison of the Means and Standard deviations of the average number of wet nights for the treatment and placebo group for each week of the study.

		Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8
Placebo (N=16)	Mean	3.75	4.25	3.62	3.75	3.06	3.69	3.56	3.00
	Std.	2.20	1.88	2.33	2.41	1.84	2.02	2.16	1.75
	Deviation								
Treatment (N=15)	Mean	3.73	4.87	3.93	4.87	4.67	4.27	4.13	3.53
	Std.	2.25	2.10	2.25	2.17	2.41	1.91	2.13	2.03
	Deviation								

The mean and standard deviation are fairly uniform across the weeks for both the placebo and treatment groups. On average there is no real change, which supports the previous discussion.

4.6 Comparisons between the placebo and treatment groups based on percentage differences

Improvement was measured as the decrease in the average number of wet nights per week, and success defined as an improvement of 50% or more. From this evaluation, an understanding of the role this method of treatment plays in the management of nocturnal enuresis can be ascertained.

Table 4.3 Comparison of the improvement in the placebo and the treatment groups based on the percentage differences between the baseline period (wk 1-2) and the trial period (wk 3-4). (Note the bold line indicates success as defined for this study).

	Neg Results	0-24% Impr.	25-49% Impr	50-74% Impr	75-100% Impr	Sample Size
Placebo	11	2	3	0	0	16
Treatment	6	7	2	0	0	15

There were no successes as defined for this study. There was, however an improvement in most of the subjects in the treatment group. This indicates that the average number of wet nights experienced was decreasing. This was however not statistically significant on non-parametric analysis.

Table 4.4 Comparison of the improvement in the placebo and the treatment groups based on the percentage differences between the baseline period (wk 1-2) and the post-trial observation period (wk 5-8). (Note the bold line indicates success as defined for this study).

	Neg Results	0-24% Impr.	25-49% Impr	50-74% Impr	75-100% Impr	Sample Size
Placebo	5	3	5	3	0	16
Treatment	4	9	1	1	0	15

In both groups there appeared to be a general improvement in the average number of wet nights over the course of the study. This is indicated by the success achieved in 3 cases in the placebo group and in 1 case in the treatment group. In both groups the majority of the subjects experienced some degree of improvement. This, however was not seen to be statistically significant or due to the effect of treatment.

An interesting point to note is that the degree of improvement of both groups, increased after the trial period (end of wk 4) i.e. The results were better after a period of time had passed.

4.7 Non-parametric Hypothesis Testing

4.7.1 Statistical procedures

The following statistical procedures were employed to statistically evaluate the effect of the homoeopathic complex and placebo treatment by means of hypothesis testing:

Statistical procedure 1 employed Wilcoxon's Signed Rank test to evaluate the response of the placebo group to the placebo treatment, in order to evaluate the role placebo played in the management of nocturnal enuresis (intra-group analysis).

Statistical procedure 2 employed Wilcoxon's Signed Rank Test to evaluate the response of the treatment group to the homoeopathic complex, in order to evaluate the role this played in the management of nocturnal enuresis (intra-group analysis).

Statistical procedure 3 employed the Mann-Whitney U test to compare the responses of the treatment and placebo group in order to evaluate the efficacy of the homoeopathic complex in the treatment of nocturnal enuresis (inter-group analysis).

4.7.2 The analysis

4.7.2.1 Statistical procedures 1 and 2: Intra- group comparisons using Wilcoxon's Signed Rank test

H_0 : It was hypothesised that there would be no significant difference between the average number of wet nights during the baseline, trial and post trial periods on analysing the intra- group data for placebo and treatment groups at a confidence level of 5%. This was an indication that there was no improvement in the condition.

H_1 : It was hypothesised that there would be a significant difference between the baseline, trial and post trial results on analysing the intra- group data for placebo and treatment groups at a confidence level of 5% This was an indication that there was an improvement in the condition, attributable to the intervention (placebo or complex respectively).

A 95% confidence interval was required to reject the null hypothesis. Thus H_0 was accepted if $p \geq 0.05$, and H_0 was rejected if $p \leq 0.05$. I.e. a 5% level of significance was used.

Table 4.5 Sample analysis of the placebo group comparing the average number of wet nights of the baseline period to the average number of wet nights of each week of the study using Wilcoxon’s Signed Rank test.

Placebo	Baseline vs Wk 3	Baseline vs Wk 4	Baseline vs Wk 5	Baseline vs Wk 6	Baseline vs Wk 7	Baseline vs Wk 8
p Value	0.388	0.660	0.031	0.528	0.222	0.024
	n/s	n/s	S	n/s	n/s	S

The null hypothesis was accepted for weeks 3,4,6 and 7 because at a 5% level of significance there was no significant difference between these weeks and the baseline period. There was therefore no significant improvement in the subject’s condition during these weeks of the study, as compared to the baseline period. During week 5 and week 8, however, there were significantly fewer wet nights than other weeks. This could be due to the end of the treatment period, and end of trial placebo effects.

Table 4.6 Sample analysis of the treatment group comparing the average number of wet nights of the baseline period to the average number of wet nights in each week of the study, using Wilcoxon's Signed Rank test.

Treatment	Baseline vs Wk 3	Baseline vs Wk 4	Baseline vs Wk 5	Baseline vs Wk 6	Baseline vs Wk 7	Baseline vs Wk 8
p Value	0.648 n/s	0.080 n/s	0.155 n/s	0.232 n/s	0.470 n/s	0.977 n/s

The null hypothesis was accepted for weeks 3-8 because at a 5% level of significance there was no significant difference between these weeks and the baseline period. There was therefore no significant improvement in the subject's condition during these weeks of the study as compared to the baseline period.

Table 4.7 Sample analysis of the placebo group comparing the average number of wet nights of each week to the average number of wet nights of the preceding week using Wilcoxon's Signed Rank test.

Placebo	Wk 3 vs Wk 4	Wk 4 vs Wk 5	Wk 5 vs Wk 6	Wk 6 vs Wk 7	Wk 7 vs Wk 8
p Value	0.788 n/s	0.244 n/s	0.085 n/s	0.677 n/s	.223 n/s

As expected from the above comparison with the baseline period no significant improvement in the average number of wet nights was achieved in any of the weeks compared to the previous week.

Table 4.8 Sample analysis of the treatment group comparing the average number of wet nights of each week to the average number of wet nights of the preceding week using Wilcoxon’s Signed Rank test.

Treatment	Wk 3 vs	Wk 4 vs	Wk 5 vs	Wk 6 vs	Wk 7 vs
	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8
p Value	0.063	0.569	0.427	0.811	0.117
	n/s	n/s	n/s	n/s	n/s

As expected from Fig. 4.5 no significant difference was noted in the average number of wet nights of the treatment group from one week to the next.

4.7.2.2 Statistical procedure 3: Inter-group analysis using the Mann-Whitney U test

H_0 : It was hypothesised that there would be no significant difference between the placebo and the treatment group with regard to the average number of wet nights per week.

H_1 : It was hypothesised that there would be a significant difference between the placebo and the treatment group with regard to the average number of wet nights per week.

A 95% confidence interval was required to reject the null hypothesis. Thus H_0 was accepted if $p \geq 0.05$, and H_0 was rejected if $p \leq 0.05$. i.e. a 5% level of significance was used.

The one-tailed p-values were obtained. The action of the homoeopathic complex was expected to reduce the incidence of bed-wetting. This expected directionality of the results determined the use of the one tailed p value I.e. was there any significant decrease in the average number of wet nights between the placebo and the treatment group.

Table 4.9 Statistical comparison between the placebo and treatment groups for the baseline period using the Mann- Whitney U test.

Baseline Period	p value (one tailed)
Week 1-2	0.654 n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant decrease in the average number of wet nights between the placebo and the treatment group for the baseline period. As no 'treatment' had yet been given to either group, this was expected and forms a check of the sampling.

Table 4.10 Statistical comparison between the placebo and treatment groups for the trial period using the Mann- Whitney U test.

Trial Period	p value (one tailed)
Week 3-4	0.572 n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant decrease in the average number of wet nights in the placebo group compared to the treatment group for the trial period.

Table 4.11 Statistical comparison between the placebo and treatment groups for the post-trial observation period using the Mann- Whitney U test.

Post trial Observation Period	p value (one tailed)
Week 5-8	0.202 n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant decrease in the average number of wet nights in the treatment group compared to the placebo group for post trial observation period.

Table 4.12 Statistical comparison between the placebo and treatment groups for each week of the trial using the Mann- Whitney U test.

	Week 3	Week 4	Week5	Week 6	Week 7	Week 8
p value (one tailed)	0.800 n/s	0.175 n/s	0.045 S	0.423 n/s	0.379 n/s	0.495 n/s

The null hypothesis was accepted for weeks 3 and 4 and weeks 6-8, however it was rejected for week 5. A significant decrease in the average number of wet nights in the treatment group as compared to the placebo group was noted for week 5. This may have been due to an initial improvement under the treatment, which wore off over the course of post trial observation period. At the 5% level of significance there was no significant difference between the placebo and the treatment groups for weeks 3 and 4 and weeks 6-8.

CHAPTER 5

DISCUSSION

The demographic data points to an almost equal gender distribution amongst subjects. The sample demonstrates a breakdown of 51.6% male and 48.4% female subjects. (section 4.4, figure 2). This neither supports nor refutes various texts that suggest a higher prevalence of enuresis amongst boys. One reason for this could be the relatively small sample size used in the study. There is a less equitable age distribution amongst subjects. 52% of the subjects were between 5-8yrs, 42% were between 9-12yrs and 6% were between 13-18yrs. (section 4.4, figure 3). This clearly indicates a higher prevalence in younger children and supports the notion that bedwetting has a spontaneous resolution rate of 15% per annum (Ullom-Minnich, 1996: 2259).

Based on a rational definition that a 50% reduction in bedwetting defines success, the results of this study demonstrate a limited success. When the baseline and post trial/observation periods are compared, the placebo group demonstrates an 18% success rate whereas the treatment group only demonstrates a 6% success rate (Table 4.4). According to the above definition there is no success in either the placebo or the treatment group when the baseline and trial periods are compared (Table 4.3). Despite the limited success, both groups demonstrate an improvement, especially when the baseline and post trial/observation period are compared. This indicates that the results were better after a period of time. Despite the majority of subjects experiencing some degree of

improvement, this was not seen to be statistically significant or due to the effect of treatment. The fact that the success was greater in the placebo group, suggests that improvement in either group may be due to the 'placebo effect' as opposed to the effect of the homoeopathic complex. The 'placebo effect' could be due to one or more of a combination of factors e.g. the impact of the initial homoeopathic consultation, receiving treatment in the form of a powder for two weeks, receiving more attention than normal, being part of a group trial or being observed for a period of 8 weeks i.e. the duration of the study.

Wilcoxon's Signed Rank test (intra-group analysis) demonstrates no statistically significant improvement in the treatment group, despite the 6% improvement cited earlier. The placebo group shows slight improvement in week 5 ($p=0.031$) and week 8 ($p=0.024$), when weeks 3-8 are compared to the baseline period.

The inter-group comparisons using the Mann-Whitney U test are all statistically insignificant in each of the three periods of the trial. However when the placebo and treatment group are compared for each week of the trial, the treatment group shows a significant decrease in the number of wet nights as compared to the placebo group in week 5 ($p=0.045$). This p value is however close to being considered insignificant i.e. $p=0.05$.

Thus the results of the study demonstrate that despite a slight improvement i.e. a reduction in the incidences of bedwetting in both groups over the duration of the trial

(figure 4), the ability of the homoeopathic complex to reduce the weekly incidences of bedwetting in subjects residing in children's homes was statistically insignificant.

Although few if any complexes are proven, they are known to be clinically effective.

Numerous practitioners prescribe combination remedies and many companies worldwide operate successful businesses based on the manufacture and distribution of homeopathic complexes. This is not an argument for the use of complexes but merely an observation on their efficacy in certain instances. However in this instance the homeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH) was not as efficacious as hypothesized.

As stated earlier, this study is a component of a group research project, each component employing a different treatment of the same problem. It seems appropriate to compare the results of this study with those from Bloch's and Reilly's study respectively. Bloch's study sought to measure the efficacy of the homeopathic simillimum in the treatment of nocturnal enuresis in children's homes in the greater Durban area (2002). Bloch's research demonstrated a 12.5-18.75% success rate in the placebo group and a 25-37.5% rate in the treatment group. The results of Reilly's study (2003), which sought to measure the efficacy of *Ilex paraguensis* in the treatment of enuresis, were statistically insignificant. *Ilex paraguensis*, like the complex, focused its treatment on the urinary bladder. Thus, with the research projects being similar apart from the treatment administered, i.e. case taking procedure, homes, diaries, appearance of medication and dosage were all the same, the treatment with the homeopathic simillimum proved to be more efficacious than treatment with the homoeopathic complex or *Ilex paraguensis*.

The simillimum prescriptions did not focus on an organic lesion i.e. they did not focus on the urinary system, but focused mainly on mental, emotional, physical and general peculiar and individualizing symptoms. Six of the sixteen repertory sheets in the Bloch study did not make reference to urination or the urinary bladder. This is in contrast to the complex used in this study, which contained remedies specifically chosen for their affinity for the urinary system and their past clinical success in the treatment of enuresis. The remedies in the complex were also made up in the 12CH potency, which is considered a medium potency and more suited to organic lesions. The *Ilex paraguensis* used in Reilly's study (2003) was made up in a 6X, a low potency also suited to treating on an organic level. The simillimum scripts were generally administered in higher potencies i.e. 30CH, 200CH and 1M, suited to addressing mental emotional states (2002).

As already discussed, nocturnal enuresis is a multifactorial problem with an unclear aetiology that will probably vary from one context to the next. The subjects in this study were all from a similar background in that they were all in children's homes separated from their parents and families for various reasons whether financial, the death of parents, or because of some form of abuse. It can be safely stated that they had all been through some form of trauma or rejection. The homes provide a safe haven for these children, but socio- economic constraints make it difficult for them to provide each child with the optimum degree of individualised care and attention. The probability that enuresis in these children's homes is part of a broader socio-economic problem with a strong mental emotional component is supported by Cortina's findings (1994: 222). Cortina concluded from his study on subjects with enuresis, that nocturnal enuresis in the

child appears to be an unconscious protest against the family or society due to repression or disciplinary excesses. He suggested that additional factors include attention-seeking behavior on the part of the child as well as parental separation or divorce.

Thus the success of the simillimum treatment, which had a strong psychosomatic emphasis, relative to the limited success of the homeopathic complex and *Ilex paraguayensis* 6X, together with the afore mentioned information on the children's shared backgrounds and circumstances, suggests that the enuresis in this study had a strong mental emotional component that needed to be addressed for any significant improvement to occur. This would support the likelihood that the improvement observed in both the placebo and treatment groups in this study was due to the placebo effect i.e. that the incidences of wet nights decreased due to factors other than the pharmacological action of the medicine e.g. additional attention the children received during the study, the relationship with the researcher, the form the medication took etc.

Thus the complex employed in this study, being organ and system specific, may be more effective in treating enuresis in a different setting, i.e. one in which there are less clear mental and emotional causative factors. In retrospect, a complex based on remedies mirroring the mental emotional states of the children as apposed to their urinary systems, would be more appropriate and hence effective in treating enuresis in subjects residing in children's homes. The potency used in the complex could also be higher, perhaps a 30CH, which would be more suited to treating on the mental emotional plane.

CHAPTER 6

CONCLUSION

The results of this study indicate that the homeopathic complex (Cantharis vesicatoria 12CH, Equisetum hyemale 12CH, Sarsaparilla 12CH, Delphinium staphysagria 12CH, Uva ursi 12CH) did not result in a statistically significant reduction in the weekly incidence of bedwetting in children between the ages of 5-18 residing in children's homes in the greater Durban area. There was however some improvement i.e. reduction in bedwetting, but the improvement on the whole was greater in the placebo group than the treatment group. Thus it is assumed that the improvement may have been due to a placebo effect.

Despite the relative shortcomings of complex prescribing as discussed in the literary review (Chapter 2), the use of a homeopathic complex in the treatment of children in children's homes is potentially very appropriate given the lack of funds, the paucity of medical and social information on the children as well as the language barrier, which all make homeopathic case taking and identifying the simillimum difficult. However, if a complex is employed, it must be tailored as much as possible to be context specific.

The execution and analysis of this study leads the researcher to make the following recommendations to any potential researchers:

- Run a trial using this complex in another context e.g. children in families where the enuresis has less of a psychological basis.
- Run a trial using the same complex in a different potency.
- If children's homes are employed, consider changing the constituents of the complex to focus on the mental emotional sphere. The potency could then also be raised, possibly to a 30CH.
- Increase the baseline period to 4 weeks to allow for a longer and thus more reliable reference period against which to compare subsequent changes.
- The treatment period could be extended to 3-4 weeks.
- The post trial/observation period could be extended to 6weeks, as more improvement was noted in this research after a period of time had passed. It is not uncommon for the effect of a homoeopathic medicine to be observed for several weeks or months after having been administered and in some cases improvement is only observed after a period of time.
- Increase the sample size.

CHAPTER 7

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CHAPTER 8 APPENDICES

Appendix 1: Parent / Guardian Consent Form

Title of research project: A double blind study to determine the efficacy of a homoeopathic complex (Cantharis vesicatoria 12ch, Equisetum hyemale 12ch, Sarsparilla 12ch, Delphinium staphysagria 12ch, Uva ursae 12ch), Ilex paraguensis 6x and the homoeopathic simillimum in the treatment of nocturnal enuresis in children between five and eighteen years, residing in children's homes.

Name of supervisor: Dr C Hall

Name of research students: M Bloch, H Lockyear and P Reilly

(Please circle the appropriate answer)

Have you read the information form? Yes/No

Have you had the opportunity to discuss this study with the above research students? Yes/No

Have you had the opportunity to ask questions regard this study? Yes/No

Have you received satisfactory answers to your questions? Yes/No

Do you understand that participants are free to withdraw from the study at any time? Yes/No

Do you understand the nature of this research project and its structure? Yes/No

Do you agree to allow your child or children under your care to participate in this study? Yes/No

Do you agree to allow the researchers access to relevant medical records? Yes/No

(If you have answered no to any of the above questions please consult the researchers.)

I,the undersigned, as parent/ guardian hereby give consent forto participate in the above mentioned study.

.....
Signature parent/ guardian

.....
Witness signature

Date.....

Appendix 2: Minor assent form

My name is.....

- I wish to take part in your research project.
- The project has been carefully explained to me.
- I am not being forced to take part.
- I understand that I can decide not to take part at any time.

.....
Signature

Date.....

Igama lami lingu.....

- Nginaso isifiso sokubamba iqhaza ocwaningweni lakho.
- Lolu cwaningo luchaziwe kabanzi kimina.
- Angiphoqelewanga ukubamba iqhaza.
- Ngiyazi ukuthi ngingawushintsha noma inini umqondo mayelana nokubamba iqhaza.

.....
Sayina

Usuku.....

Appendix 3: Patient information sheet

The purpose of this study is to determine the efficacy of a homoeopathic complex, Ilex paraguensis and the homoeopathic simillimum in the treatment of nocturnal enuresis.

Homoeopathy: According to the World Health Organisation homoeopathy is the second most widely used form of therapy worldwide. Homoeopathic remedies produce no side effects and thus bring about cure in a gentle manner and are safe for use in children. Homoeopathy was founded by S. Hahnemann two hundred years ago and is based on the law of similars. This implies that a homoeopathic remedy will cure a disease state similar to that which it can cause when administered to a healthy person.

Homoeopathic complex: A homoeopathic complex comprises a number of remedies that are known to have an effect on a particular condition. For the purposes of this research the complex will be specially formulated for bed-wetting.

Homoeopathic simillimum: The simillimum is a single remedy that most accurately reflects the state of the patient. Rather than being specific for a given complaint it reflects the state of the patient on the mental, emotional and physical plane. For this reason there are a number of remedies that can be used for bedwetting, each with an entirely different symptom picture.

Ilex paraguensis: Ilex paraguensis is a herb which is used for a tea in Paraguay. This herb when homoeopathically prepared is reputed to be effective in the treatment of bed-wetting.

Double blind study: A double blind study is one in which neither the researchers nor the patients know the nature of the medication. For the purpose of this study this implies that neither patient nor researcher will know who is receiving placebo, complex, simillimum or Ilex paraguensis.

Placebo: Sixteen patients out of sixty-six will receive placebo. For the purposes of this study the placebo will be non-medicated powders that have an identical appearance and taste to medicated powder. The use of placebo or a control in clinical trials is considered to be in keeping with the scientific method. Its main purpose is to provide a base line against which results can be measured. Patients who received placebo will be offered treatment free of charge after completion of the study.

Powders: The medication to be used will be dispensed in lactose powders (see example provided). These powders are sweet tasting and easy to use.

The powders are to be administered in numerical order prior to going to sleep. The child should not eat, drink nor brush teeth fifteen minutes before or after administration.

Nocturnal enuresis: (bed-wetting) Nocturnal enuresis is the inability to maintain bladder control during sleep. It is a common disorder that is thought to be 80% psychogenic. Other causes of enuresis include chronic bladder infection, delayed maturation and neurological abnormalities. It is divided into primary and secondary

types. Subjects who have never achieved voluntary bladder control are considered to fall into the primary type. Those who have had bladder control and then develop enuresis at a latter stage are considered to fall within the secondary type. Both categories of children will be considered.

Outline of study: The study will comprise sixty-six children. The supervisor will randomly divide them into four groups (simillimum, complex, I. paraguensis and control). Each child will receive a physical examination as well as have his / her case taken by the students. Part of the case taking will include interviewing the caregivers, particularly for the very young children. Once the case taking is complete there will be a two-week observation period during which the incidence of bedwetting will be noted. Thereafter the treatment period of two weeks will commence with each child receiving a single powder each evening before bed. Once this period is complete, post treatment observation of four weeks will commence with completion of enuresis diaries. Once the study is over children on placebo will be offered free treatment.

Enuresis diary: This will comprise a simple calendar that will be filled in with a yes/no answer each day by either the caregivers or the students.

Contact: The student researchers will be in regular contact with the caregivers and children. In addition they will be telephonically available, as will their supervisors.

Dr C Hall

Michael Bloch

Heather Lockyear

Paddy Reilley

Confidentiality: All data collected will be confidentially handled. The final thesis will be presented in such a way that the confidentiality of participants will be ensured.

Follow up: The aim of this project is to evaluate the use of homoeopathy in the treatment of enuresis, with the well being of the participants being of foremost importance. For this reason children who have improved or who wish to improve will be encouraged to attend our day clinic after the trial. The clinic offers a free service (consultation and medicine) to those willing to be observed.

Risks: Homoeopathic treatment has no side effects. For this reason it is an ideal treatment method and poses no risk to the user.

Benefits: The researchers hope that the participants will directly benefit from participating in this research. The research is aimed at reducing the incidence of nocturnal enuresis.

Costs: The research will be at no cost to participants or the children's' homes.

Appendix 3.1: Simplified patient information sheet

We want to welcome you to our study. This page explains what we are doing in our study. It is important for you to understand that it is your choice to be in the study, and that you know how it works. This sheet gives you information about our study.

The reason we are doing this study is to see how homoeopathy works in bedwetting.

Bedwetting: Bedwetting is weeing in your bed at night.

Homoeopathy: is a type of natural medicine that helps the body to heal itself. It is safe for children.

Homoeopathic complex: The homoeopathic complex is a medicine made of a mixture of five different medicines. All of these medicines are used to treat bedwetting.

Ilex Paraguensis: A plant from South America used to treat bedwetting.

Placebo: Some children will get a placebo. A placebo is something that looks like a medicine but isn't a medicine. Children who get placebo will be given medicine at the end of the study.

Double blind study: This means that you do not know and the researcher will not know if you are given a placebo. This is done to make the study scientific.

Medicine: The medicine being used is given out in powders that we will show you. They are sweet tasting and easy to use. The powders are to be taken every night before going to bed. The powders are numbered, and are to be used in order e.g. 1,2,3 etc. You should not eat, drink or brush your teeth fifteen minutes before or after taking the powder. Your mouth must be clean. The powders should be put straight onto the tongue and do not need to be put in water.

The study: The study will last eight weeks. The first two weeks we will count the number of time that each child wets their bed. The next two weeks the children will get their medicine. The last four weeks we will again count the number of times that each child wets their bed. We will meet with each child and their house parent to get to know them.

Assent form: This is a form that each child must sign. This form makes sure that the children are not being forced to take part in the study.

Diary: Every day the house parent will tick off on a calendar whether the child wet their bed or not.

Telephone numbers: We can be phoned at the following telephone numbers.

- Dr C Hall
- Michael Bloch
- Heather Lockyear
- Paddy Reilly

We will visit you each week during the study.

Confidentiality: This means that all the information will be private and not shared with other people. It will also mean that at the end of the study no one, except us, your house parent and the principal of your home will know that you have been in this study.

Appendix 3.2: Zulu translation of simplified patient information sheet

Siyakwamukela kulolucwaningo. Lelikhazi lichaza esikwenzayo kulolucwaningo. Kubalulekile ukuba wazi ukuthi ungenela lolucwaningo ngokuthanda kwakho, nokuthi ulwazi ukuthi lusebenza kanjani.

Homeopathy:- Uhlobo lwemithi yemvelo olusiza umzimba ukuba uzelaphe ngokwawo. Uphephile kubantwana.

Homeopathy Complex:- Uhlobo oluthile lomuthi olwenziwe ngengxube yemithi emihlanu. Lusetshenziswa ukwelapha ukuchama uma ulele.

Homeopathic Similimum:- Uhlobo lomuthi olukhethelwa lowo muntu oluqondene naye, okusho ukuthi umntwana ngamunye uthola lowo muthi oqondene nesimo akuso.

Ilex Paraguensis:- Isithalo esitholakala e South America eselapha ukuchama uma ulele.

Placebo:- Abanye abantwana bazonikezwa I placebo. I placebo into ebukeka sengathi umuthi, kodwa kungeziwo. Abantwana okudingeka banikezwe I placebo bayonikezwa ekupheleni kocwaningo.

Double blind Study:- Loku kusho ukuthi wena kanye nomcwaningi wophenyo angeke nasiswe ukuthi unikezwe I placebo. Loku kwenzelwa ukuba ucwaningo lube lula kwezesayensi (scientific).

Medicine: Imithi enizoyinikezwa iyobe izimpushana. Inambitheka ngokusashukela, kulula futhi nokuyisebenzisa. Imithi lena kumele ithathwe zonke izinsuku ebusuku ngaphambi kokuba ulale. Imithi lena inezinombolo futhi kumele ithathwe ngokulandelana kwezinombolo e.g. 1,2,3...etc. Akumele udle, uphuze noma uwashe amazinyo imizuzu engu 15 ngaphambili noma ngemuva kokusebenzisa lempushana. Umlomo kumele uhlanzeke. Umuthi kumele umnyungwe ngolimi, asikho isidingo sokuwuxuba namanzi.

Bedwetting:- Ukuchama ebusuku uma ulele.

The Study:- Amasonto amabili okuqala sibala izikhathi umntwana azichamela ngazo ebusuku uma elele. Amasonto amabili alandelayo abantwana bazonikwezwa imithi (impushana). Amasonto alandelayo amane (4 weeks) siphinde sibale izikhathi umntwana azichamele ngazo ebusuku uma ulele. Sizohlangana nomntwana kanye nomzali ukuze sithole ukwazana nabo.

Assent Form:- Ifomu okumele umntwana ngamunye alisayine.
Lelifomu lenzela ukuqinisekisa ukuthi akekho umntwana
ophoqiwe ukuba angenele lolucwaningo.

Diary:- Zonke izinsuku umzali kumele abeke uphawu
kwikhalenda oluchaza ukuba umntwana uchamile yini
ngenkathi elele noma cha.

Izinombolo zocingo:- Sitholakala kulezizinambolo ezilandelayo:

- Dr C Hall
- Michael Bloch
- Heather Lockyear
- Paddy Rielly

Sizonivakashela wonke amasonto

CONFIDENTIALITY:

LONKE ULWAZI OLUZOTHOLAKALA KULOLUCWANINGO LUYOBE
LUYIMFIHLO, AKEKHO OMUNYE UMUNTU OZOLWAZI. AKUKHO
MUNTU OZOKWAZI UKUTHI UBUNGOMUNYE WABANGENILE
KULOLUCWANINGO.

Appendix 4: Homoeopathic case history

PATIENT'S DETAILS

Name: _____ Date: _____

Address: _____

Date of Birth: _____ Age: _____

Sex: M/F Consultation: initial / follow up

PARENTS' DETAILS

Name of parent(s) / guardian(s) _____

Telephone (H) _____ (W) _____

MAIN COMPLAINT: _____

PAST MEDICAL HISTORY AND TREATMENT: (including childhood diseases)

Medication: _____

Vaccinations: _____

Allergies: _____

FAMILY HISTORY: _____

BIRTH HISTORY: Pregnancy _____

Labour _____

MILESTONES: _____

GENERALS:

Sleep: (patterns and positions) _____

Weather preference: _____

SYSTEMS REVIEW:

HEAD: _____

ENT: _____

RESPIRATORY: _____

CARDIOVASCULAR: _____

GIT: Feeding / diet _____

Cravings and aversions _____

Appetite _____

Thirst _____

Stool (colour, consistency, frequency) _____

GENITO-URINARY: _____

Urine _____

Discharges _____

MUSCULOSKELETAL AND CNS: _____

SKIN: _____

Perspiration _____

PERSONALITY: Temperament _____

Relations with others _____

Fears _____

Comments and observations

Appendix 5: Physical examination

VITAL SIGNS:

Temperature _____ Pulse rate _____
Respiratory rate _____ BP _____
Height _____ Weight _____

GENERAL EXAMINATION:

Jaundice/ anaemia/ cyanosis/ clubbing dehydration/ Odessa/ lymphadenopathy

ENT: _____

CHEST EXAMINATION: _____

ABDOMINAL EXAMINATION: Abdominal masses, distension, sphincter tone

NEUROLOGICAL EXAMINATION: Gait, reflexes, observation of spinal cord, dermatomes and myotomes L2, L3, L4, L5 _____

TESTS: Urine dipstick _____

Appendix 6: Enuretic diary

Week Eight

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week Seven

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week Six

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week Five

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week Four

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week Three

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week Two

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Week One

Researcher:

Patient:

Care-giver/ cottage:

Mon	Tues	Wed	Thurs	Fri	Sat	Sun

Appendix 7: Side effects of allopathic drugs commonly used in the treatment of nocturnal enuresis

Imipramine hydrochloride (Tofranil):

Insomnia

Personality changes

Nervousness

Danger of overdose

Oxybutin chloride (Ditropan):

Constipation

Dizziness

Tremors

Desmopressin acetate (DDVAP):

Weight gain

Convulsions

Coma

Headaches

Allergic skin reactions

Serum sodium loss if there is not a restricted water intake