
***Assessment Of The Efficacy Of Desmopressin In
The Treatment Of Primary Monosymptomatic
Nocturnal Enuresis In Egyptian Children***

Thesis

**Submitted For The Partial Fulfillment Of
The Master Degree In Pediatrics**

By

Marian Khairy Hakim

(M.B., B.Ch.)

Ain Shams University

(٢٠٠٧)

Under The Supervision Of

Professor Doctor: *Farida El-Baz Mohammed*

Professor of Pediatrics

Faculty of Medicine

Ain Shams University

Doctor: *Sally Soliman Zahra*

Lecturer of Pediatrics

Faculty of Medicine

Ain Shams University

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

CAIRO, EGYPT

٢٠١٣



List Of Contents

<i>Subject</i>	<i>Page</i>
Lists:	
• List of abbreviations.	i
• List of figures.	ii
• List of tables.	iv
I. Introduction.	۱
II. Aim Of The Work.	۳
III. Review Of Literature.	۴
<u>Chapter One: Nocturnal Enuresis.</u>	۴
• Definition.	۴
• Classification.	۶
• Epidemiology.	۶
• Etiology.	۹
• Assessment.	۱۷
• Prognosis.	۲۶
• Complications.	۲۷
<u>Chapter Two: Physiology of micturition & pathophysiology of enuresis.</u>	۳۶
• Normal development of bladder and sphincter control.	36
• Pathophysiology of nocturnal enuresis.	44
<u>Chapter Three: Treatment Of Nocturnal Enuresis.</u>	۵۱
• Practical management tips.	54
• Enuresis alarm.	54
• Behavioural treatment.	56
• Pharmacological treatment.	61
• Desmopressin.	65
• Combined treatment with alarm and desmopressin.	77
• Non responders.	79
IV. Subjects And Methods.	۸۱
V. Results.	۱۰۰
VI. Discussion.	۱۲۷
VII. Conclusions.	۱۴۶
VIII. Recommendations.	۱۴۷
IX. Summary.	۱۴۸
X. References.	۱۵۱
XI. Arabic Summary.	۱۸۲



List Of Contents





List Of Abbreviations

ADH	Antidiuretic hormone.
ADHD	Attention deficit hyperactivity disorder.
AVP	Arginine vasopressin.
CA	Chronological age.
DDAVP	1-deamino 8 D-arginine vasopressin.
DSM	Diagnostic and statistical manual of mental disorders.
FDA	Food and drug administration.
ICD	International classification of diseases.
IQ	Intelligence quotient.
IVP	Intravenous pyelography.
MA	Mental age.
MCC	Maximum cystometric capacity.
NE	Nocturnal enuresis.
NSAID	Non steroidal anti inflammatory drugs.
PANDAS	Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections.
PMNE	Primary monosymptomatic nocturnal enuresis.
SIADH	Syndrome of inappropriate antidiuretic hormone secretion.
VCUG	Voiding cystourethrogram.

List Of Figures

<i>Figure Number</i>	<i>Figure Title</i>	<i>Page</i>
Figure (١)	Variations of NE prevalence according to gender.	٧
Figure (٢)	Variations of NE prevalence according to age.	٨
Figure (٣)	Inheritance of NE from affected parents.	١٠
Figure (٤)	Dandelion.	١٦
Figure (٥)	Schematic work-up in patients presenting with night time wetting only.	١٧
Figure (٦)	Symptoms of depression in children.	٢٨
Figure (٧)	Neural circuits that control continence and micturition.	٣٧
Figure (٨)	Basic pathophysiology of nocturnal enuresis or nocturia.	٤٥
Figure (٩)	Pragmatic approach to the diagnosis and treatment of nocturnal enuresis.	٥٣
Figure (١٠)	The alarm device.	٥٦
Figure (١١)	Parasympathetic innervation of the urinary bladder and action of anti muscarinic drugs.	٦٢
Figure (١٢)	Desmopressin.	٦٧
Figure (١٣)	Antidiuretic hormone.	٦٧
Figure (١٤)	Chemical structure of vasopressin and desmopressin.	٦٨
Figure (١٥)	Desmopressin ٠,١ mg tablets bottle.	٩١
Figure (١٦)	Star chart.	٩٥
Figure (١٧)	Comparing the study groups regarding gender.	١٠٣
Figure (١٨)	Comparing the study groups regarding order of birth.	١٠٤
Figure (١٩)	Comparing the study groups regarding family history.	١٠٥
Figure (٢٠)	Comparing the study groups regarding anxiety scale at the beginning of study.	١٠٧



List Of Figures (cont.)

<i>Figure Number</i>	<i>Figure Title</i>	<i>Page</i>
Figure (٢١)	Comparing the study groups regarding depression scale at the beginning of study.	١٠٨
Figure (٢٢)	Comparing the study groups according to response at the end of the treatment period (٨ weeks).	١٠٩
Figure (٢٣)	Tracing wet nights frequency in patients and controls throughout the study (at ٢ weeks intervals).	١١١
Figure (٢٤)	Evaluation of drug (desmopressin) response at different intervals of the study (٨ and ١٦ weeks).	١١٣
Figure (٢٥)	Evaluation of drug (desmopressin) response at different intervals of the study (٨ and ١٦ weeks).	١٢٥

List Of Tables

<i>Table Number</i>	<i>Table Title</i>	<i>Page</i>
Table (١)	Subjective view of wetting in children of nocturnal enuresis and urinary incontinence aged from ٥-١١ years.	٣٢
Table (٢)	Pharmacokinetics of different desmopressin formulations.	٧٠
Table (٣)	Comparison between different modalities of treatment of nocturnal enuresis according to full response and cure rates.	٧٨
Table (٤)	Intelligence classification according to IQ scores.	٨٧
Table (٥)	Depression score according to age and gender.	٩٠
Table (٦)	Characteristics of the patients and control groups.	١٠٠
Table (٧)	Comparing the study groups regarding age.	١٠٢
Table (٨)	Comparing the study groups regarding gender.	١٠٣
Table (٩)	Comparing the study groups regarding order of birth.	١٠٤
Table (١٠)	Comparing the study groups regarding family history.	١٠٥
Table (١١)	Comparing the study groups regarding body measurements.	١٠٦
Table (١٢)	Comparing the study groups regarding IQ testing.	١٠٦
Table (١٣)	Comparing the study groups regarding anxiety scale at the beginning of study.	١٠٧
Table (١٤)	Comparing the study groups regarding depression scale at the beginning of study.	١٠٨
Table (١٥)	Tracing wet nights frequency in patients and controls throughout the study (at ٢ weeks intervals).	١١٠
Table (١٦)	Comparison of number of wet nights in the two groups at ٨ and ١٦ weeks in relation to ٠ point.	١١٢

List Of Tables (cont.)

<i>Table Number</i>	<i>Table Title</i>	<i>Page</i>
Table (١٧)	Evaluation of drug (desmopressin) response at different intervals of the study (٨ and ١٦ weeks).	١١٣
Table (١٨)	Correlation of Desmopressin response with sex, order of birth, family history and number of wet nights at the beginning of the study at ٨ weeks	١١٥
Table (١٩)	Correlation of Desmopressin response with anxiety grades at the beginning of the study and the end of the study, and depression grades at the beginning of the study and the end of the study.	١١٧
Table (٢٠)	Correlation of Desmopressin response with age, weight, height, body mass index, head circumference and IQ test at ٨ weeks.	١١٩
Table (٢١)	Correlation of Desmopressin response with sex, order of birth, family history, anxiety grade at the beginning and the end of the study, depression grade at the beginning and the end of the study and number of wet nights at the beginning of the study at ١٦ weeks.	١٢٠
Table (٢٢)	Correlation of Desmopressin response with age, weight, height, body mass index, head circumference and IQ test at ١٦ weeks.	١٢٢
Table (٢٣)	Comparison of anxiety score in the patients group before and after treatment.	١٢٣
Table (٢٤)	Comparison of depression score in the patients group before and after treatment.	١٢٣
Table (٢٥)	Comparison of anxiety score in the controls group before and after treatment.	١٢٤
Table (٢٦)	Comparison of depression score in the controls group before and after treatment.	١٢٤
Table (٢٧)	Comparing the study groups according to incidence of relapse.	١٢٥

INTRODUCTION

Nocturnal enuresis has been described in early medical texts dating back in antiquity to the Ebers papyrus, with multiple causes and remedies across the centuries. Daytime urinary incontinence, strangely enough, did not attract much attention (*Belman et al, 1999*).

Enuresis and other elimination disorders were initially perceived as volitional acts occurring as a function of character defect, thus treatment tended to be highly punitive. Although a cultural residue of this early perspective remains (i.e. children are still frequently punished for urinary accidents). Toward the middle of this century, this idea was superseded by a psychological perspective. This position lifted the emphasis on volition and personal responsibility and instead emphasized variables such as aberrant family dynamics and toilet training practices and their potentially maladaptive influence on subsequent psychic development (*Watson & Gresham, 1967*).

However, over the last two decades, physicians have developed a better understanding of the different subtypes of patients that constitute the heterogeneous population of children with enuresis, and this has been associated with an increasing awareness of the need for a more active treatment attitude (*Hogg, 1997*).



Failure to obtain urinary continence during the day and/or night is one of the most common disorders of childhood. Although only a minority of incontinent children have an underlying pathologic condition associated with morbidity, "wetting" is still one of the most feared events among children especially when school age is reached. Nevertheless, members of the medical community have been reluctant to treat children with these conditions actively, often referring to the lack of morbidity, and to the misconception that the symptoms are most often mild and short lived (*Hogg, 1997*).

The improved knowledge about various subtypes of wetting has resulted in such children being carefully differentiated with respect to both their evaluation and treatment (*Hogg, 1997*).

AIM OF THE WORK

The aim of this study was the assessment of the efficacy of desmopressin in the treatment of primary monosymptomatic nocturnal enuresis in Egyptian children.

CHAPTER ONE

NOCTURNAL ENURESIS

All children start life being incontinent of urine both by day and night and, as neurological maturation occurs, voluntary control of the bladder is gained first by day then by night. Very few never gain control of the bladder unless there is obvious neurological disease, including gross mental handicap. In most cases, nocturnal enuresis in children should be seen not as disease but as a variation of the normal rate of neurological maturation (*Robson, 1997*).

Enuresis comes from the Greek- Enourein – to void urine. It is a part of elimination disorders, which include also encopresis (*Kanitkar & Dua, 2008*).

Nocturnal enuresis (NE), commonly called bed-wetting, is the most common childhood urologic complaint (*Paredes, 2008*) and one of the most common pediatric health issues (*Robson, 1997*).

Definitions:

Over the years, various terms have been used to describe wetting problems. This practice has created confusion and impeded standardization of diagnosis.

The International Children's Continence Society defined nocturnal enuresis as the involuntary loss of urine that occurs

only at night. It is normal voiding that happens at an inappropriate and socially unacceptable time and place (*Van Gool et al,* 2004).

Another definition is: involuntary urination while asleep after the age at which bladder control usually occurs (*Paredes,* 2002).

American Psychiatric Association's Diagnostic & Statistical Manual Of Mental Disorders-IV (DSM-IV), 2000, defined NE as repeated urination into bed or clothes, occurring twice per week for at least three consecutive months in a child of at least 6 years of age and not due to either a drug side effect or a medical condition. Even if the case does not meet these criteria, the DSM-IV definition allows psychiatrists to diagnose nocturnal enuresis if the wetting causes the patient clinically significant distress (*Mellon and McGrath,* 2003).

On the other hand nocturnal enuresis is defined in the International classification of diseases (ICD 10) as: at least one wet night per month for 3 consecutive months (*WHO,* 2000).

Some researchers consider bed-wetting as a clinical problem if: the child regularly wets the bed after turning seven years old (*Evans and Radunovich,* 2004).

D'Alessandro refines the previous definition to: bed-wetting more than twice a month after six years old for girls and seven years old for boys (*Thiedke,* 2003).

Classification: (Thiedke, 1997)***A) According to previous periods of dryness:***

- *Primary NE (PNE):* bed-wetting in a child who has never been dry.

Also PNE can be defined as: persistent bed-wetting in the absence of any urologic, medical or neurological anomaly in a child beyond the age when over 90% of children are normally dry.

- *Secondary NE:* bed-wetting in a child who has had at least six months of nighttime dryness.

B) According to presence of other symptoms:

- *Monosymptomatic or uncomplicated NE:* normal voiding occurring at night in bed in the absence of other symptoms referable to the urogenital or gastrointestinal tract.
- *Polysymptomatic or complicated NE:* bed-wetting associated with daytime symptoms such as urgency, frequency, chronic constipation, or encopresis.

Epidemiology:

70%-80% of bed-wetters have PNE and 10%-20% have secondary NE (Wan and Greenfield, 1997).

A) Variations according to gender:

- NE occurs three times more often in boys than in girls.

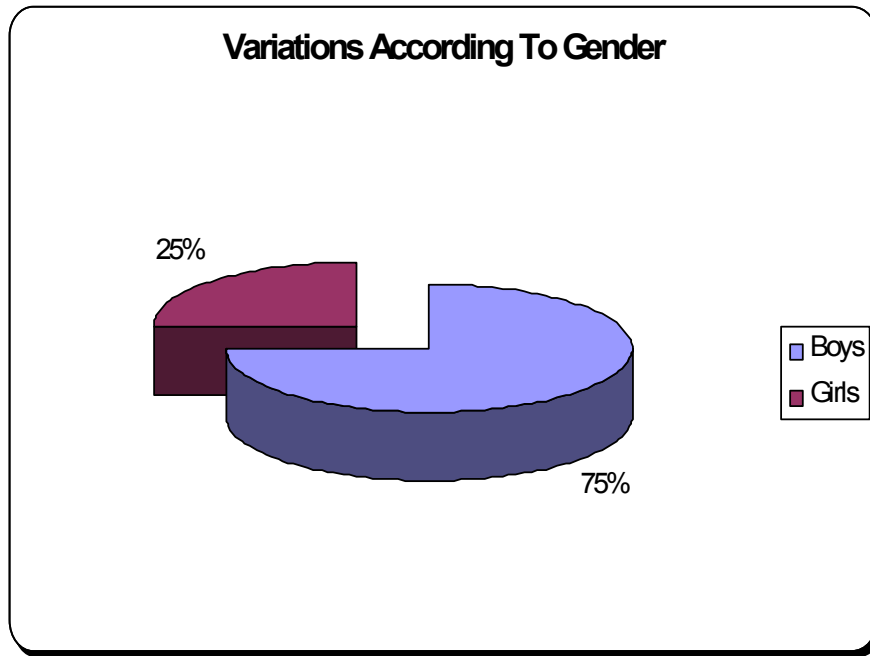


Figure (1): Variations of NE prevalence according to gender
(*Thiedke, 2007*).

- Most girls can stay dry at night by age six and most boys stay dry by age seven.
- Males of all ages are more likely to wet the bed than females and girls tend to be a little ahead of boys in terms of achieving control.
- Moreover, in some children, the problem can persist, with around 1,8% of girls and 1,6% of boys aged 10-16 years wetting at least once every 3 months (*Thiedke, 2007*).