

## Treatment of primary enuresis in adolescent with a combination of fluoxetine and imipramine: A case report

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*About 15 to 20 percent of children have some degree of nighttime wetting, diagnosed as primary enuresis at five years of age. The symptom has a spontaneous resolution rate of approximately 15 percent per year. Therefore, at the age of 15 years old, only 1 to 2 percent of teenagers still wet their beds. Enuresis is not related to sex, birth order, LBW, socioeconomic, marital and parental educational status. Parents are not concerned about their child's enuresis. This report describes a case of primary enuresis in 15 years old female adolescent. Her enuresis began at the age of four years. The patient was depressed and full of guilt of her habit. The physical examination and laboratory tests revealed no abnormality. The patient was started on fluoxetine 20 mg/day and imipramine 25 mg/day and underwent supportive psychotherapy. There was significant reduction in nocturnal urination and free of symptoms in 2 weeks. No side effects were noticed. After 2 months of follow-up, no medication was needed. The combination of the drugs might be an effective answer to the disorder, with low side-effects.*

**Keywords :** *Enuresis, Fluoxetine, Imipramine, Adolescent, Treatment.*

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โรคปัสสาวะรดที่นอนชนิดปฐมภูมิ พบได้บ่อยในเด็กอายุ 5 ปี ประมาณร้อยละ 15 ถึง 20 ซึ่งมักจะหายเองประมาณร้อยละ 15 ต่อปี และที่เป็นต่อเนื่องในเด็กวัยรุ่น อายุมากกว่า 15 ปี พบได้เพียงร้อยละ 1-2 เท่านั้น อาการจะไม่สัมพันธ์กับเพศ ลำดับการเกิด น้ำหนักแรกคลอด เศรษฐฐานะ และการศึกษาของผู้ปกครอง แต่พบว่าผู้ปกครอง ไม่ค่อยสนใจกับปัญหานี้มากเท่าใดรายงานผู้ป่วยหญิงวัยรุ่น อายุ 15 ปี มีอาการปัสสาวะรดที่นอน มาตลอดตั้งแต่ อายุ 4 ปี ไม่เคยได้รับการรักษามาก่อน ผู้ป่วยมีภาวะซึมเศร้า และรู้สึกผิดต่ออาการเจ็บป่วย การซักประวัติ การตรวจร่างกาย และการตรวจทางห้องปฏิบัติการ อยู่ในเกณฑ์ปกติ การรักษาประกอบด้วย การให้ ยาฟลูออซิทิน 20 มิลลิกรัม และ อิมมิพรามิน 25 มิลลิกรัม และการให้จิตบำบัดประคับประคองผู้ป่วยมีอาการดีขึ้น ไม่มีผลข้างเคียง จากยา และไม่มีอาการอีกเลย ใน 2 สัปดาห์ สามารถหยุดยาได้ ใน 2 เดือน อภิปรายถึงเหตุผลการใช้ ยา เพื่อเพิ่มประสิทธิภาพการลดอาการ และลดผลข้างเคียงของยา

This report describes a case of primary enuresis in a depressed female adolescent, and the disorder responded to fluoxetine combined with imipramine. The American Psychiatric Association has defined bed-wetters as children older than the age five who have urine incontinence at night (Table 1).<sup>(1)</sup> When the condition takes place without any medical cause is called primary enuresis. In practice, children who have never maintained continence for more than one year are referred to as having primary enuresis, whereas children who have achieved continence for one year or longer and then lost it are labeled as having secondary enuresis.

It is now generally accepted that 15 to 20 percent of children have some degree of nighttime wetting at the age of five. The condition usually has a spontaneous resolution at the rate of approximately 15 percent per year. Therefore, at the age of 15 years old, only 1 to 2 percent of teenagers still wet their beds. At the age of five, about 15 – 20 % of children

have some nighttime wetting; the numbers are similar for daytime voiding dysfunction. Since the rate of spontaneous resolution is about 15 % per year, by age of 15 only 1 – 2 % of the children are affected. Most studies report that boys about twice as frequent as girls for nocturnal; varies for types of diurnal. Usually, parents are not concerned about their child's enuresis.<sup>(2)</sup>

The prevalence of enuresis in adolescent in Thailand the prevalence of primary, secondary and total enuresis was 15.4, 2.7 and 18.1 percent respectively in 5 -15 years old children. Of these, 88.5 percent had nocturnal enuresis, 0.6 percent had diurnal enuresis, 10.6 percent had diurnal and nocturnal enuresis.<sup>(3)</sup>

Enuresis can persist well into adolescence and cause a significant problem; 80 % of these patients have severe enuresis; and 31 % also have associated daytime urinary symptoms, with 40 % of them received no previous therapy.<sup>(4)</sup>

**Table 1.** Diagnostic criteria for enuresis.

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- A. Repeated voiding of urine into bed or clothes (whether involuntary or intentional).
  - B. The behavior is clinically significant as manifested by either a frequency of twice a week for at least 3 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 behavior is not due exclusively to the direct physiological effect of a substance (e.g., a diuretic) or a general medical condition (e.g., diabetes, *spina bifida*, a seizure disorder).

**Specify type:**

Nocturnal only

Diurnal only

Nocturnal and diurnal

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The standard treatments of enuresis consist of pharmacological treatment, psychological, behavioral and family intervention. The pharmacological treatment recommended in enuresis is imipramine. This report shows the efficacy of combined pharmacological treatment of imipramine and fluoxetine which have the good response of treatment.

### Case report

A 15-year-old unmarried female adolescent, from middle socio-economic status, was brought to clinic by her mother who complained that patient had repeated episodes of enuresis. She was born with normal labor. Her motor, social and language developmental milestones were normal but she could not control her bladder. Her enuresis persisted through out her childhood and early adolescence. According to her parents, she was a child with easy temperament, compared to other children. There was no family history of mental illness and psychiatric history of treatment of the symptom.

At the age of 4 years old after the divorce of her parents, the patient was noticed to have repeated episodes of enuresis. The symptom appeared every night. There was no associated sense of lack of urinary control over the day. She had average normal education level. Over the time, there was no change in her eating habit. There was no past or present history suggestive of eating disorder. Her menstruation began at 12 years old, and the cycles were regular and adequate. There were no other associated psychiatric symptoms and behaviors.

Her physiological and neurological examinations reveal no abnormality. Her laboratory tests including complete blood count, renal function tests,

liver function tests and serum electrolytes were within normal limits. Her mental examination showed depressed mood and guilt of the habit. After initial assessment, she was started on fluoxetine 20 mg/day and imipramine 25 mg/day. She also underwent supportive psychotherapy including stress management and family sessions. There was significant reduction in nocturnal urination and she was free of the symptom in 2 weeks. No side effects were reported or noticed. After 2 months of follow-up, no medication was need.

### Discussion

The study of 5 - 15 years of 179 cases of enuresis in Thailand about the risk factors which significantly correlated with enuresis were the history of bed-wetting in the parents/sibling and inconsistent toilet training. Enuresis in Thai patients is not related to sex, birth order, LBW, socioeconomic, marital and parental educational status.<sup>(3)</sup> Most parents thought that enuresis was normal for their children, and therefore sought no treatments.<sup>(5)</sup> Patients usually come for treatment rather late, such as this patient.

Behavioral modification techniques such as bedwetting alarms yield the highest long-term cure rate, but they require a strong commitment and are hardly successful before the age of 7-8 years.<sup>(6)</sup> A treatment of primary nocturnal enuresis with desmopressin (DDAVP) is based upon the hypothesis that antidiuretic hormone (ADH) secretion is insufficient during the night. Pharmacotherapy has been revolutionized by DDAVP which gives a response rate of up to 70 % and relatively free from side-effects but it has a high relapse rate after medication.<sup>(7)</sup> Imipramine is less expensive than DDAVP but may

be fatal in case of overdose. Imipramine restores nocturnal ADH excretion; it increases morning plasma ADH levels, and causes consistent changes in other biochemical variables. <sup>(8)</sup> Anticholinergics should be reserved for those patients who have significant diurnal symptoms or those who have failed with the first-line pharmacotherapy. Overall, patients and parents should be reassured that the spontaneous cure rate is high. In this case, medication was the first line of treatment because of the suitability of the patient's age and it has low cost of treatment.

Complete history, examination and laboratory tests were taken for the patient. Comparing with the adult onset of nocturnal enuresis with absent daytime incontinence which is a serious symptom that usually heralds significant urethral obstruction, and a high incidence of bladder diverticulum, hydronephrosis and vesicoureteral reflux. It requires urological investigation and aggressive therapy. <sup>(9)</sup>

There were few studies about the efficacy of selective serotonin reuptake inhibitor such as fluoxetine<sup>(10)</sup>, fluvoxamine<sup>(11)</sup> in enuresis. Imipramine alone gives a response rate of 30 % with high relapse rate in enuresis. <sup>(12)</sup> The major disadvantage of imipramine is its anticholinergic and sedative side-effects that increase with higher dose.

The low response treatment rate and the high side effects of imipramine may be the limitation of treatment especially in adolescent which may need the higher dose. According to the succession report of fluoxetine in enuresis, it may be possible for the combination of treatment in order to augmentation of efficacy and decrease the side effect of imipramine.

So a combination of serotonergic with anticholinergic activity may be an answer in the

antidiuretic activity with fewer side effects which is shown in this case. Psychotherapy in this case consists of supportive and family intervention. The future studies of control trial should be done this aspect.

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