SYNERGISTIC EFFECT OF LOXOPROFEN AND TCAD IN TREATMENT OF NOCTURNAL ENURESIS IN

PATIENT OLDER THAN 15 YEAR

Anis Hasan Haleem Albu-Salih

Al-Hussein Teaching Hospital, Samawah, Al-Muthanna, Iraq M.B.Ch.B.
FIBMS (Urosurgery)

Alsalhianees@gmail.com 009647807483020

Abstract:

The study was aimed to compare between two medication regimens in treatment of nocturnal enuresis in children older than 15 year and young adult. A study was conducted on 48 children suffering from nocturnal enuresis, divided into two groups, the first group included 25 children treated with tricyclic antidepressant (TCAD) in combination with loxoprofen tab. The second group included 23 child treated with TCAD alone. Our results showed significant preference to group I (loxoprofen and TCAD) as compared with group II (TCAD alone) in treatment of nocturnal enuresis after 1-3WK and 3-6WK respectively. From this study we can conclude that loxoprofen plus TCAD could reduce number of NE significantly as compared with TCAD alone.

Keywords: Nocturnal enuresis . Urinary Incontinence, loxoprofen, Tricyclic antidepressants

Introduction:

Nocturnal enuresis (NE) as defined by the International Continence Society (ICS) is the involuntary passing of urine during sleep [1]. It can result in sleep deprivation which can affect a patient's mood as a result. Commonly, it is an isolated symptom, starting as primary nocturnal enuresis, which persists from childhood into adult life [2]. Nocturnal enuresis (enuresis or bedwetting) is the most common type of urinary incontinence in children. Depending on the definition, prevalence is 8-20% for 5 year olds, 1.5-10% for 10 year olds, and 0.5-2% for adults, with 2.6% of 7.5 year old children wetting on two or more nights a week [3]. A large epidemiological study showed that nocturnal enuresis is more common in males at all ages, and is more likely to persist in those with frequent wetting [4]. Nocturnal enuresis is usually idiopathic and is

commonly associated with daytime urinary incontinence (seen in 3.3% of 7.5 year olds in a large epidemiological study), faecal incontinence, and chronic constipation. In a tertiary continence service, 36% of children with nocturnal enuresis reported constipation[5]. And enuresis resolves in about two thirds of such children when constipation is treated[6]. About 30% of children with sleep disordered breathing have nocturnal enuresis, probably because of impaired sleep quality[7]. Similarly, about 30% of obese children have nocturnal enuresis[8]. Which is more resistant to treatment[9]. Nocturnal enuresis is more common in children with developmental delay, physical or intellectual disabilities, and psychological or behavioural disorders. It occurs in 20-40% of children with psychological or behavioural disorders, such as attention-deficit/hyperactivity disorder (ADHD) (the most common), autism spectrum disorder, anxiety, and depressive or conduct disorders[10]. In these children, enuresis is more likely to be persistent, possibly because of lower adherence to treatment. Tricyclic antidepressants (TCAs) are a class of medications that are used primarily as antidepressants[11]. A systematic review of 58 trials showed that tricyclic antidepressants can be effective with a reduction in the frequency of bedwetting by one night per week compared with placebo (WMD -0.92, -1.38 to -0.46)[12]. Loxoprofen is a nonsteroidal anti-inflammatory drug (NSAID) in the propionic acid derivatives group[13]. it can be effective and useful for patients with nocturia that the main mechanism of this effect is to decrease urine production during a night's sleep[13] and by inhibiting prostaglandin synthesis, prostaglandinestmulate bladder smooth muscle contraction and its inhibition lead to bladder smooth muscle relaxation an thus decreasing the urination episodes [14]. Aims of this study is to compare between medical regimens in treatment of NE.

Materials and methods:

Between January 2017 and December 2019, 25 chlid with nocturnal enuresis Received TCAD (tofranil tab 25mg), and a single dose of 60 mg of loxoprofen at night half hour before sleep and considered as group I. During the same period, 23 child with nocturnal enuresis selected as the group II received TCAD tofranil tab25mg alone at night half hr before sleep, They were reevaluated after 1-3wk and 3-6wk of treatment by the number of nocturnal enuresis episodes. Both groups received the same instruction of fluid restriction 4hr before night sleep.

SAS, (2012) Statistical Analysis System- program was used to effect of difference factors in study parameters. Independent samples T- test was used to significant compare between means in this study[15].

Results and discussions:

Results of this study illustrate that the mean of nocturnal enuresis was 26.1 in group I and 22 in group II 6wk before treatment. After 1-3wk of treatment the mean of NE reduced significantly (P>0.05) in group I and record 2.92 as compared with 4.5 recorded to group II.While after 3-6wkof treatment the mean of NE reduced significantly (P>0.01) in group I and record 1.1 as compared with 2.5 recorded to group II table (1). Our results in group II is nearly similar to finding of Caldwell et al, (2016) whom suggesting that tricyclic reduce bedwetting by about one night per week during treatment and about a fifth of the children achieve 14 dry nights[16]. While disagreed with our finding in group I as the number of bedwetting is more than those recorded in our study, this is may be due to the synergistic effect of loxoprofen in combination with tricyclicthat used in group I.In both groups the NE episodes in the 2ed half of the study (after treatment) is significantly lesser than that in the 1st half of the study (before treatment). This result is due to Tricyclic are antidepressants that probably work by their antispasmodic effect on the bladder[16]. Results of current

study are compatible with those results obtained by Saito et al, (2005) whom suggested that loxoprofen improves nocturia, and the main mechanism of this effect is by decreasing urine production during] sleeping[17]

Table (1)Number of NE 6wk before] treatment, 1-3wk and 3-6wk after treatment in group I and group II

Group	Number	6wk before Treatment	1-3wk after	3-6wk after
		Mean± SE	treatment	treatment
Group I	25	26.1**± 2.3	2.92 ± 0.4	1.1 ± 0.2
Group II	23	22**± 1.7	4.5*±0.6	$2.5**\pm 0.3$
** significant at P<0.01				
* significant at P<0.05				

Conclusion:

From this study we can conclude that loxoprofen plus TCAD could reduce number of NE significantly as compared with TCAD alone.

References

- 1. Abrams, P., Cardozo, L., Fall, M., Griffiths, D., Rosier, P., Ulmsten, U., ...&Wein, A. (2003). The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology .49-37,(1)61,
- 2. Yeung, C. K., Sihoe, J. D. Y., Sit, F. K. Y., Bower, W., Sreedhar, B., & Lau, J. (2004). Characteristics of primary nocturnal enuresis in adults: an epidemiological study. BJU international.345-341,(3)93,
- 3. Butler, R. J., Golding, J., Northstone, K., & ALSPAC Study Team. (2005). Nocturnal enuresis at 7.5 years old: prevalence and analysis of clinical signs. BJU international .410-404 ,(3)96,
- 4. Jain, S., & Bhatt, G. C. (2016). Advances in the management of primary monosymptomatic nocturnal enuresis in children. Paediatrics and international child health .14-7,(1)36,
- 5. Austin, P. F. S. B., Bower, W., Chase, J., Franco, I., Hoebeke, P., Rittig, S., ...&Nevéus, T. (2013). The standardization of terminology of bladder function in

- children and adolescents: update report from the Standardization Committee of the International Children's Continence Society (ICCS .(
- 6. Yeung, C. K., Sreedhar, B. I. J. I., Sihoe, J. D., Sit, F. K., & Lau, J. (2006). Differences in characteristics of nocturnal enuresis between children and adolescents: a critical appraisal from a large epidemiological study. BJU international ,(5)97, .1073-1069
- 7. McGrath KH, Caldwell PHY, Jones MP. The frequency of constipation in children with nocturnal enuresis: a comparison with parental reporting. *J Paediatr Child Health* 2008;44:19-27.
- 8. McGrath, K. H., Caldwell, P. H., & Jones, M. P. (2008). The frequency of constipation in children with nocturnal enuresis: a comparison with parental reporting. Journal of paediatrics and child health, 44(1-2), 19-27. 9.Carson VB (2000). Mental health nursing: the nurse-patient journey W.B. Saunders. ISBN 978-0-7216-8053-8.pp.423.
- 10. Weintraub, Y., Singer, S., Alexander, D., Hacham, S., Menuchin, G., Lubetzky, R., ...&Pinhas-Hamiel, O. (2013). Enuresis—an unattended comorbidity of childhood obesity. International Journal of Obesity .78-75,(1)37,
- 11. Guven, A., Giramonti, K., & Kogan, B. A. (2007). The effect of obesity on treatment efficacy in children with nocturnal enuresis and voiding dysfunction. The Journal of urology .1462-1458 (4)178,
- 12. Daiichi Sankyo Co. (January 24, 2006). "Percutaneous Absorption-Type Analgesic and Anti-inflammatory Drug Loxonin Poultice 100mg Receives Approval for Manufacture" (Press release).Doctor's Guide Global Edition.Retrieved 2007-04-19.
- 13. Saito, M., Kawatani, M., Kinoshita, Y., Satoh, K., &Miyagawa, I. (2005). Effectiveness of an anti-inflammatory drug, loxoprofen, for patients with nocturia. International journal of urology .782-779, (8)12,
- 14. Andersson KE, Persson K. The L-arginine/nitric oxide pathway and non-adrenergic, non-cholinergic relaxation of the lower urinary tract. Gen Pharmacol 24:833, 1993.
- 15. SAS. (2012). Statistical Analysis System, User's Guide. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA.
- 16. Caldwell PHY, Sureshkumar P, Wong WCF.(2016). Tricyclic and related drugs for nocturnal enuresis in children. Cochrane Database of Systematic Reviews, Issue 1. Art.

17. Saito, M., Kawatani, M., Kinoshita, Y., Satoh, K., &Miyagawa, I. (2005). Effectiveness of an anti-inflammatory drug, loxoprofen, for patients with nocturia. International journal of urology .782-779 ,(8)12,