Evaluation of the Effectiveness of a Short-term Treatment and Repeat Treatment of Nocturnal Enuresis Using an Enuresis Alarm

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OBJECTIVE To evaluate the effectiveness of a 3-month enuresis alarm (EA) treatment and repeat EA treatment among pediatric patients with nocturnal enuresis, and to compare patient characteristics among "responders" and "nonresponders" to treatment.

MATERIALS AND METHODS Clinical outcomes were retrospectively evaluated for 137 children (94 boys and 43 girls, mean age, 10.1 years). Effectiveness was evaluated after an initial 3-month treatment, using the International Children's Continence Society criteria. Among children in the no-response group at 3 months, those who continued the EA treatment for ≥4 months were subclassified into group 1, whereas children who repeated the EA treatment at an interval ≥6 months were subclassified into group 2.

RESULTS Among our 137 cases, 19 achieved complete response and 47 achieved partial response at 3 months, for an overall treatment effectiveness rate of 48%. Among the no-response group, treatment was extended in 17 cases (group 1), with 3 (18%) achieving a successful outcome. Treatment was repeated in 18 cases (group 2). In group 2, 8 (44%) achieved successful outcome at 3-month time point. Daytime urinary incontinence did not modify treatment effectiveness.

CONCLUSION EA treatment should be given for a short period of time and should not be continued without a definite purpose or clear response. Suspending and then repeating this treatment after an appropriate interval is effective for patients who do not respond to the initial course of treatment. UROLOGY 105: 153–156, 2017. © 2017 Published by Elsevier Inc.

Enuresis alarm (EA) is a standard treatment for nocturnal enuresis (NE), with proven effectiveness to increase bladder capacity and improve arousal thresholds for NE.[1-3] However, research is required to improve our understanding of mechanisms underlying EA treatment, including the level of arousal to NE developed and the role of family cooperation in treatment effectiveness. Moreover, evidence is needed to identify patient characteristics associated with positive and negative outcomes of EA treatment, as well as the duration of treatment associated with a negative therapeutic outcome. Therefore, the aims of our study were to evaluate the effectiveness of a 3-month EA treatment and repeat EA treatment among pediatric patients with NE at our institution, and to compare patient characteristics among "responders" and "nonresponders" to treatment.

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MATERIALS AND METHODS

Patient Selection

The retrospective study group comprised 137 children (94 boys and 43 girls, mean age, 10.1 years) who underwent EA treatment at the Department of Pediatric Urology of Jichi Medical University, Children's Medical Center Tochigi, between April 2008 and September 2015. Some children had a clinical diagnosis of non-monosymptomatic NE (MNE). For children treated with other treatment approaches, such as anticholinergic agents or antidiuretic vasopressin analog, EA treatment was implemented ≥1 month after initiation of a prior treatment.

Standardized Enuresis Alarm Treatment

At our institution, we used the following standard approach to the treatment of NE. First, we introduced healthy lifestyle guidance and corrected bowel habits. The healthy lifestyle guidance included is as follows: to limit fluid intake within 3 hours of bedtime, to sleep and wake up earlier, and not to scold that NE was not improved. For bowel movement, based on a bowel diary for 2 weeks, we diagnosed and treated bowel movement as follows: when the frequency of defecation was less than 3 times per week, or the frequency of hard stool (Bristol Stool Chart types 1-2) was more than 50%, or they had bowel pains and anal bleedings. EA

and pharmaceutical treatments were implemented if behavioral interventions did not improve NE.

For all patients, the EA was donned before sleep. When the EA was triggered, children were awakened by their parents to void in the toilet. The EA was not donned again after voiding. This protocol was continued over a 3-month duration as a guide. If a child did not respond to the treatment at the 3-month time point of evaluation, the decision to either continue treatment or not was made in consultation with the child and the child's family. Even if initial EA treatment was not successful, EA treatment was repeated at an interval of ≥6 months after completion of the initial treatment. For repeat EA treatment, method and duration of treatment were the same as in the initial treatment.

Clinical Evaluation

Effectiveness of EA treatment at 3 months was evaluated on a monthly basis, using the criteria of the International Children's Continence Society (ICCS), as follows: no response (NR), defined by a decrease in NE incidence ≤49%; partial response (PR), defined by a 50%-99% decreased in NE incidence; and complete response (CR), defined by full resolution of NE. If the patients underwent less than 2 months' duration of treatment, we evaluated the effectiveness of EA treatment at the time of completion of the treatment. In our study, we regarded CR and PR as successful treatment outcomes.[4]

The following patient-specific characteristics were compared among children obtaining a successful treatment outcome (CR or PR group) and the NR group: age, sex, frequency of NE, prior treatment, simultaneous treatment, and concurrent daytime urinary incontinence (DUI). To evaluate frequency of NE, we assessed the wet nights from last 2 weeks to 1 month.

Among children in the NR group at 3 months, those who continued the EA treatment for ≥4 months were subclassified into group 1, whereas children who repeated the EA treatment at an interval ≥6 months were subclassified into group 2.

Statement of Ethics

Our study was approved by the Ethics Committee of Jichi Medical University. In accordance with ethical guidelines of the Ministry of Health, Labour and Welfare in Japan for clinical research, the description document was posted on our department's website, and the content of the study was published in our hospital.

Statistical Analysis

Between-group differences (ie CR or PR vs NR) were evaluated using a Mann-Whitney *U* test for continuous variables and a Fisher exact test for categorical variables. A *P* value <.05 was considered to be a significant difference.

RESULTS

The mean and median frequencies of NE were 79.1% and 89%, respectively. Among our 137 cases, an incidence rate of NE of 90% was reported in 67 (48%) of cases. Other patient characteristics are shown in Table 1. Prior or simultaneous bowel treatments were performed in 45 patients (33%). At the 3-month time point, the ICCS distribution was as follows: CR, 19 cases; PR, 47 cases; and NR, 71 cases. Therefore, a treatment effectiveness rate of 48% (66 cases) was obtained.

Comparisons of patient characteristics between the CR or PR group and the NR group are summarized in Table 2.

Table 1. Characteristics of all patients

	Patients (n = 137)
Age (mo)	120.6 ± 19.7
Frequency of NE (%)	79.1 ± 23.2
Girl-to-boy ratio	43:94
Prior treatment	108 (79%)
Simultaneous treatment	62 (45%)
Daytime urinary incontinence	16 (12%)

Patients in both groups were comparable in terms of age, sex, frequency of NE, prior treatment, and simultaneous treatment. The simultaneous treatment included anticholinergic agents, antidiuretic vasopressin analog, alpha blockers, tricyclic antidepressants, and bowel treatment. The mean duration of EA treatment was 3.2 months. Among children in the NR group at 3 months, 17 (13 boys and 4 girls) extended their EA treatment of ≥4 months to a mean treatment duration of 6.5 months. These patients were subclassified in group 1, with 3 cases (18%) achieving a successful outcome at the end of treatment extension. Eighteen children in the NR group at 3 months (15 boys and 3 girls) were subclassified into group 2. As for treatment outcome of group 2 at the 3-month time point, CR and PR were achieved in 2 and 6 patients, respectively. Therefore, a successful outcome was achieved in 9% (3 of 17 cases) in group 1 and in 44% (8 of 18 cases) in group 2.

At the initiation of EA treatment, DUI was reported in 16 (12%) cases. The age of these children was comparable with those of all other children in our study group. Among these patients, CR was achieved in 3 cases and PR in another 3 cases at 3 months, a rate of successful outcome that was comparable with the rate for children without DUI.

DISCUSSION

EA treatment is effective when it is given for a short period, that is, for 3 months. Continuing this therapy for a longer period does not increase efficacy. There is, however, no consensus as to the optimal duration of alarm treatment. Oredsson and Jorgensen reported that a period of 6 weeks was too short to provide a therapeutic effect.[5] The therapeutic guideline and the ICCS recommend that EA treatment be given for at least 2-3 months,[6,7] although no study has compared different periods of treatment. EA treatment should reportedly be discontinued when it fails to provide an effect within 6-8 weeks because a longer treatment period imposes an enormous burden on children with NE and their families.[8] In this study, the efficacy of EA treatment was limited when it was continued in patients who did not respond within the first 3 months.

Repeat EA treatment after an appropriate interval is effective for some patients who failed to respond to the initial course of treatment. Repeat EA treatment was reported to be useful for patients who experienced a relapse after responding to the initial course of treatment.[9] However, according to our review of the relevant literature, no studies

Table 2. The comparisons of patient characteristics

	CR or PR Group (n = 66)	NR Group (n = 71)	*P* Value
Age (mo)	119.2 ± 16.1	121.8 ± 22.6	.77
Frequency of NE (%)	77.8 ± 23.3	80.2 ± 23.1	.522
Girl-to-boy ratio	24:42	19:52	.27
Prior treatment	50 (76%)	58 (82%)	.412
Simultaneous treatment	28 (42%)	34 (48%)	.607
Daytime urinary incontinence	6 (9%)	10 (14%)	.431

have examined repeat treatment in patients who failed to respond to the initial course of treatment. Because EA was reported to influence the arousal threshold,[3] it may exert its effect by maturing the cognitive functions involving urination. Considering that the motivation of children with NE and their families is closely related to the effects of this treatment, we found that it would be more suitable, from a motivational viewpoint, for patients who did not respond to EA treatment to suspend and then repeat treatment after an appropriate interval than to continue for a prolonged period with no apparent efficacy. Continuing the initial course of EA treatment for a long period poses another problem because it renders patients reluctant to participate in treatment and to refuse the second course of this treatment. In contrast, suspending the initial course of EA treatment early may facilitate the introduction of a second attempt. Because the bladder function and sleep-wake mechanism have not fully matured in patients with enuresis,[8,10-12] their maturation has a positive effect on the treatment of enuresis. One study found that patients who did not respond to EA treatment were unlikely to respond to pharmacotherapy,[13] suggesting that repeat treatment will become a more important option.

Another study found that patients with enuresis had more frequent daytime voiding symptoms than normal children without enuresis,[14] indicating that immature bladder function is one of the causes of enuresis. The ICCS reported that patients with daytime voiding symptoms were classified as non-MNE and did not respond well to EA.[6,7,9,13] Kajiwara et al reported that, of patients with enuresis, those with non-MNE accounted for as high a proportion as 41%.[15] However, it was also reported that making an accurate diagnosis of voiding symptoms in children was difficult, and that the borderline between MNE and non-MNE was unclear.[6] Furthermore, yet another study showed that the efficacy of EA was comparable between patients with MNE and patients with non-MNE.[16]

Some patients reportedly have bladder conditions varying between the daytime and the nighttime, irrespective of the presence or absence of daytime voiding symptoms, such as those with reduced bladder volume during the nighttime as compared with the daytime and those who had detrusor overactivity at night but not during the day.[17] The existing classification of MNE and non-MNE is based on daytime voiding symptoms and therefore may not reflect nighttime bladder function and thus may not be essential for predicting the therapeutic effect of EA on nighttime bladder function. Our study including patients with non-MNE showed the efficacy of EA even in those with DUI, with no significant difference in the effect of EA being observed between patients with and without DUI.

The limitation of this study was its retrospective design. This study was limited in that the response rate to EA treatment was low as compared with other studies. This is partly attributable to our hospital being a referral-based university hospital, which often receives intractable cases, irrespective of the presence or absence of referral. Another potential limitation is that, given a report that EA treatment was more effective in patients 8 years of age or younger,[18] our patients had a rather high mean age of 10 years and 1 month and were therefore considered to be more refractory to EA treatment. In addition, although our patients used concomitant drugs, we examined the efficacy of EA alone because none started any additional concomitant drugs concurrently with EA treatment. Last, these were short-term results and sustainability was not assessed.

CONCLUSION

EA treatment should be given for a short period of time and should not be continued without a definite purpose or a clear response. Suspending and then repeating treatment after an appropriate interval is effective for patients who do not respond to the initial course of treatment.

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