A.L. Malykh[1], I.N. Zakharova[2], M.I. Pykov[2]

1 Ulyanovsk State University, Russian Federation
2 Russian Medical Academy of Postgraduate Education, Ministry of Health of the Russian Federation, Moscow

Enuresis in adolescents and conscripts: modern approaches to diagnostics

Author affiliation:
Malykh Andrei L'vovich, MD, assistant professor of the department of healthcare organization and public health
Address: 5, Aviastroitelei Str., Ulyanovsk, 432069, **tel.:** +7 (8422) 20-35-73

Article received: 23.10.2013. Accepted for publication: 14.01.2014.

The article lists results of a complex examination of adolescents and conscripts of 15–23 years of age with enuresis performed according to the Ulyanovsk Region military commissariat's referral in 2003–2012. The main methods of diagnostics were pelvic ultrasound, Doppler sonography of renal arteries, electric encephalography, uroflowmetry and sexual hormones level determination. Increase in size and volume of prostate gland, reduction in total testosterone and luteinizing hormone blood levels, high spread of vesicoptosis (prolapse of urinary bladder) and nephroptosis were revealed in 67.3 % of conscripts with nocturnal enuresis in comparison with healthy conscripts.
Key words: *functional constipation, prostate gland, enuresis, urinary bladder dysfunction, differentiated therapy, adolescents.*

The issue of lower pelvic organs dysfunctions is one of the most topical for pediatrics and pediatric urology [1]. The issue is urgent due to high spread of this pathology. According to epidemiologic trials, 20% of 5-7-year-old children have urination disorders; the amount of primary school students with urinary bladder (UB) dysfunction reaches 17-26% [2, 3]. Enuresis is the most frequent form: it is present in 5-7% of 7-year-old children. Urinary incontinence regresses with age due to maturation of central nervous system and gradual formation of adult urination. However, according to the literature data, enuresis persists in 1.5% of adolescents and 0.5-1% of adults [4, 5].
Nocturnal urinary incontinence occurs more often than it is diagnosed. On the one hand, some of the conscripts undergoing examination on the grounds of enuresis have signs of malingering: such adolescents are found restrictedly fit for military service (fitness category B) according to article "Diseases Timetable". On the other hand, enuresis in adolescents and conscripts is of high medical and social significance. The disease induces considerable discomfort of male youths and their social circle. Adolescents are denied the opportunity to study at boarding schools, serve in the army, have lower quality of life and acquire accentuated personality traits [5, 6]. Long-term psychotraumatic factor of both the disease per se and awareness of one's physical inferiority makes a negative impact on the adolescent's behavior and leads to emotional-volitional disorders with markedly anxious mental state. The **objective** of this research was to study risk factors and reveal morphofunctional and clinical peculiarities of enuresis in adolescents and conscripts.

PATIENTS AND METHODS

The trial involved 143 15-23-year-old (16.3±1.8) adolescents with enuresis examined at the Ulyanovsk central clinical hospital (State Healthcare Institution) in 2003-2012 upon request of the Ulyanovsk regional joint military commissariat. All conscripts were divided into 3 groups. Group 1 was comprised of 98 (68.5%) adolescents with verified diagnosis "Enuresis"; group 2 (convalescents) was comprised of 12 (11.2%) conscripts without complaints of nocturnal urinary

incontinence having a record of urinary incontinence in medical history; the health group was comprised of 33 (20.2%) patients with signs of malingering.

All adolescents underwent a complete physical examination in order to reveal morphofunctional peculiarities of enuresis. The conscripts with nocturnal urinary incontinence as one of the symptoms of an organic nervous or urinary disease were excluded from the trial. The examination algorithm consisted of somatic and neurological status determination, electroencephalography, lower pelvic ultrasound, including Doppler sonography of renal arteries and veins, uroflowmetry, radiography of lumbosacral spine and determination of sexual hormones level. Apart from that, we studied emotional-volitional and cognitive functions of conscripts with nocturnal urinary incontinence using questionnaire "Psychological General Well-Being Index" and performed STAI in order to assess state and trait anxiety.

Noninvasive methods of diagnostics have become top-priority in pediatric practice in the recent decades. The primary method we used was lower pelvic ultrasound with transperineal and transrectal access. We examined condition of lower pelvic organs and pelvic floor muscles through the anterior abdominal wall and transperineally in B mode. Patients were put in the left lateral jackknife position to perform scanning. The sensor was put directly in the ischioanal fossa. Scanning was performed in 2 perpendicular planes – sagittal and frontal. Doppler sonography aimed at assessment of renal blood flow in conscripts and adolescents was performed on three vascular levels. We assessed peak systolic velocity (Vmax, cm/s), end diastolic velocity (Vmin, cm/s) and time-averaged maximum blood flow velocity (TAMX, cm/s) out of absolute parameters, resistance (RI) and pulsatility indices (PI) – out of relative parameters.

We additionally assessed diameters of portal and renal veins and determined condition of venous blood flow. Volume of conscripts' prostate glands was calculated according to formula:

$V = 0.522 \times A \times B \times C$ (cm^3),

where A is superior-inferior, B – anteroposterior and C – cross-sectional dimensions in cm (S. Patel, 2002).

We used a 16-channel apparatus Nycon Choden (Japan) to determine functional state of bioelectrical brain activity (BEA). Type of electroencephalogram (EEG) was determined according to the E.A. Zhirmunskaya's classification (1991) and the N.K. Blagosklonova technique (1994) adapted for pediatric practice, the latter distinguishing between organized, disorganized (delayed or accelerated α-rhythm), desynchronized and hypersynchronized BEA types.

We used functional system Bonito (Italy) to perform urodynamic examination. Adaptive and reservoir/evacuation functions of urinary bladder were assessed on the basis of urination time (T, s), maximum volumetric urine flow rate (Q_{max}, ml/s), maximum urine flow rate achievement time (T Q_{max}, s) and effective volume of urinary bladder (V, ml). We performed qualitative assessment of uroflowgrams on the basis of interconnection of parameters "volume" and "rate", which are non-specific for various pathologies of lower urinary tracts. Uroflowmetric curve was plotted automatically according to the results of direct graphic recording of volumetric urine flow rate during urination. It was later evaluated according to the standards by E.L. Vishnevsky and T.V. Gadzhiev (2006). On the basis of this evaluation we determined the urination type: normal, obstructed, fast and ambiguous (intermittent) [4].

Apart from that, we examined concentration of sexual hormones in blood serum of all conscripts: follicle-stimulating hormone, luteinizing hormone, prolactin and total testosterone – using a solid-phase immunochemiluminescent analyzer BioRad-680 (Japan).

To perform statistical data manipulation we used software Statistica 8.0. The following parameters were calculated: geometric average (G), standard deviation (SD) and interquartile range. We used Mann-Whitney U test to determine significance of differences between the average compared values (p) in unconnected groups. Fisher's exact test (F test) was used to analyze categorical data.

TRIAL RESULTS AND DISCUSSION

Analysis of complaints and medical histories of adolescents with enuresis showed that the disease was primary in 93 (94.9%) and secondary (after adult urination has been formed) in 5 (5.1%) adolescents [4]. Urinary incontinence rate was 1-2 times per week in 58 (59.4%) patients, 2-4 times per month in 23 (23.4%) patients and 6-12 times per year (rare enuresis episodes) in 10 (10.2%) conscripts. 7.8% of adolescents suffered from nightly urinary incontinence accompanied by various urination and defecation disorders, urinary/rectal urgency, urination acceleration, occasional fecal retention, including such retention with formation of functional constipation. It should be noted that increase in enuresis episodes associated with considerable physical stress, intercurrent disease overlay and excessive fluid intake before bed was observed in 35 (35.9%) conscripts.

63 (64.2%) conscripts underwent regular therapy of nocturnal urinary incontinence, primarily on an outpatient-ambulatory basis; treatment yielded no marked clinical effect in 54 (85.7%) patients. According to medical histories, enuresis duration in group 1 conscripts was 12.8±3.6 years, in group 2 adolescents – 6.9±2.5 years, in the patients found healthy – 5.4±2.8 years.

Analysis of the risk factors assistant to formation of urinary system dysfunction, especially of enuresis, revealed that the only significant differences between patients of all the clinical groups concern hereditary burden and urinary bladder position. The morphofunctional alterations revealed in conscripts in the process of examination are given in tb. 1.

We established that vesicoptosis (prolapse of urinary bladder) is statistically significantly more often diagnosed in patients with enuresis (72%) than in the conscripts with the record of urinary incontinence in medical history only (25.0%; Fisher's exact test: $p = 0.03$) and healthy adolescents (39.3%; Fisher's exact test: $p = 0.04$). UB neck atony rate is statistically significantly higher in patients with enuresis (36.7%) than in group 2 adolescents (16.6%) without clinical manifestations of UB dysfunction (Fisher's exact test: $p = 0.03$), whereas the difference between patients with enuresis and healthy adolescents (24.2%; F test: $p = 0.35$) was not statistically significant.

Analysis of the obtained data revealed that the main biochemical blood parameters did not vary between healthy and sick adolescents, except for the amount of platelets, which was significantly higher in conscripts with nocturnal urinary incontinence ($p < 0.05$; tb. 2).

Electroencephalography of conscripts with enuresis revealed organized BEA in 48.9%, desynchronized BEA – in 5.3%, hypersynchronized BEA – in 14.2%, disorganized BEA with accelerated α-rhythm – in 3.1%, disorganized BEA with delayed α-rhythm – in 28.% of patients. Organized BEA was revealed in 66.6% of group 2 patients (with the record of enuresis in medical history) and in 54.5% of healthy adolescents (group 3). Dysfunction of midline brain stem structures affecting behavioral and cognitive functions was diagnosed in 30.6% of conscripts with enuresis and 10.1% of group 3 adolescents (F test: $p = 0.04$). Non-specific alterations of bioelectrical brain activity were observed in 69 (70.4%) conscripts with urinary incontinence, which manifested themselves with moderate non-focal cerebral alterations in 50 (51.1%) adolescents, intense non-focal cerebral alterations in 13.3% and marked non-focal cerebral alterations in 6.1% of adolescents accompanied by sympathetic and parasympathetic nervous system balance upset. According to the A.M. Veyn questionnaire, 99 (69.2%) conscripts of all groups suffered from autonomic dysfunction syndrome.

Assessment of cognitive functions (memory, attention, thinking) revealed moderate alterations of these functions. Overall, general attention fluctuation was observed in 85 (59.4%) conscripts involved in the trial, slower and shorter speech – in 62 (47.5%), memory alterations – in 34 (23.7%) adolescents.

Analysis of renal hemodynamics in adolescents with enuresis revealed blood flow disorders on the trunk level of renal and segmental arteries (right). IR differences between patients with urinary incontinence and healthy conscripts were significant: 0.63±0.02 in the right interlobar artery and 0.58±0.02 in the left interlobar artery (tb. 3).

Prostate gland volume determination in conscripts with enuresis revealed increase in volume, anteromedian and cross-sectional dimensions, which were significantly bigger in the conscripts with this pathology and adolescents with the combination of urinary incontinence and vesicoptosis than in any other adolescents ($p < 0.05$; tb. 4).

Urodynamic examination of lower urinary tracts determined normal urination in 57 (58.1%) conscripts with enuresis, obstructed urination in 34 (34.6%) and fast urination in 7 (7.3%) adolescents. Normal and obstructed urination was observed in 26 (78.8%) and 7 (21.2%) youths found healthy (according to the emergency hospitalization results), respectively. Uroflowmetric parameters of conscripts with enuresis and healthy adolescents were not significantly different ($p > 0.05$).

Neurological examination revealed minor central nervous system alterations in 48 (48.9%) adolescents with enuresis. The following microsymptoms were observed in 51.1% of conscripts: slight tongue deviation, increase in tendon reflexes, dissociation of tendon and periosteal reflexes and asymmetry of facial muscles. Tremor of closed eyelids and fingers of outstretched arms was statistically more often diagnosed in adolescents with enuresis (36.3%) than in healthy conscripts (18.1%; F test: $p = 0.04$).

Examination of hormonal state revealed that the level of total testosterone was significantly lower (down to 7.32 [6.58-9.26] nmol/l) in adolescents and conscripts with enuresis than in healthy conscripts (15.86 [12.6-19.83] nmol/l ($p < 0.001$)). It also revealed moderate reduction of luteinizing hormone ($p = 0.03$; tb. 5). Moreover, apparently, pituitary-hypothalamic secretion alterations are associated with bioelectrical brain activity peculiarities and indicate its functional immaturity and moderate limbic-reticular complex formation delay in conscripts with urinary incontinence; this was confirmed by non-focal cerebral alterations of varying severity (according to EEG data), pathological activity focus and impaired functioning of background brain rhythms in 68 (69.3%) examined adolescents. That is why complex diagnostics of functional alterations requires introduction of sexual hormones level and EEG in the examination algorithm for conscripts with enuresis [7, 8].

CONCLUSIONS

1. Neurological examination of conscripts with enuresis revealed focal, primarily residual, symptoms associated with disorganized delayed α-rhythm (28.5%) or hypersynchronized BEA (14.2%).
2. Moderate non-focal cerebral alterations of bioelectrical brain activity accompanied by reduction in the total blood testosterone and luteinizing hormone levels were revealed in 70.5% of conscription-aged adolescents with enuresis; this indicated dysfunction of midline brain stem structures and impaired pituitary-hypothalamic secretion of sexual hormones.
3. Adolescents with enuresis had increase in dimensions and volume of prostate gland (17.35 ± 3.20 cm^3), which is why this morphological symptom may be used to analyze urinary incontinence.
4. 36.4% and 7.3% of adolescents with enuresis had obstructed and fast urination, accordingly; this fact characterized urodynamic disorders of lower urinary tracts.

REFERENCES

1. Zorkin S.N., Borisova S.A., Gusarova T.I. Performance evaluation of oxybutynin (Driptan) use in children with hyperactivity of urinary bladder. *Pediatriya – Pediatrics*. 2006; 5: 67–71.
2. Abramova A.A., Gurevich A.I., Menovshchikova L.B. Menovchshikova. Method of diagnosing paradoxical movement of pelvic floor in patients with voiding dysfunctions. *Detskaya khirurgiya – Pediatric surgery*. 2012; 5: 37–41.

3. Dzhavatkhanova R.I. *Funktsional'noe sostoyanie pryamoi kishki pri khronicheskikh zaporakh u detei. Avtoref. dis. … kand. med. nauk* [Functional Status of Rectum at Chronic Constipations in Children. Author's abstract]. Moscow, 2013. 21 p.
4. Vishnevskii E.L., Pushkar' D.Yu., Loran O.B. et al. *Urofloumetriya* [Uroflowmetry]. Moscow, Pechatnyi gorod, 2004. 220 p.
5. Bryazgunov I.P. *Nochnoi enurez u detei i podrostkov* [Nocturnal Enuresis in Children and Adolescents]. Moscow, Medpraktika, 2006. 76 p.
6. Ganina E.Yu. *Enurez u yunoshei prizyvnogo vozrasta. Avtoref. dis. … kand. med. nauk* [Enuresis in Conscription-aged Adolescents. Author's abstract]. Moscow, 2008. 23 p.
7. Baleva L.S., Kazanskaya I.V., Korovina N.A., Studenikin V.M., Blistinova Z.A., Zavadenko N.N., Zakharova I.N., Novikov P.V., Petrukhin A.S., Proshin V.A., Tamazyan G.V., Chumakova O.V., Shevchenko Yu.S., Tatochenko V.K., Lavrent'eva E.B., Doskin V.A., Belousova E.D. Primary nocturnal enuresis diagnostics and treatment algorithm (children). *Voprosy sovremennoi pediatrii – Current pediatrics*. 2005; 4 (2): 103–108.
8. Baleva L.S., Kazanskaya I.V., Korovina N.A., Studenikin V.M., Blistinova Z.A., Zavadenko N.N., Zakharova I.N., Novi kov P.V., Petrukhin A.S., Proshin V.A., Tamazyan G.V., Chuma kova O.V., Shevchenko Yu.S., Tatochenko V.K., Lavrent'eva E.B., Doskin V.A., Belousova E.D. Primary nocturnal enuresis diagnostics and treatment algorithm (children). *Voprosy sovremennoi pediatrii – Current pediatrics*. 2005; 4 (3): 66–70.

Table 1. Pathologies revealed in conscripts of various clinical groups

Pathology	Clinical groups					
	Enuresis (n=98)		Convalescents (n=12)		Healthy conscripts (n=33)	
	Abs.	%	Abs.	%	Abs.	%
Pyelonephritis	10	10.2	1	8.3	2	6.6
Chronic glomerulonephritis	2	2.0	-	-	1	3.0
Vesicoptosis (total):	68	69.4	5	41.6	13	39.3
degree 1;	13	13.3	1	8.3	9	27.2
degree 2;	44	44.9	2	16.6	3	9.1
degree 3;	11	11.2	2	16.6	1	3.0
Urinary bladder neck atony	36	36.7	2	16.6	8	24.2
Nephroptosis	12	12.2	-	-	2	6.6
Spina bifida posterior	62	63.2	5	41.6	16	48.5
Prostate gland fibrosis	5	5.1	-	-	-	-
Scoliosis (degrees I-II)	10	10.2	1	8.3	3	9.1
Flat feet	27	27.5	2	16.7	7	21.2
Vegetative-vascular dystonia	18	18.4	1	8.3	10	30.3
Other	24	24.4	12	16.6	5	15.1

Table 2. Biochemical blood parameters of the examined conscripts

Parameter	Conscripts with enuresis (n=68)	Healthy conscripts (n=30)	p*
Creatinine, mcmol/l	84.56 [76.62−89.17]	72.6 [64.6−84.61]	0.12
Urea, mcmol/l	6.4 [6.27−6.84]	6.23 [6.05−6.54]	0.46
Rest nitrogen, mcmol/l	26.3 [22.3−28.46]	20.5 [18.6−2.34]	0.38
Alkaline phosphatase, IU/l	428.63 [269.17−563.7]	251.6 [175.0−346.1]	0.17
Lactate dehydrogenase, IU/l	328.65 [168.45−478.5]	336.4 [134.7−436.5]	0.72

Amount of platelets ($x10^9$/l)	288.6 [195.4−305.4]	185.27 [191.6−216.41]	**0.05**
Total protein, mcmol/l	64.5 [64.2−68.6]	62.4 [60.0−65.6]	0.46
Total bilirubin, mcmol/l	22.54 [24.83−26.1]	21.8 [22.46−25.9]	0.15

Note. * - U test *p* (statistically significant differences are shown in bold).

Table 3. Hemodynamics in conscripts with enuresis and adolescents found healthy (G±SD)

Level of renal artery	Parameter	Enuresis (n=48)		Convalescents (n=12)		Healthy adolescents (n=33)	
		Right	Left	Right	Left	Right	Left
Trunk of renal artery	IR	0.79±0.03*	0.72±0.04	0.74±0.03	0.78±0.04	0.69±0.03	0.71±0.03
	TAMX, cm/s	55.4±9.15	51.9±8.32	52.5±14.64	60.45±15.17	42.4±9.25	45.0±10.3
	Diameter, mm	5.72±0.59	5.27±0.72	4.9±0.61	4.7±0.43	4.87±0.72	4.6±0.64
Segmental artery	IR	0.76±0.02*	0.72±0.02*	0.70±0.04	0.71±0.04	0.69±0.03	0.64±0.03
	TAMX, cm/s	51.5±10.62	49.7±9.53	52.2±7.83	50.1±11.64	49.4±9.12	46.1±13.35
	Diameter, mm	4.8±0.93	4.25±0.85	4.65±0.79	5.01±0.84	4.5±0.18	5.45±1.06
Interlobar artery	IR	0.63±0.02	0.58±0.03	0.62±0.06	0.56±0.03	0.62±0.04	0.61±0.03
	TAMX, cm/s	38.3±9.47	36.85±9.67	21.64±5.42	36.6±4.73	23.5±7.87	23.5±5.96

Note. * - $p < 0.05$ (significance of differences between groups).

Table 4. Prostate gland dimensions in conscripts (G±SD)

Prostate gland dimensions, cm	Clinical groups			
	Enuresis (n=54)	Convalescents (n=15)	Healthy conscripts (n=32)	Conscripts with enuresis and vesicoptosis (n=41)
Superior-inferior	31.41±5.93	32.93±4.6	31.63±6.0	28.0±4.73
Anteroposterior	31.4±6.42*	22.63±2.0	22.4±2.28	37.7±4.81*
Cross-sectional	31.36±3.35*	24.4±1.9	25.8±3.38	33.6±2.17*
Volume, cm^3	17.35±3.2*	10.5±1.93	10.6±2.54	19.9±2.93*

Note. * - $p < 0.05$ (significance of differences between groups of healthy and sick conscripts).

Table 5. Amount of sexual hormones in conscripts

Hormones	Conscripts with enuresis (n=30)	Control group (n=30)	p*
Follicle-stimulating hormone, mIU/l	5.0 [2.6−9.27]	8.1 [4.0−9.73]	0.012
Luteinizing hormone, mIU/l	3.64 [2.96−4.28]	4.72 [3.26−4.95]	**0.03**
Prolactin, mIU/l	310.35 [281.4−346.5]	328.52 [296.1−375.1]	0.25
Total testosterone, nmol/l	7.32 [6.58−9.26]	15.86 [12.6−19.83]	< **0.001**

Note. * - U test *p* (statistically significant differences are shown in bold).