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CORRECTION OF SLEEP DISORDERS IN CHILDREN

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Abstract

The article is devoted to a critical theme: sleep disorders in children. An open, prospective, randomized, comparative, controlled observational study was performed in the representative group of 114 patients aged 6 months to 2.5 years with sleep and sleep initiation disorders, where 64 patients received treatment with Dormikind and 50 patients received behavioral therapy for 28 days. It was reliably proved that sleep initiation reduced by 1.7 times and reached 26.2±4.8 (95% CI, 25.0-27.4) minutes in the main group. The number of children sleeping on hands dropped by 8.7 times and by 2 times in the parents' bed in the main group, according to Brief Infant Sleep Questionnaire scale, in the control group the same characteristics changed by 1.1, 1.3 and 1.5 times, correspondingly, and sleep initiation reached 33.4±2.9 (95% CI, 32.6-34.2), U-criteria, U=742.5 (p<0.001). The number of patients rocked to sleep in their own beds increased by 3.2 times (vs. 1.2 times in the control group) on the background of treatment with Dormikind. Duration of night sleep increased on average by 1.5 ±0.96 (95% CI, 1.26-1.74) hours; in the control group – by 0.5±0.81 (95% CI, 0.27-0.73) hours (U-criteria, U=383.5; p<0.001) and frequency of awakening reduced by 2.1 times and reached 1.8±0.7 (95% CI, 1.6-2.0) hours. In the control group frequency of awakening reduced only by 1.2 times in average and reached 2.8±0.7 (95% CI, 2.6-3.1), U-criteria, U=579.5; p<0.001. Significant positive dynamics was noted in the emotional-behavioral state of children after therapy: decreased irritation, excitability, fatigue, anxiety and till the end of treatment total score significantly improved by almost 3 times (1.3 times in the control group, that is 2.8±0.7, 95% CI, 2.6-3.0; U-criteria, U=266.0, p<0.001) and reached 1.3±0.7 (95% CI, 1.1-1.5) in the main group. According to positive dynamics in all sleep parameters, IMOS score showed significant difference in groups concerning valuation: "total recovery" – 31% (20 patients) in Dormikind group and 0% in the control one (F-criteria, p=0.0008). Valuation "significant improvement" – 58% (37 patients) in the main group vs. 10% (5 patients) in the control, valuation "improvement" – 6% (4 patients) in the main group vs. 46% (23 patients) in the control. Parents noticed absence of dynamics only in 5% (3 patients) in the main group vs. 38% in the control and in 3 children of the control group parents noticed worsening of the state after therapy. Thus, the high efficacy and safety of Dormikind were verified, and it can be recommended for wide use in pediatric healthcare practice.

Keywords: *sleep, children, Dormikind.*

Introduction

Sleep is a special genetically determinate state of the body characterized by regular sequential change of certain cycles, phases and stages [*Kovalzon V, 1993; Poluektov M et al., 2001; Levin Y, 2005; Abashidze E et al., 2008; Guzeva V, 2014*].

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The state of sleep is an obligatory part of normal human physiology and its disorders are reflected in all spheres of human activity: social, physical, cognitive. One of the most common sleep disorders is insomnia. According to International classification of sleep disorders [*ICD-10, 2003; American Academy of Sleep Medicine, 2005*], insomnia is defined as "repeated disorders of initiation, duration, consolidation and quality of sleep occurred despite sufficient time and conditions for sleep".

The frequency of insomnia in children is sig-

nificant and varies from 30 to 56% [*Poluektov M et al., 2001; Levin Y et al., 2005; Roth T, 2007; Bassetti C et al., 2011; Khachatryan L et al., 2016*]. As a rule, the highest percentage of the disorder is observed in infants up to 3 years that is related to immaturity of multiple hypnogenic centers in the CNS and their frequent dysfunction in the perinatal period (Table 1). The synthesis and maintenance of melatonin level also plays a critical role. It is well known that melatonin takes part in many vital processes: cardiovascular, endocrine, immune systems and, what is of great importance, in sleep regulation. Melatonin is the main hormone produced by pinealocytes in the epiphysis (80%), retina, intestine, thymus, and the pancreas [*Anisimov V, 2007; Kaladze N et al., 2010; Cardinali D et al., 2012 a,b; Gromova O et al., 2012; Hardeland R, 2012*]. Melatonin synthesis in the epiphysis increases with darkness and decreases in the light time.

It is known that syndrome of vegeto-visceral disorders takes 58% [*Johnston M et al., 2001; Johnston M, 2005; Ratcliff R et al., 2009; Grebennikova O et al., 2014; Jong M et al., 2016; Khachatryan L et al., 2016*] within the structure of sequelae of perinatal distress of the nervous system, from which the specific share of insomnia is 39%. The actual value can be higher as parents not always attend physician with complaints of sleep disorder in children; and in practice, we often observe light-headed attitude to sleep both in adult population and among parents of pediatric cohort. Meanwhile, it is known [*Poluektov M et al., 2001; Levin Y et al., 2005; Buysse D et al., 2008*] that critical processes, which not only allow the body to restore but also maintain neuroendocrine and metabolic balances in the body occur during different phases of sleep. For instance, somatropin is secreted, cell proteins and ribonucleic acids, phosphatergic binds are synthesized in delta-sleep (slow sleep phase), and processing of information obtained during the previous wakening and creation of future behavior program occur in rapid sleep phase [*Levin Y, 2005; Abashidze E et al., 2008; Buysse D et al., 2008; Jong M et al., 2016; Khachatryan L et al., 2016*]. Cerebral cells are very active during rapid sleep, although information from sensory organs does not reach them and does not efferent to muscular system [*Zakharov A, 2004; Kryger M et al., 2005; Levin Y, 2005; Jackson M et al., 2001; Guzeva V, 2014*]. Insomnia cannot be referred to mild disorders. Sleep deficiency results in rapid fatigue in daytime, decreased activity and working ability, growth and development disorders in children and decrease in their parents' quality of life. Moreover, studies showed that in rare cases, long-term and significant disorders could lead to more serious sequelae: increase in mental disorders and decrease in cognitive activity.

Table 1

Structures of hypnogenic centers in the brain [*Kovalzon V, 1993; Degtyareva M et al., 2006*]

1. Structures providing development of slow sleep:
➢ Anterior parts of hypothalamus (preoptic nuclei)
➢ Nonspecific thalamus nuclei
➢ Raphe nuclei (contain serotonin, inhibitory transmitter)
➢ Morucci center (medial part of the pont)
2. Centers of rapid sleep:
➢ Locus coeruleus
➢ Vestibular nuclei of medulla oblongata
➢ Superior colliculus of mesencephalon
➢ Reticular formation of mesencephalon
3. Centers regulating sleep cycle:
➢ Locus coeruleus (stimulation - awakening)
➢ Some parts of the cortex

Naturally, the search of medications neutralizing sleep disorders is reasonable. Correction of sleep in infants is extremely complicated due to deficiency of drugs and age limitations for available formulations, e.g. Phenybut (from 2 years old), Nervochel (from 3 years old), Persen (from 12 years old) [*Zyablitseva E, Shulgina G, 2006; Kuzenkova L et al., 2009; Gozal D, Kheirandish-Gozal L, 2010; Bagmetova V et al., 2011; Namazova L et al., 2016; Pchelina P, Poluektov M, 2016*]. Due to the above, the appearance of safe and efficient medication as Dormikind in the pediatric practice is relevant and well-timed. According to native and foreign authors [*Bochkareva E, 2013; Sineva T et al., 2015; Khachatryan L et al., 2016*], Dormikind has proved itself as a medication of first choice in infants that caused interest to its wide use for insomnia correction in children.

Material and methods

To verify the efficacy of Dormikind, we conducted an open, prospective, randomized, com-

parative, controlled observational study. The study was carried out in the period from November 2016 to October 2017. Patients' enrolment lasted during 10 months on the basis of consulting-diagnostic center of Sechenov University and Moscow children state policlinic No 120. Inclusion criteria were patients of 6 months - 2.5 years old; sleep and sleep initiation disorders, absence of serious neurological and somatic diseases, written informing agreement of parents/patients representatives, and their ability to adequate and constructive cooperation with doctors-researchers in the process of the study.

After establishment of compliance of child to all criteria of inclusion/exclusion and receipt of written informing agreement children were divided in 2 groups with the method of simple randomization (program Statistica 10.0). Parents of every child pulled out a paper, where "control" (I group) or "main" (II group) were written. In accordance with this information, children were randomized to one of the two groups. Patients of the Control group took Dormikind 1 medicinal tablet 4 times a day during 28 days (preliminary the tablet was solved in 20 *ml* of the water). Dormikind is a German combination drug produced by DHU (Deutsche Homoeopathie-Union, Germany), containing herbal-mineral complex: Cypripedium pubescens, Magnesium carbonicum, Zincum valerianicum in low dilutions. Excipients include lactose monohydrate, microcrystalline cellulose, talc, magnesium stearate. Each of the ingredients has an important target in insomnia correction. Dormikind's composition and mechanism of action of its ingredients are shown in table 2.

The control group received correction using behavioral therapy for children's insomnia. Usually, behavioral therapy includes an approach of "delay and control" or a method of "gradual redemption". In the first method, the child goes to sleep only in his own bed, and parents ignore protests and crying creating by this a "correct" stereotype of sleep initiation (to sleep alone in his bed). Another way (less radical) is when parents leave the child to fall asleep in the room alone but return to it with certain frequency, and gradually the intervals of their absence increase and the frequency of visits reduces. For objective correction, we trained parents only in the second method of behavioral therapy, and II group children – psychological-behavioral correction, which carried out together with parents for right sleep process organization in children.

All patients were observed and evaluated 3 times: before treatment start (visit 1), on 14th day (visit 2) and on 28th day (visit 3) after treatment start. Evaluation of the therapy conducted with account of Clinical efficacy scale (in points, table 3), BISQ[1] (Brief Infant Sleep Questionnaire) scale (modified variant of The Pittsburgh Sleep Quality Index [*Buysse DJ et al., 1989; Shahid A et al., 2011*], IMOS[2] (Integrative Medicine Outcomes Scale) [*Matthys H et al., 2003; Chuchalin A et al., 2005; Poluektov M.G. et al. 2016*], a self-report questionnaire that assesses sleep quality), IMPSS[3] (Integrative Medicine Patient Satisfaction Scale). Tolerability of the treatment [*Chuchalin A et al., 2005; Kamin W et al., 2010*] analyzed with 4 points

TABLE 2

Composition and indications for use of Dormikind

Substance	Active ingredient / tablet (100 *mg*)	Indications for use
Cypripedium pubescens (plant from Orchid family)	D4 - 15 *mg*	• Irritation, hysteria signs; • Insomnia; • Increased excitability in children
Magnesium carbonicum	D10 - 20 *mg*	• Neurotic manifestations; • Irritation; • Sleep disorders with frequent and behind night myoclonia of children
Zincum valerianicum	D12 - 15 *mg*	• I insomnia in children; • Б insomnia due to strong • irritation

TABLE 3

Clinical scale for assessment of emotional and behavioral sphere

Characteristics	Assessment variants	Points
Irritation, increased excitability	Absent	0
	Episodically	1
	Constant	2
Fatigue	Absent	0
	in the evening	1
	during the whole day	2
Anxiety	Absent	0
	Episodically	1
	Often	2

evaluation (very good tolerability – 4 points, 2. Unsatisfactory -1 point). All abovementioned evaluations made on the 2nd and 3rd visits.

1. In the questionnaire the next criteria are accounted: sleep conditions (in separate room, with relatives (adults or other children) in room, in bed with parents); the time of going to night sleep; body position during sleep; duration of night and day sleep (hours); number of awaking and duration of awaking in the night; duration of the period falling asleep (minutes); conditions of falling asleep (during the feeding, rocking on sleep in the bed or in parents bed); the level of relationship (mother, father, grandmother etc) between baby and adult sleeping with him; the level of severity of sleep disorder.
2. Contains 5 variants of evaluation: total recovery – significant improvement – nonsignificant improvement – without changes – worsening, in the range from 5 till 1 points correspondingly.
3. Contains 5 variants of evaluation: totally satisfied – satisfied – neutral – not satisfied – extreme not satisfied, in the range from 5 till 1 points correspondingly.

Electroencephalography in the awakening and sleep state was performed in all patients in compliance with International protocol "10-20" using Encephalan-131-01. Neurosonography was performed in the case of open fontanelle before and after treatment.

Statistical analysis and result processing were performed using Statistica 10.0 (Statsoft Inc., USA); differences were considered significant at $p \leq 0.05$. Difference significance was assessed by Mann-Whitney U test, differences in shares between groups – by criteria $\chi 2$, Fischer tests, Student t-test using IBM SPSS Statistics V22 and Microsoft Excel 2010.

RESULTS AND DISCUSSION

In accordance with study protocol 114 children (58% boys and 42% girls) were observed. In I group – 64 children of average age 13.4±6.9 months (95% CI, 11.7-15.1) were randomized, 50 children of average age 13.1±6.6 months (95% CI, 11.3-15.0) were included in II group. All observed children had practically normal physical development and somatically good health (Index Ketle II in I group was 16.2±1.3 *kg/m²* (95% CI, 15.9-16.5), and in II – 15.8±1.4 *kg/m²* (95% CI, 15.4-16.2). Totally 342 observations was conducted with analysis of 42 indexes with evaluation in the dynamics.

The single complaint at the visit was sleep and sleep initiation disorder. In I group, 28 infants (43.7%) had acute insomnia, 36 (56.3%) – chronic insomnia (for more than 3 months); in II – 46% and 54 %, respectively. The family history showed that 65.6% of infants in I group were single children in the family, 31.3% – the second child, 3.1% – the third one; in II group: 64%, 24% and 12%, respectively. Most of sleep disorders in the first-borns were likely related to higher frequency of obstetric-gynecological and perinatal complications on the one side, and large parent experience in proper arrangement of sleep initiation and sleep pattern in having many children.

At primary visit psychoneurological status assessed by means of the clinical efficacy scale I group children had 3.8±0.7 (95% CI, 3.7-4.0) points and in II group – 3.5±0.9 (95% CI, 3.3-3.8) points that verified group similarity. Insignificant neurological changes in the form of increased muscular tone were noted in 23.4% (15 children) in I group, 26% (13 children) – in II). According to neurosonography data, mild ventriculomegaly was noted in 15.6% of I and 14% of II groups. According to electroencephalogram results, no significant disorders of cerebral bioelectrical activity (epileptiform disorders, regional or generalized pathologic activity, disorder of sleep patterns formation) were found in 96.4% of children in the awakening and sleep state [*Orekhova E et al., 2007*].

The results of electroencephalogram [*Stroganova T et al., 2005*]:

- Sleep initiation disorder – increase of duration of sleep initiation (to 30-50 minutes and more), also

due to negative child's attitude to the process of bedtime often requiring long baby rocking;
- Sleep maintenance disorder – increase in the number of fragment and full awakenings during sleep initiation often requiring parent's intervention;
- Disorder of sleep depth with prevailing of surface sleep stages (1 and 2 stage of slow sleep phase);
- Decrease in sleep duration (due to long sleep initiation and frequent awakening) with absence of paradoxal sleep phase in most examinations and rapid awakening with motor and emotional anxiety;
- Frequent benign myoclonia of sleep including with further fragment and full awakening and anxiety.

BISQ scale was used for results evaluation, qualitative and quantitative characteristics were analyzed separately.

Duration of night sleep in I group was 9.3±0.5 hours (95% CI, 9.2-9.4), in II – 10.13±0.5 (95% CI, 9.3-10.2); 3.7±0.8 (95% CI, 3.5-3.9) times of awakening during sleep were noted in I and 3.3±0.9 (95% CI, 3.2-3.6) in II groups.

Duration of sleep initiation was 44.2±3.1 (95% CI, 43.5-45.0) minutes, and night wake – 2.2±0.6 (95% CI, 2.1-2.4) hours in I group. In II group the same indexes were 38.2±4.6 (95% CI, 36.9-39.5) minutes and 1.9±0.6 (95% CI, 1.7-2.1) hours.

Detailed assessment of qualitative indexes of sleep initiation showed that only 8 infants in I group (13%) had independent sleep initiation in the bed; 26 infants (41%) were rocked in arms and 16 children (25%) – slept in the bed together with their parents (Table 4). In II group, the picture was almost similar: 15 children (30%) were rocked on hands, 7 children (14%) slept in the bed alone and 12 children (24%) slept in the bed together with their parents. Meanwhile, only 30% of parents of I group children and 26% in II group considered the problem with sleep very serious; 28% in I and 32% in II groups – as not very serious, others – did not consider it a problem at all and tried to explain regular insomnia in their children by teeth cutting and other not objective reasons.

The following dynamics was observed in the groups after 14 days of treatment. In I group, against the background of Dormikind correction, significant tendency toward normalization of the emotional-behavioral background was noted with a score of 2.4±0.7 (95% CI, 2.2-2.6) versus 3.3±0.8 (95% CI, 3.1-3.5), U-criteria, U=723.5, p<0.0001 in II group. During comparison dynamics of indexes, it was discovered that decrease of average point of total valuation of emotional-behavioral background in I group was 1.4±0.9 (95% CI, 1.2-1.6) vs. 0.2±0.7 (95% CI, 0.1-0.4), U-criteria, U=489.0, p<0.0001 in II group. Analysis according to IMOS integrative scale demonstrated average estimation of I group3.1±0.8 (95% CI, 2.9-3.3) vs. 2.1±0.8 (95% CI, 1.9-2.3) for II group children (U-criteria, U=701.0, p<0.001). Analysis demonstrated that significant improvement of sleep quality and condition was registered in I group in 34.4% of children (22 children); parents of 39.1% of children noticed some improvement, and no progress was observed in 26.5% of children (17 patients). The following trend was registered in II group subjected to behavior therapy: recovery or significant improvement was registered in no child, 36% of children (18 children) had some improvement, no change was registered in 40% of children, and in 24% of children (12 patients) sleep initiation worsened, awakening frequency increased, and sleep became more superficial. Testing according to therapy tolerability scale showed that 19% of children (12 patients) tolerated Dormikind very well, 75% (48 patients) tolerated it well, which indicated absence of any adverse events, but parents were dissatisfied with dosage schedule of the drug, and slight excitability was registered in 4 patients (6%) during the first 3 days of intake, which did not require cancellation of the drug. The parents of II group children reported good tolerance of behavior therapy in 14% of cases (7 cases, criteria $\chi 2$, p<0.001, vs. the I group), satisfactory reaction in 52% of cases (26 children) and unsatisfactory reaction – in 34% (17 children) of cases in the

TABLE 4

Characteristic of the process of sleep initiation on the basis of descriptive part of BISQ

Criteria	I group	II group
Falls asleep in separate room, pat. (%)	7 (11%)	8 (16%)
Falls asleep alone in the room, pat. (%)	8 (13%)	7 (14%)
Falls asleep during feeding, pat. (%)	4 (6%)	5 (10%)
Falls asleep during rocking in bed, pat. (%)	10 (16%)	11 (22%)
Falls asleep during rocking in arms, pat. (%)	26 (41%)	15 (30%)
Falls asleep with parents in bed, pat. (%)	16 (25%)	12 (24%)

form of deteriorated sleep parameters, which required repeated conversation on the necessity to continue the correction in order to rearrange the pattern of sleep initiation and sleep.

In view of the above, IMPSS integrative scale (patient satisfaction with treatment results) demonstrated that 12,5% of parents of I group children were completely satisfied with the treatment on the 14th day of therapy (no one was completely satisfied in II group), 48.4% of I and 18% (criteria $\chi 2$, $p<0.001$) of II groups were satisfied, 20.3% of I and 36% of II groups had neutral assessment, and 19% of I and 32% of II groups were unsatisfied (in addition, 14% of II group were extremely unsatisfied with behavior therapy, which may be associated to individual personal characteristics of these parents).

Analysis of correction efficiency after 28 days (i.e. after completion of therapy course) discovered significant improvement of emotional and behavioral sphere of patients of I group 1.3±0.7 (95% CI, 1.1-1.5) (T-criteria Wilcoxon, $p<0.001$ vs. initial results) and 2.7±0.7 (95% CI, 2.6-3.0) in II (T-criteria Wilcoxon, $p<0.001$). Difference among groups were statistically significant (U criteria, U=266.0, $p<0.001$ vs. II group). No significant change in neurological and somatic status was registered; physical signs were within the age norm. Data analysis according to BISQ scale discovered positive dynamics in the quality and amount of sleep. For example, nighttime sleep of I group children became significantly longer 10.8±0.8 hours (95% CI, 10.1-11.0) (T-criteria Wilcoxon, $p<0.001$ vs. initial indexes), the number of awakenings has decreased down to 1.8±0.7 times (95% CI, 1.6-2.0) (T-criteria Wilcoxon, $p<0.001$ vs. initial indexes) and duration of nighttime wakefulness has decreased down to 0.9±0.7 hours (95% CI, 0.7-1.1) (T-criteria Wilcoxon, $p<0.001$ vs. initial indexes), The same parameters in II group children were 10.6±0.6 hours (95% CI, 10.4-10.8), 2.8±0,7 times (95% CI, 2.6-3.1), 1.4±0.5 hours (95% CI, 1.3-1.6), parameters of this criteria significantly differentiated from initial level, T-criteria Wilcoxon, $p<0.001$.

In I group, duration of falling asleep period was 26.2±4.8 minutes (95% CI, 25.0-27.4) T-criteria Wilcoxon, $p<0.001$ vs. initial result and U-criteria, U=383.5, $p<0.001$ vs. II group: 33.4±3.0 minutes (95% CI, 32.6-34.2), T-criteria Wilcoxon, $p<0.001$ vs. initial result. Average parameters of abovementioned changes in comparison with initial level are demonstrated on figure 1.

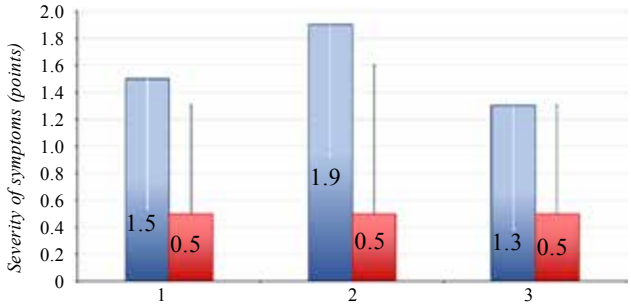

Figure 1. *Average differences in quantitative parameters of sleep before and after (M±SD)*

Notes: *I group - left column and II group - right column in each pair; 1 – increase of nighttime awakening, abs.; 2 – shortening of duration of night awakening, hours; 3 - shortening of sleep initiation duration, minutes;* – Differences in groups are significant, U-criteria, $p<0.002$*

Moreover, the qualitative characteristics of sleep initiation has changed significantly. Children of I group in 14% cases fell asleep during nursing (initially 6%), 19% fell asleep in bed without assistance (initially – 13%), 50% were rocked to sleep in bed (initially 16%), 5% in arms (initially 41%) and 13% in the parents' bed (initially 25%), i.e. all quality parameters of sleep initiation have improved (Table 5). Therefore, sleep initiation in children of the main group treated with Dormikind has become significantly shorter by 1.7 times (vs. 1.1 times in II group), the number of children falling asleep in arms has decreased by 8.7 times (1.3 times in II group), and falling asleep in the parents' bed has decreased by 2 times (1.5 in II group). The number of patients successfully rocked to sleep in their beds has increased by 3.2 times (vs. 1.2 in II group). Average duration of nighttime sleep has increased by 1.5 hours (0.5 hours in II group). Significant dynamics was reported in emotional and behavioral condition of the children after therapy: irritability,

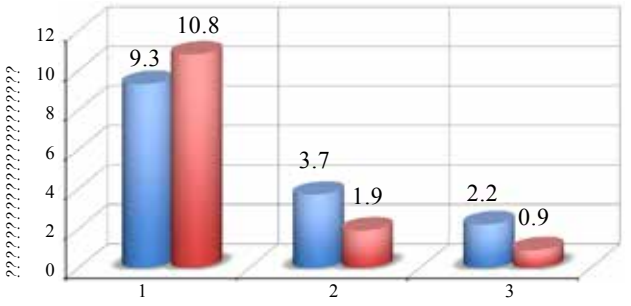

Figure 2. *Dynamics of sleep quality parameters before and after Dormikind therapy*

Note: *1 - duration of nighttime sleep in hours, 2 number of awakenings, 3- duration of wakefulness in hours; left column - before therapy and right column - after therapy in each pair;*

TABLE 5

Dynamics of sleep initiation in treated children

Characteristics	Groups			
	I (n=64)	II (n=50)	I (n=64)	II (n=50)
	Before treatment %		After treatment %	
Sleep initiation duration *(min)*	44±3.1	38±4.6	26±4.8*, **	33±3.0
Sleep initiation during nursing, abs (%)	4 (6)	5 (10)	9 (14)	8 (16)
Sleep initiation in bed alone, abs (%)	8 (13)	7 (14)	12 (19)	9 (18)
Rocked to sleep in arms, abs (%)	26 (41)	15 (30)	3 (5)#	12 (24)
Rocked to sleep in bed, abs (%)	10 (16)	11 (22)	32 (50)##	13 (26)
Sleep initiation in the parents' bed, abs (%)	16 (25)	12 (24)	8 (13)	8 (16)
Sleep initiation in the individual room, abs (%)	8 (13)	7 (14)	12 (19)	9 (18)

*NOTE: * – ingroup differences (before and after treatment) are significant, T-criteria Wilcoxon, p<0.001*
*** – ingroup differences are significant, U criteria, U=383.5, p<0.001*
 # – ingroup differences are significant, F-criteria, p=0.004
– ingroup differences of frequencies are significant, criteria χ2, p=0.009

excitability, fatigability and anxiety have decreased and total assessed rating has significantly improved virtually by 3 times (by 1.3 times in II group).

Average parameters of evaluation according IMOS scale after treatment finish was 4.2±0.7 (95% CI, 4.0-4.3) in I group vs. 2.6±0.7 (95% CI, 2.4-2.8) in II group, U-criteria, U=271.0; p<0.001. Certainly, all these changes were reflected on the integrative assessment scale of treatment results, where 30% (20 parents of the children) under treatment with Dormikind described the change in their children's condition as complete recovery, 59% (37 parents) – as significant improvement, 6% (4 parents) noticed some improvement, and 5% (3 parents) have not noticed any dynamics. Complete recovery was not registered in II group; 10% (5 parents) noticed significant improvement, in 46% (23 parents) there was some improvement, and 38% (19 patients) showed no dynamics. In addition, worsening was observed in 6% (3 patients) of II group under behavior therapy. Thus, to the moment of treatment finish in I group the share of children totally recovered or with significant improvement was more higher in comparison with II group (89% vs. 10%, F-criteria, p<0.001). Comparative characteristic of the IMOS scale in I and II groups is shown on figure 3.

Questioning of parents regarding tolerability of the therapy by their children after completion of the correction process (after 28 days) demonstrated average evaluation of tolerability as 3.3 ±0.5 (95% CI, 3.2-3.5) points in I group vs. 1.9±0.7 (95% CI, 1.7-2.1) points in II, U-criteria, U=235.0; p<0.001. Parents of 38% (24) of I group noticed excellent tolerability of treatment (0% of II group), 59% (38 parents) – good tolerability in I group (20% of II group), and satisfactory tolerability in 3.1% (2 parents) of I group (50% of II group). The same parameters were 0%, 20%, 50%. Parents (30%) of II group children were unsatisfied with the tolerability of behavior therapy. In total excellent and good tolerability of insomnia treatment was more frequent in I group: 97% cases (62 children) in comparison with II one – 20% (10 children), F-criteria, p<0.001.

The final assessment according to IMPSS demonstrated that 70.3% of parents of I group patients were completely satisfied with the therapy (14% of II

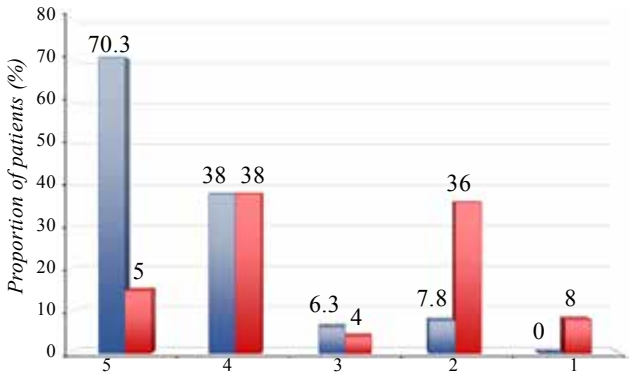

FIGURE 3. Spreading of different variants of evaluation IMOS on 28th day of treatment
NOTES: 5 – complete recovery, 4 – significant improvement, 3 – improvement, 2 – no dynamics, 1 – worsening; I group - left column and II group - right column in each pair

group), 15.6% (38% of II group) were satisfied, 6.3% in I group and 4% in II group had neutral assessment, and 7.8% of I and 36% of II groups were unsatisfied (Fig. 4). Average parameters according to IMPSS in I group was statistically higher than in II: 4.5±0.9 (95% CI, 4.3-4.7) points vs. 3.1±1.3 (95% CI, 2.8-3.5) in II group, U-criteria, U=588.0, p<0.001.

According to electroencephalography data, the following changes were observed: decrease of neurotic manifestations intensity (excitability and irritability, hyperactivity manifestations) accompanied with more comfortable sleep initiation, often with no need for long rocking of the child. The following dynamics was registered:

Decrease of sleep initiation duration (less than 15-20 minutes) with faster attainment of superficial sleep stage in 84% of I and in 40% of II groups.

Decrease of the number of fragmentary and complete awakenings (in certain cases by 2 times and more) and anxiety of the child with attainment, in certain cases, of deep sleep stages (3rd stage of slow sleep phase) in 45.3% of I and in 18% of II groups.

According to Doppler neurosonography data, reduction of changes in the anterior cerebral artery and normalization of blood velocity in the Galen vein was registered.

Conclusion

Sleep initiation and sleep disorders in children of early years are poliethiological problem more often. Experts show the main reason behavior insomnia, linked with incorrect association and arrangement of sleep initiation. Moreover, child reaction on unpleasant atmosphere in the family, CNS diseases and other organs and systems disorders, e.g. functional disorders of digestion (colics, regurgitation), could influence child sleep seriously.

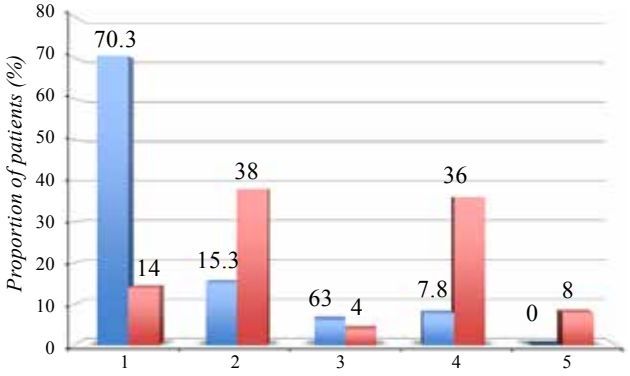

Figure 4. *Comparative integrative scale for assessment of satisfaction with the treatment*

Note: *I group - left column and II group - right column in each pair; 1 – % of completely satisfied with the treatment, 2 – satisfied, 3 – neutral attitude, 4 – unsatisfied, 5 – extremely unsatisfied*

Taking into account share of behavior insomnia, and the role of CNS in sleep disorders development, the method of psychological-behavior method of therapy took the place. It also should be marked that the influence of the method the sleep develops relatively slow. Usually it is very difficult for parents to follow all requirements of such method of the therapy, as it touches regimen and behavior particularities. That is why usage of medicamental method is actual.

Dormikind demonstrated high clinical efficacy in the study, that confirmed by methods of objective evaluation of CNS condition and sleep processes together with very good tolerability.

In I group the period of sleep initiation decreased statistically significant 1.7 times (1.1 times in II group), the number of children, abled to fall asleep only rocking in arms decreased 8.7 times in I and in 1.3 in II groups. The number of children falling asleep in parents' bed decreased by 2 times in I group (1.5 times in II group).

Duration of night sleep decreased in 1.5 hours in average (in II group – in 0.5 hours). Significant dynamics was noticed in emotional-behavioral condition of the children after the therapy: in Dormikind group irritation, excitability, fatigue, anxiety decreased, total point statistically significant decreased almost in 3 times (in II group – in 1.3 times). Stipulated dynamics of clinical symptoms was totally confirmed by electroencephalography: duration of sleep initiation period decreased in 84% in I group (in 40% in II group, that took behavior), and frequency of fragmental and total awakening decreased in I group in 2.4 times (in 0.6 times in II group).

Therefore:

1. Dormikind is the complex medicine, used in sleep and sleep initiation disorders, that confirmed via positive changes both subjective and objective marks and criteria.
2. Dormikind medical effects become statistically significant to 14th day of treatment.
3. Dormikind differs with mix of high efficacy and good tolerability among children from 6 month of life.
4. Dormikind is the medicine of choice in the treatment of sleep and sleep initiation disorders in children of early age, which could be recommended for wide usage in pediatric practice.

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