INTRODUCTION

Despite the apparent harmlessness, infant colic is a significant problem in Pediatrics, and it can cause considerable distress for the family and difficulties for health care physicians [1-5]. The causes and mechanisms of infantile colic development remain unclear, and all attempts to correct known etiological or pathophysiological factors are not quite successful [3].

METHODS:

The analysis of available publications about the results of clinical trials for relieving infantile colic

RESULTS:

The diagnosis of infantile colic is based on the typical clinical symptoms, characterized by a sudden attack of crying and restlessness, that can last at least 3 hours a day and be repeated at least 3 times a week for at least 3 weeks, mostly in the evening and at night in a 3-month-old baby having normal weight gain and age-appropriate psychomotor development [1-6, 8-9]. Infant colic has no specific diagnostic laboratory and instrumental tests and it remains a diagnosis of exclusion [10,11,12].

According to the unified health care clinical protocol approved by the order of Ministry of Health of Ukraine №59 from 01.29.2013, the "The unified clinical protocols of medical care for children with diseases of the digestive system", the treatment of colic includes complex psychotherapy, physical, dietary and pharmacological methods, the effectiveness of which has different levels of evidence [9].

Psychotherapy
The majority of researchers considered a favorable psycho-emotional environment, the identification and, if possible, the elimination of the stress factors and the help the family to overcome this difficult period as the first line therapy [4-6,13-15]. According to evidence-based medicine, the effectiveness of psychotherapy has a low level of evidence (D) on reduction of the duration and intensity of colic in infants [9,14], but it can significantly reduce the risk of a
dangerous condition, such as “shaken baby syndrome”, which may be the result of neurological disorders and psychomotor retardation, and sometimes be fatal [8,16-18].

So, Gelfand A. cites the research indicating that about 2.2% of parents of 1-month-old infants with colic in an attempt to stop the crying spells shake, beat, and even strangle the child. Already 5.6% of parents of the babies up to the age of 6 months admitted that they were tempted, or had used one of these "dangerous practices" [7].

Levitsky S, Cooper R. (2000) studied the effect of infant colic on the emotional state, found that all the mothers experienced physical and psychological symptoms in response to colic of their child, 90% of mothers reported significant family stress and violations of their social contacts, while 70% of the mothers were identified overt aggressive thoughts and fantasies. At the same time 26% said, they even had thought of physical abuse and infanticide during episodes of colic their baby [20].

Parents’ education, active support and advice are critical for physical and emotional well-being of the family and reduce the risk of injury and physical abuse of infants [16].

**Physical methods to relieve colic**

The effective soothing techniques including visual, tactile and auditory stimuli can have a calming effect. The creation of conditions for the child as close to the womb, and maximum tactile contact are recommended. A gentle rocking and rhythmic clapping, moving in a horse-drawn carriage or in a car, etc. is effective [5,13]. A special type of sound characterized by uniformity and monotony (the sound of running water, some working appliances such as washing machine, dryer or vacuum cleaner), so-called "white noise" may calm many kids [4,10,13,19,21].

Another recommendation for the infant colic prevention is a postural therapy (evidence level D): after feeding the parent should hold the baby in an inclined position (grade 45 °, tummy down) for 10-15 minutes, for a burping [9,12].
Widely recommended and used the abdomen massage has not shown the expected efficacy [4,19,22], but improves the communicative interaction between the child and his/her mother. The methods of manual therapy such as chiropractic and cranial osteopathy are not convincing [4.23]. Acupuncture as another alternative colic treatment is popular in several countries. A number of studies have shown the effectiveness of the acupuncture method on the intensity of colic [4.24].

**Dietary recommendations**

First of all, it is necessary to explain the necessity of breastfeeding. There is an evidence that melatonin contained in breast milk at night, may improve sleep and reduce the intensity of infant colic [4,25]. However, many parents associate a crying baby with hunger or "poor-quality milk" and early start bottle-feeding, or in the attempt to calm the child, they often begin to overfeed, causing excessive weight gain [2,10,26]. Various elimination diets of nursing mothers have no proven effectiveness in the correction of colic in children, and many studies indicate that the composition of breast milk is less dependent on a diet of feeding mother, that used to be considered [27,28]. The hypoallergenic diet of the mother with the elimination of cow's milk has the evidence of the effectiveness (level of evidence B) [4,9,13,19,28,29]. At the same time, according Moravej H et al. (2010) only 2.6% of children with infantile colic had a positive skin test to cow's milk protein, and the result of reducing the crying due to the appropriate diet of the mother was received only in this group. It is therefore advisable to recommend the exclusion of cow's milk for all nursing mothers for the prevention of colic [5,30].

The diet therapy with the formula of a partial or complete protein hydrolyzing for bottle-feeding children has the highest level of evidence [A] and is considered to be the most effective to reduce the symptoms of colic [4,9,13,19,27,29,32].

Even though some studies have shown to be particularly effective of soy-milk formula to facilitate colic, the routine use in infants under 6 months of age is not recommended, because the
number of cases of allergy to soy protein is growing every year [5,13,27,32]. In addition, the concern is the content of phytate, aluminum and phytoestrogens in the soy formules [32]. The use of lactose-free formula has not confirmed its efficacy and is not recommended for children with infantile colic [13,27,29]. The preliminary results demonstrate the effectiveness of special formules containing partially hydrolyzed protein, prebiotic oligosaccharides, low amount of lactose and enriched beta palmitic acid [4,8,25,33,36].

**Pharmacotherapy**

The methods of the pharmacological correction of infantile colic are most controversial. Although it is not conclusively shown that gastrointestinal factors are a sole and main cause of infant colic, basically all used pharmacological agents targeted at correction of gastrointestinal disorders. However, the majority of medicines influencing the certain proven pathophysiological mechanisms in the gastrointestinal tract have no advantage over placebo or have serious side effects.

The results of randomized, placebo-controlled, multicenter studies have not demonstrated the benefits of the effectiveness of simethicone to placebo for the treatment and the prevention of infantile colic, and therefore it is not recommended for routine use [4,5,10,13,19]. Dicyclomine hydrochloride (an anticholinergic drug that blocks predominantly M-cholinergic receptors) appeared much more effective and statistically reliable for the relief of colic (level of evidence A). However, because of the detection of serious side effects (apnea, seizures, hypotonia, coma), its use is not recommended for children under 6 months of age [4,15,19]. Another drug with proven efficacy in the reduction of crying compared to placebo is cimetropia bromide (not registered in Ukraine), a derivative of belladonna. The side effect is drowsiness, dangerous effects are not reported [5]. The new pharmacological agents (Nepadutant), acting on
the motility and sensitivity is going through a phase of clinical trials in a multicenter, international, randomized, double-blind, placebo-controlled study [4].

The results of studies on the effect of probiotics on infant colic are discrepant. Some studies confirm the significant efficacy of *L. reuteri* DSM 17938 to reduce the duration of crying infants [34-37, 39], but according to other researchers there is no effect [38]. In general, the effectiveness of probiotics for relief of infant colic currently has a level of evidence C [9].

Traditionally in many countries the agents of plant origin, having a carminative and mild antispasmodic effect for the relief of infant colic. Their effectiveness may be due to the anticholinergic and antiadrenergic activity [38]. A small amount of clinical studies and the lack of standardization in the evaluation of the composition and the dosage do not make possible to estimate the efficiency of scientific data resources. In general, it is believed that they are ineffective, and often even dangerous [4,5,22].

Based on the evidence of a transient lactase deficiency in most infants with infantile colic [2], it’s possible to use lactase preparations in the children who are breastfed and suffer from persistent colic [9]. However, the evidence of the effectiveness of lactase in reducing the symptoms of infant colic in large-scale clinical trials is not received, and therefore the enzyme therapy is not recommended for wide use in these children [27].

**CONCLUSION:**

The lack of clear understanding of the mysterious phenomenon of infant colic and approaches to its correction requires further research. Today the only undisputed "healing factor" of colic relief is time. The search for effective and safe means to relieve infant colic will be a significant step forward in public health.