INFANTILE COLIC

Infantile colic presents in otherwise healthy and well-developing infants as episodes of excessive paroxysmal crying, which is not helped by routine comfort measures. Colic begins at about 2 to 3 weeks of age and ends anywhere between 3 and 6 months of age. There is no laboratory test to diagnose colic. Doctors have to rule out all the other conditions that can make the baby cry excessively, some of which can be life-threatening. One of the most widely used definitions, which was proposed by Dr. Wessel back in 1954 (1) and is used by many today, states the "Rule of 3": crying lasting longer than 3 hours per day, 3 days per week and continuing for more than 3 weeks. The crying of an infant with colic has a typical pattern described as loud, piercing, high-pitched and aversive. The crying may be accompanied by tensing of the abdominal muscles, flexing of the legs, lifting of the head, flushing of the face, clenching fingers and passing gas. The peak period of crying usually occurs in the evening. The attack may terminate when the infant is completely exhausted, or with the passage of stool or gas (2).

The estimated number of babies affected by colic published by different researchers varies from as low as 3% to as high as 40%. Most researchers agree the number is somewhere between 10% to 20% (3). With the current birth rate in the United States of about 4,000,000 babies a year, this translates into about 400,000 – 800,000 cases of colic a year. The cause, or causes of infantile colic are still unknown. However, doctors who study colic, have reported many interesting observations:

Colic is more common among the first born (4).
Colic is more common among breast fed infants (5).
Colic infants have an increased amount of the hormone motilin in their blood, which is known to stimulate gastrointestinal tract (Motilin can cause cramping) (6).
Colic infants have an increased amount of serotonin by-products in the urine, suggesting an increased production of serotonin (Serotonin can also produce cramping) (7).
Colic infants have abnormal contractility of the gallbladder (8).
Colic infants have increased intestinal permeability (9).
Mothers of colic infants experience more stress and anxiety (10).
Mothers of colic infants are older, with higher level of education (5).
Mothers of colic infants are more likely to consume broccoli, cauliflower, cabbage, onions, chocolate and cow's milk (11).

All theories that explain colic fall into several categories:

1. Psychological
   Psychological, such as an abnormal interaction between mother and infant. One theory suggests that maternal anxiety is sensed by an infant, and an infant responds to such with colic, which in turn makes the mother more anxious, setting a vicious cycle. Possibly, an anxious mother actually has increased levels of yet unidentified substances in her breast milk that cause intestinal cramps in an infant. A combination of an increased level of maternal anxiety and more frequent breast feedings among the colic infants points toward this theory.

2. Gastrointestinal
   Gastrointestinal: hyperactivity, or immaturity of gastrointestinal tract response to either external, or internal stimulation, intestinal spasms, or excessive production of gas (12, 13, 14). There is a substantial amount of evidence, such as increased level of motilin, decreased gall bladder activity, and increased hydrogen production, indicating, abnormal function of gastrointestinal tract in colic infants. Gastroesophageal (GE) reflux also has been proposed as a potential cause of colic. It is true that GE can make the baby cry excessively and simulate colic, however, GE can be successfully treated with either dietary changes, or appropriate anti-reflux medicine. GE is a condition in its own right and should not be confused, or mixed with colic.

3. Allergic disorders
   Allergic reactions: such as reaction to cow's milk, or other food constituents consumed either by an infant, or a mother. There is indirect evidence that some infants may suffer from milk protein allergies, or lactose intolerance, or even from general sensitivity to foods consumed by nursing mothers. However, only a minority of colic infants respond to hypoallergenic formulas.

4. Misbalance between serotonin and melatonin production.
   According to this new and intriguing theory, colic infants have increased production of serotonin, which is not opposed by production of melatonin (15). Production of melatonin normally starts at approximately three months of age, when colic frequently ends. Since allergies may be responsible for increased production of serotonin, there
may be a link between the last two theories.

Many different theories try to explain colic. However, none of these theories explains all cases of colic. No unifying theory takes into account all the known facts of colic. It is likely that colic is a multifactorial condition, which has a similar presentation, but is produced by different causes in different infants.

**USUAL TREATMENT**

Infantile colic is considered to be one of the most frequent reasons parents seek medical attention for their children during the first weeks of life. Despite the benign and self-limiting course, infantile colic carries a substantial psychological, emotional and physical burden for the parents. Colic can interfere with parent-child bonding, cause strain in a marriage, lead to unnecessary hospitalizations, and in some unfortunate cases, lead to child abuse (16). Mothers of colic babies may experience fantasies of infanticide (17). Unlike previously thought, colic does not always disappear without a trace, and some children, who suffered from colic in infancy, may experience gastrointestinal problems later in their lives (18). Some families may experience abnormal interaction levels after colic has ceased (19). Therefore, it is important for health care providers to offer parents of a colic baby, simple, inexpensive and effective medical advice and assistance.

The typical therapeutic interventions for infantile colic offered to parents fall into the four categories listed below:

1. **Dietary**
   
   Dietary manipulations include professional advice on various feeding techniques, or the use of hypoallergenic milk, soy or lactose-free formulas, and an early introduction of solids. (20, 21, 22). However, neither the use of soy formulas, or changes in feeding techniques work effectively. A review of the data studying these recommendations showed that use of hypoallergenic formula, such as partially hydrolyzed or amino acid-based, may benefit approximately 25% of infants (23, 24). Occasionally, elimination of offending foods from the maternal diet also may help.

2. **Physical**

   Physical strategies include carrying, swaddling, applying abdominal pressure, or massaging the baby. Other methods include taking an infant for a car ride, use of a car ride stimulator, crib vibrator, or infant swings (25, 26). Another approach is to play recordings of sounds that supposedly soothe the baby. However, a car ride past midnight is an extremely impractical method. There is evidence in the medical literature that these methods do not work (27).

3. **Pharmacological**

   Hyoscyamine (levsine™, or gastrosed™) and Dicyclomine are two anticholinergic drugs, (anticholinergic drugs are similar in their effect to atropine. They dilate pupils, increase heart rate, decrease production of saliva, relieve spasms of gastrointestinal and urinary tracts, as well as bronchi) which are the only prescription medications on the U.S. market that consistently have been shown to effectively treat infantile colic. Unfortunately, up 5% of treated infants may develop side effects, including breathing difficulties, apnea, seizures, syncope, asphyxia, coma and muscular hypotonia (28, 29). In addition, several cases of death have been reported in infants taking dicyclomine (30). It is not surprising that these drugs are rarely prescribed by physician for infantile colic (16, 31). Several sedative or sleep-inducing drugs, including diphenhydramine (benadryl™), phenobarbital, chloral hydrate, and even alcohol have been reported as effective treatment for infantile colic. However, there is the potential for serious side effects associated with these agents, thus limiting their widespread use in treating colic (16, 32). Simethicone (Mylicone), a non-absorbable, over-the-counter drug, which reduces the size of intestinal gas bubbles is frequently recommended, despite several studies that demonstrate the effectiveness of simethicone on infantile colic is no better than placebo (33, 34).

4. **Behavioral**

   Recommendations for behavioral interventions are the most inconsistent therapies available. Some authors advocate increasing sensory stimulation, while others advocate decreasing such stimulation (16, 31, 35). Other recommendations include early response to crying, or allowing THE infant to cry, offering a pacifier, implementation of a routine feeding schedule, using eye contact and interactive playing.

   The lack of a safe, effective, practical and affordable therapeutic modality for infantile colic has led many physicians to believe that counseling, education, reassurance and empathy are the best forms of colic therapy available (2, 16, 27).

**USE OF FENNEL**

Various plants have been used to relieve of infantile colic, including catmint (Nepeta cataria), chamomille
(Matricaria chamomilla), dill (Anethum graveolens), fennel (Foeniculum vulgare), lemon balm (Melissa officinalis), and others. Among these plants, fennel is the most frequently recommended by herbologists and naturopaths. All of these listed plants are rich in volatile oils, and their beneficial effects are attributed to volatile oils. The highest concentration of the fennel oil, ranging from 2 to 7%, is found in the seeds. Fennel volatile oil is a mixture of at least a dozen of different chemicals. The main ingredients of fennel seed oil are: anethole, 40 to 70%; fenchone, 10 to 30%; and estragole, 2 to 9%. Other components are present in concentrations usually less than 1%. Animal experiments have shown that fennel oil regulates contractility of the small intestine (36, 37, 38). Anethole has a chemical structure similar to a chemical that is naturally present in the body, called dopamine. Dopamine is known to have a relaxing effect on the intestine, and perhaps, explains why fennel has a beneficial effect on infantile colic.

Fennel has a long documented history of use, dating to an ancient Egypt. Even today, many lactating mothers in Asian countries routinely take fennel.

Preparations of fennel seed available on the market today exist as either teas or extracts, and contain variable and unpredictable concentrations of the volatile oil. This variability in oil concentration results from many factors, including soil and climate of the growing region, harvesting methods, manufacturing, and storage conditions. The inconsistency in the concentration of oil makes it difficult to obtain an effective, predictable and reproducible response. That explains why until recently there has only been one clinical study supporting the use of herbs, including fennel for infantile colic (47).

SAFETY OF FENNEL

Fennel has the remarkable qualities of being both effective and very safe. No acute or chronic toxic reactions to fennel, or to fennel products in humans have ever been reported. Laboratory animals given 3000 milligrams of fennel extract per kilogram of weight showed no sign of toxicity (39). Likewise, fennel seed oil tested in animal experiments has been found to be non-toxic at doses significantly higher, than those used in humans. For example, animals fed a diet containing 1% of anethole, the main component of fennel seed oil, had no toxic effects (40). The recommended daily amount of fennel seed oil for an average colicky 1 month old, who weighs approximately 4 kilograms (9 lbs.), would be 20 to 40 milligrams. Such an infant consumes approximately 600 gram (20 oz) of formula, or milk per day. Therefore, 20 to 40 mg. of fennel seed oil given to an infant daily would be equal to 0.0035 to 0.007% of the total daily food consumption, which is 140 to 280 times less, than in a study quoted.

Besides its antispasmodic qualities, fennel seed oil has antioxidant and antimicrobial activity, probably attributed to anethole, which itself has been shown to have anti-inflammatory, antibacterial and also anticarcinogenic effects (41, 42, 43).

Even though fennel is mentioned as an allergen, the allergenicity of fennel is extremely low, probably much lower than of milk, soy or eggs. In fact, since 1948 there were only two reports of allergic reaction to fennel plant in the English literature (44, 45). However, all statements of experts regarding the allergenicity of fennel are based on these two reports. It has been shown that fennel allergy is caused by pollen (46), which is always present in unprocessed seeds. Fennel seed oil, which is produced by distillation of fennel seeds, has no pollen particles in it, and therefore, cannot produce allergic reactions.

Undiluted, or 100% fennel seed oil applied to the skin for a long period of time can produce local irritation. However, diluted fennel seed oil is not irritating. In an experiment on human volunteers, application of 4% oil did not produce any reactions.

The Council of Europe included fennel in the list of spices and seasonings in 1973. Fennel seed oil has been on the FDA's GRAS (Generally Recommended As Safe) list of flavoring substances in the United States since 1970's.

PEDIACALM

After several years of research and study, Lev Laboratories has created uniquely formulated fennel based product for colic, Pediaclalm.

- Pediaclalm is a stable emulsion of standardized* volatile oil of fennel in water.
- Pediaclalm is the only standardized herbal dietary supplement for infantile colic. This guarantees the amount of active ingredients in each bottle.
- Pediaclalm is safe, contains no alcohol, bicarbonate or sugar. All ingredients in Pediaclalm are FDA approved for human consumption.
- Pediaclalm is the only fennel preparation with patented composition. (US 6 346 250 B2)
- Pediaclalm is conveniently packaged as a ready to use product into 6 oz nursing bottles.
PediaCalm is effective. This was supported by a recently conducted clinical study. A randomized, double-blinded, placebo controlled trial, which involved a total of 125 infants demonstrated significant improvement (65%) among the infants taking this product in comparison with infants taking placebo (23.7%) (submitted for publication).

\[ \text{PEDIA CALM VS. PLACEBO IN INFANTILE COLIC} \]

\[ \begin{array}{c}
\text{TREATMENT GROUP} \\
65\% \\
\hline
\text{CONTROL GROUP} \\
24\% \\
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