Infantile colic is a distressing condition in infants, pathogenesis of which is still not clear. Several treatment strategies have been attempted before, but only some of them proven successful. The aim of this paper is to review studies on treatment options for infantile colic. For this, a systematic literature review was done on studies regarding pathophysiology, medical and conventional interventions for infantile colic from 1954 to March 2011. Forty nine articles included in Cochrane database were reviewed. Fourteen studies on pathophysiology and risk factors, 7 studies on effect of infantile colic on parents and family, 19 studies on management, 5 studies on other related factors and 4 literature reviews were included for review. Pathophysiology has been described in various ways in different studies and yet not conclusive. Regarding studies on management, simethicone could not significantly control colic, dicyclomine hydrochloride had serious side effects and cimetropium bromide results were favourable, but milder side effects were noted. Some nutritional studies reported low-allergen maternal diets in breastfed infants but suitability of these methods are questionable in Bangladesh. Behavioural studies on the use of decreased stimulation and contingent music were favourable in some studies. Mixed herbal tea and probiotic like Lactobacillus reuteri studies showed encouraging results. There are some scientific evidences to support a low-allergen maternal diet in breastfed infants with infantile colic. Some encouraging results exist for mixed herbal tea, cimetropium bromide and probiotics.

Key words: Infantile colic, Probiotics, Low-allergen maternal diet

Introduction

Colic is a frustrating nuisance for the parents. It is a condition in which an otherwise healthy baby cries or displays symptoms of distress (cramping, moaning etc) frequently and for extended periods, without any discernible reason. According to Wassel, colic is a condition of a healthy baby in which it shows periods of intense, unexplained fussing/crying lasting for more than 3 hours a day, more than 3 days a week for more than 3 weeks.1

Incidence and course

Infantile colic is a widespread clinical condition in infancy, which is observed in 10–30% of infants.2,3 The condition typically appears within the first month of life and often disappears suddenly, before three to four months of age, but can last up to 12 months.4 One study concludes that the chance of having colic is lower in breastfed babies.5 The crying episodes tend to increase at 6 weeks of age and are most frequent in the late afternoon and evening hours. Further, colic affects infants of all socioeconomic status in the same way without any evidence of family history, and there are no reported differences in prevalence between boys and girls.2

Crying associated with exhaustion can trigger serious problems, such as parental stress,6 breastfeeding failure,6 postpartum depression (affecting 10-15% of new mothers),7,8 excess visits to the doctor/emergency room (1 in 6 children are brought to the doctor/emergency rooms for evaluation of persistent crying)9 and unnecessary treatment for acid reflux.10

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Aetiopathogenesis

The word ‘colic’ is derived from the ancient Greek word for intestine (sharing the same root as the word ‘colon’). Despite its name that suggests gastrointestinal tract problems, the prolonged crying episodes may be related to individual differences in central nervous system functioning rather than gastrointestinal tract dysfunction.11

Colic may be due to the process of ‘hyperalgesia’ (which refers to a reduced pain threshold or a greater or longer duration of response to a painful stimulus) and ‘allodynia’ (when painful or discomforting experiences are due to stimuli that do not normally produce pain or discomfort). This hypersensitivity occurs in the primary afferent neurons or in secondary dorsal horn neurons.3,12 The pathogenesis is still hypothetical.

Many other possible aetiopathogenic hypotheses have been described. Most of the hypotheses proved relationship of the following factors with infantile colic indirectly.

- Lactose intolerance
- Dysmotility
- Gastro-oesophageal reflux
- Gut hormones (motilin, ghrelin)
- Gut microflora (Lactobacillus spp.)
- Feeding disorders
- Food hypersensitivity (cow’s milk allergy)
- Psychological factors (infant–parent interaction)

Lactose intolerance

In recent decades, lactose intolerance due to a relative lactase deficiency has been identified as a possible causative factor in infant colic. Fermentation of lactose by the bacteria in intestine leads to production of lactic acid and hydrogen. The rapid production of hydrogen and the osmotic pressure generated by lactose and lactic acid in the colon cause an influx of water, leading to distension of bowel and pain.2

Recently, the hypothesis which stated that colicky symptoms could be relieved by reducing the lactose content of the infant's feed has been tested once again in a small double-blind study in which the feed of colicky babies was preincubated with lactase.13,14

Motility disorder

In some infants during the first few weeks of life there is transient intestinal hypermotility which may lead to colic. This concept of hypermotility is supported by the documented beneficial effects of drugs with antispasmodic effects, such as dicyclomine hydrochloride, cimetropium bromide and by the release of high motilin levels in colicky infants.15,16

Gastrooesophageal reflux (GOR)

It has been thought that there may be a cause-effect relationship between GOR and infantile colic, especially in view of the prevalence of GOR during infancy. According to some authors, GOR and infantile colic are two different clinical conditions. Occasionally, GOR does not show its typical symptoms but is only characterised by excessive crying, similar to colicky infants.17

Gut hormones

GIT hormones are involved in the regulation of intestinal motility, and these include vasoactive intestinal peptide (VIP), gastrin, motilin and the newly discovered ghrelin. More recently, it has been shown that colicky infants also have higher serum levels of ghrelin compared to their healthy counterparts, even though it is not clear whether the high values observed are a cause or a consequence of infantile colic.18

GUT microflora

Among the organic hypotheses, the role of intestinal microflora in the aetiopathogenesis of infantile colic has been re-proposed recently. Savino et al found that differences in the composition of intestinal lactobacilli might influence the aetiopathogenesis of infantile colic.19 Lactobacilli are nonpathogenic, anaerobic, Gram-positive bacteria that play an important role in the development of local and systemic immune responses.20 Lower count of lactobacilli (Lactobacillus brevis and L. lactis lactis) has been found in colicky infants compared to healthy ones.21
A recently published study examined the hypothesis that modulating the intestinal microflora of colicky infants by administering a probiotic (*Lactobacillus reuteri*) would alleviate colic symptoms.\textsuperscript{22, 23}

**Feeding practices**

Incidence of colic is more in infants with disorganized feeding behaviour, less rhythmic nutritive and non-nutritive suckling, more discomfort following feeding and less responsiveness during feeding interactions.\textsuperscript{24} Evans et al compared the effect of two methods of breastfeeding (prolonged emptying of one breast at each feed vs both breasts equally drained at each feed) on breast engorgement, mastitis, infantile colic and duration of breast-feeding.\textsuperscript{24}

**Food allergen**

There are clear evidences that colic is related to food allergy and sometimes it is the first clinical manifestation of atopic disease.\textsuperscript{25} In a recent systematic review, Lucassen et al confirmed that hypoallergenic formulas were effective in the treatment of colic in some formula-fed infants.\textsuperscript{26} Jakobsson and Lindberg previously reported that exclusion of cows milk from mothers’ exclusion of cows milk protein from infants diet resulted in significant colic resolution.\textsuperscript{27} Estep et al\textsuperscript{28} suggests that a new formula with partially hydrolyzed proteins, a low amount of lactose, and a brief intervention with amino acid based formula may improve colic. For colicky breastfed infants, research has shown that simply modifying the mother's diet could be also effective.\textsuperscript{29, 30}

**Psychosocial factors**

Infants who experiences colic often considered irritable and hypersensitive, with a ‘difficult’ temperament. It is a frequently held view that colic results from an unfavourable climate created by inexperienced and anxious parents, in particular, mothers, and that behavioural problems could result from a less than optimal parent–infant interaction.\textsuperscript{31}

**Differential diagnoses of infantile colic**

Some clinical conditions may have similarities with infantile colic. These are:

- Infections (acute otitis media, urinary tract infection, meningitis)
- Cow’s milk protein allergy
- Candidal dermatitis
- Incarcerated hernia
- Occult fracture
- Neurological abnormalities, including Arnold–Chiari malformation
- Maternal drug effect (both illicit and prescription drugs)
- Overdose (e.g. excessive Vitamin D, excessive sodium)

**Danger signs**\textsuperscript{32, 33}

Physicians should be especially suspicious of other illnesses if cry is accompanied by at least one of the following "red flag" symptoms.

- Persistent moaning or weak crying or high pitched shrill cry
- Vomiting (more than 5 times/day, green or blood mixed)
- Change in stool (constipation or diarrhoea, especially with blood or mucus)
- Hypothermia or hyperthermia
- Irritability or lethargy (persisting for >6 hours continuously)
- Bulging fontanelle
- Poor weight gain (gaining less than 15 gm a day)

**Management**

Parental counselling and support are effective strategy for reducing parental anxiety and infant crying. It is important to assure parents that colic is a temporary problem. Studies on different treatment strategies have been published and some of these have been successful. The current treatment options for infantile colic, including trial data and measured outcomes, are presented in Table 1.
Feeding

- Breast feeding should be continued.
- There are indirect evidences that, breastfeeding babies may be improved by maternal avoidance of caffeine, dairy products, citrus fruits, soy products, broccoli, cauliflower, cabbage, and spicy foods.\(^{33}\)
- Mothers should be advised to finish the first breast before offering the second. The concentration of breast milk changes during a feeding. At first, the foremilk is low in calories and fat. But the hind milk is richer and sometimes more soothing. If the baby still seems uncomfortable or is eating too much, then offering only one breast (as often as desired) over a 2-3 hour period. This might give the baby more hind milk.\(^{34}\)
- Infant's head should be elevated during and after feedings.

How to comfort the baby

- Singing lullabies to the baby can be soothing.
- The infant should be held in an upright position during crying. This helps in burping up the swallowed stomach air.
- A warm towel or warm water bottle on the baby's stomach may be comforting. Some babies may be benefited from a warm bath.\(^{35}\)
- If the baby likes to lie on their stomach, babies may become calm by giving them a back stroke.\(^{36}\)
- Safe swaddling, careful avoidance of overheating, covering head, using bulky or loose blankets and

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dicycloverine, dicyclomine</td>
<td>elimination of colic</td>
<td>placebo-controlled trial showed significant benefit; however, some serious adverse effects were reported and so dicyclomine is contraindicated in infants under 6 months</td>
</tr>
<tr>
<td>Herbal tea</td>
<td>elimination of colic</td>
<td>significant benefit observed; however, data on the side-effect profile are limited and infants consumed a lot of tea in place of milk</td>
</tr>
<tr>
<td>Hypoallergenic diet</td>
<td>daily symptom reduction</td>
<td>poor study design, with a large drop-out rate in the hypoallergenic milk group</td>
</tr>
<tr>
<td>Decreased stimulation, eg, quiet room</td>
<td>improvement observed</td>
<td>significant improvement observed, but biased as babies without true colic were also included in this study</td>
</tr>
<tr>
<td>Simethicon</td>
<td>only 1 trial showed benefit</td>
<td>this study reported no details on colic definition or how cases were ascertained</td>
</tr>
<tr>
<td>Lactase enzyme</td>
<td>duration of crying reduced</td>
<td>double-blind, randomised, placebo-controlled trial with crossover – significant reduction in crying time and breath hydrogen excretion observed</td>
</tr>
<tr>
<td>Cimetropium bromide</td>
<td>duration of crying reduced</td>
<td>double-blind, randomised, placebo-controlled trial and daily duration of symptoms reduced by over 41%</td>
</tr>
<tr>
<td>Probiotics</td>
<td>duration and frequency of crying reduced</td>
<td>double-blind, randomised, placebo-controlled trial and daily duration of symptoms reduced by over 35-85%</td>
</tr>
<tr>
<td>Hydrolysed whey formula</td>
<td>duration of crying reduced</td>
<td>double-blind, randomised, placebo-controlled trial and daily duration of symptoms reduced by over 25%</td>
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allowing the hips to keep in flexed position may reduce crying. 

- Some babies keep calm when riding a device that mimics car motion and sound. The sound of a fan, vacuum cleaner, washing machine, or dishwasher has been tried for comforting the baby, but no controlled trial has proven the efficacy. 

- Swinging the baby with tiny jiggly movements (no more than 1" back and forth) with head and neck support helps in comforting the baby.

**Cholinergic drugs**

Systematic reviews of studies using anti-cholinergic drugs in the treatment of colic found to be more effective than placebo. Cimetropium, which is not available in many countries but is widely used in Italy to treat infantile colic, showed a decrease in duration of crying crises in the treated group compared with placebo. The major side effect was sleepiness; there were no reports of life-threatening events.

**Herbal medicines**

Studies have suggested a possible benefit of herbs. Tea containing Camomile (white and yellow daisy like flowers, aromatics herb), Linden, Fennel (yellow flowered herb, used in cooking, Mouree), Elm Bark (Debdaru), Lemon balm (Tulshee), Peppermint (Pudina) have been found to be effective in controlling colic.

**Chiropractic**

There are scientific evidences that chiropractic may lessen crying in colicky babies, chiropractors frequently treat colic with a form of gentle spinal manipulation specially modified for infants. Usually treatment lasts three to four visits over a period of 2 weeks.

**Probiotics**

Recently, a randomized, controlled study demonstrated that *Lactobacillus reuteri* improved colicky symptoms in breast-fed infants more than simethicone, supporting the hypothesis that probiotic supplementation could lead to health advantages in colic. Many other studies have proven the efficacy of probiotics in controlling the colic.

**Outcome**

At one-year follow-up, a group of colicky infants compared with non-colicky infants showed no differences in behavior in nine dimensions assessed using the Toddler Temperament Scale. Once colic resolves, there is little lasting effect on levels of maternal anxiety or depression.

**Conclusion**

Infantile colic is a common problem, and crying babies can cause stress, frustration and anxiety for families. There is no scientifically defined cause for infantile colic. Regarding the management, cimetropium bromide, mixed herbal tea and probiotic like *Lactobacillus reuteri* studies showed encouraging results. Low-allergen maternal diet in breastfed infants has found to be effective. Reassurance of the parents is the mainstay of treatment. Considering the distress of the baby and anxiety of the parents a safe therapeutic approach and guideline suitable for our country should be adopted. However, there is still a need for further research and modification of current remedies.

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