All babies cry, but when it is too much, and when it is colic? Crying is a normal primitive protective reflex in infants that serves as an alarm to alert parents and to get their attention. However, infants suffering from colic cry exclusively without any identifiable need. Such babies are difficult to console and provoke much anxiety among parents. Sleep is interrupted for infant and caregiver. Parents become desperate for resolution and accept advice and therapies from a variety of resources.1

INTRODUCTION

Infantile colic concerns about 10-30% of all newborns and is defined as a condition characterised by paroxysmal episodes of unexplained full force crying for at least three days a week and continuing for one week or more in a thriving, well-nourished infant.2

Crying is an important means of communication available to babies during their early infancy. In small babies, it is the only method of communicating their physical discomfort or emotional distress. All babies cry when they are hungry, thirsty, wet, and have pain anywhere in the body or sometimes for no obvious reason. Crying can also be a symptom of various medical conditions. Shaken Baby Syndrome is an extreme response to infant crying. Usually, a child cries for short periods and 5 to 10 minutes of crying several times in a day is considered normal. In fact, this is a good exercise for the lungs and it puts the arms, legs, and other muscles into action. But if the baby cries excessively, it will make him/her gulp in air, which may lead to stomach distension. The most common cause of crying is hunger. Some parents prefer to stick to fixed feeding schedules, but once in a while food should be given on demand, especially when the child puts his/her fingers into the mouth repeatedly. If the baby begins to cry a few minutes after the feed, the possible causes are wind or gas formation in stomach. Small babies often swallow air during feeds especially in the beginning when they try to gulp greedily. Also if the infant cries for a long time, he/she may swallow air, which can cause discomfort in the stomach.
The child may remain calm most of the day but starts crying excessively in the evening. It starts when the baby is 6 weeks old and ceases after months. In its most extreme manifestations, this increased crying has been considered a clinical problem, often referred to as "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. One of the most widely used definitions, 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.

ETIOLOGY

The various causes & symptoms of infantile colic are:

- Lactose intolerance
- Dysmotility
- Gastroesophageal reflux
- Gut hormones (motilin, ghrelin)
- Gut microflora (Lactobacillus sp)
- Feeding disorders
- Food hypersensitivity (allergic to cow’s milk)
- Psychological factors (infant–parent interaction) (Figure 1)

PATHOGENESIS OF INFANTILE COLIC

Several theories have been advocated to explain pathogenesis of infantile colic. Some of them are listed below. (Table 1)

Psychological Causes

Psychological causes such as an abnormal interaction between the mother and the 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 has increased levels of yet unidentified

Table 1. Differential diagnosis of infantile colic

<table>
<thead>
<tr>
<th>Common</th>
<th>Infrequent</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Feeding disorders</td>
<td>• Disaccharidase deficiency</td>
</tr>
<tr>
<td>• Constipation</td>
<td>• Renal pathology including uretero-pelvic obstruction</td>
</tr>
<tr>
<td>• Anal fissures</td>
<td>• Biliary tree pathology including stones</td>
</tr>
<tr>
<td>• Gastroesophageal reflux disease</td>
<td>• Acute abdomen diseases, including intussusceptions and volvulus</td>
</tr>
<tr>
<td>• Infections including otitis media</td>
<td>• Incarcerated hernia</td>
</tr>
<tr>
<td>• Cow’s milk protein allergy</td>
<td>• Occult fracture</td>
</tr>
<tr>
<td>• Urinary tract infection</td>
<td>• Neurological abnormalities</td>
</tr>
<tr>
<td>• Rashes, including Candidal dermatitis</td>
<td>• Ocular foreign body or abrasions or infection</td>
</tr>
<tr>
<td></td>
<td>• Maternal drug effect (both illicit and prescription drugs)</td>
</tr>
</tbody>
</table>
substances in her breast milk that causes intestinal cramps in an infant. A combination of an increased level of maternal anxiety and more frequent breast feeding among the infants, suffering from colic are the major points of this theory.

Gastrointestinal Causes
The newborn period of life exhibits a stage of readjustment and adaptation of the gastrointestinal tract. Newborns experience a series of complaints, which are mainly mild or insignificant but cannot be left untreated as these complaints have a bearing on the digestive process and may significantly affect the well being and growth of the baby. It is a known fact that most of the common discomforts in the newborn period are caused by indigestion and flatulence. Gastrointestinal hyperactivity, or immaturity of gastrointestinal tract response to either external, or internal stimulation can lead to intestinal spasms, or excessive production of gas.4,5 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 infants with colic. 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 antireflux medicine. Gastroesophageal reflux is a condition in its own and should not be confused, or mixed with colic. Furthermore, newborns lack the beneficial bacterial flora (probiotics) that develop over time to aid in digestion. This explains why almost all infants outgrow colic within the first 6 months.

Gut Microflora and Motility
An aberrant gut microbial composition in the first few months of life, such as inadequate lactobacilli levels may affect intestinal fatty acids profiles and could thereby favour the development of infantile colic. Indeed, intestinal colonisation by lactobacilli may be prerequisite for normal mucosal immune function.

Lactobacilli are nonpathogenic, anaerobic gram-positive bacteria that play an important role in the development of local and systemic immune responses. It was found not only in lower counts of intestinal lactobacilli in colicky infants compared with healthy ones, but also that Lactobacillus brevis and Lactobacillus lactis might even be involved in the pathogenesis of infantile colic by increasing meteorism and abdominal distension. An inadequate balance of lactobacilli in colicky infants might underlie immaturity in the gut barrier, which may lead to aberrant antigen transfer and immune responses, and increased vulnerability to the breakdown of oral tolerance.

Allergic Disorders
Allergic reactions such as reaction to cow’s milk or other food constituents consumed either by an infant or 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. The resulting failure to break down all the lactose in the food allows significant amounts to enter the large bowel, where it becomes a substrate for lactobacilli and bifidobacteria in the colon. Fermentation by these bacteria leads to the production of lactic acid and hydrogen. The rapid production of hydrogen in the lower bowel distends the colon, and sometimes causes pain. The osmotic pressure generated by the presence of lactose and lactic acid in the colon cause an influx of water, which may lead to further distension of the bowel. Through lactation, trace elements of cruciferous vegetables and other gas-producing foods may pass via breast milk to baby and cause gas and bloating. However, only a minority of infants suffering from colic respond to hypoallergenic formulae.

Imbalance Between Serotonin and Melatonin Production
According to this new and intriguing theory, infants suffering from colic have increased production of serotonin, which is not opposed by the production of melatonin.6 Production of melatonin normally starts at approximately 3 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.
Swallowing air
Infants often swallow air while feeding or during strenuous crying, which increases gas and bloating, further adding to their discomfort. 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.

INCIDENCE
Colic is a very common condition, which affects about one in five babies. It is more commonly seen in boys and firstborn children. 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 to be somewhere in between 10% and 20%.

THERAPEUTIC OPTIONS FOR INFANTILE COLIC
The typical therapeutic interventions for infantile colic offered to parents fall into the 4 categories listed below:

Dietary Treatment
Dietary treatments include professional advice on various feeding techniques, or the use of hypoallergenic milk, soy, or lactose-free formulas, and an early introduction of solids. However, neither the use of soy formulas nor the changes in feeding techniques work effectively. In some diet interventions, all major allergens, such as egg, wheat, and nut products, are eliminated from the mother’s diet. A review of the data comprising these recommendations showed that the use of partially hydrolyzed or amino acid-based hypoallergenic formula may benefit approximately 25% of infants.

Physical and Psychological Treatment
Physical strategies include swaddling, applying mild 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. However, a car ride past midnight is an extremely impractical method. Another approach is to play recordings of the sounds that supposedly soothe the baby. There is evidence in the medical literature that these methods do not work.

Behavioral Treatment
Recommendations for behavioral interventions are the most inconsistent therapies available. Some advocate increasing sensory stimulation, while others advocate decreasing such stimulation. 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.

Pharmacological Treatment
- Anticholinergic drugs: Hyoscyamine and dicyclomine 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 and have been shown to effectively treat infantile colic. Complications such as difficulty in breathing, apnea, seizures, syncope, asphyxia, coma, and muscular hypotonia develop in 5% of anticholinergic drug-treated infants. In addition, several deaths have also been reported taking dicyclomine. It is not surprising that these drugs are rarely prescribed by physicians for infantile colic.
- Sedative drugs: Several sedative or sleep-inducing drugs such as diphenhydramine (Benadryl), phenobarbital, chloral hydrate have been reported to be effective in the treatment of infantile colic. However, serious side effects such as drowsiness, dry mouth and throat, flushed skin, rapid or irregular heartbeat (Tachycardia) are associated with these agents, thus limiting their widespread usage in the treatment of colic.
- Simethicone: It is a non absorbable, over-the-counter drug that changes the surface tension of gas bubbles allowing them to coalesce and disperse, and aid in expulsion of gas. Despite several studies that demonstrate the effective-
ness of simethicone on infantile colic, it is no better than placebo.22

- **Lactobacillus reuteri**: The bacterium is endogenous to the human gastrointestinal tract and is found to relieve colic symptoms in breast fed infants within one week of treatment.

- **Methylscopolamine**: A muscle relaxant, which may be used to treat gastric or intestinal hypersensitivity or secretions. The drug was found not to be effective in treating colic and may in fact be unsafe to use.

- **Sodium bicarbonate (baking soda)**: Sodium bicarbonate is an alkali (antacid) which alters the naturally occurring pH of baby’s stomach acid. It may counteract some discomfort caused by acid reflux in cases of acidic stomach. However, changing the delicate pH balance in baby’s system can cause over-alkalinity and exacerbate a colicky condition. Furthermore, sodium bicarbonate is also absorbed into the bloodstream and thus can have side effects. Studies have shown that sodium bicarbonate can deplete and interfere with folic acid and iron, indicating that it may affect the function or absorption of both.

### HERBAL DRUGS IN THE MANAGEMENT OF INFANTILE COLIC

The drugs that possess carminative, digestive, antispasmodic properties can be used for the treatment of abdominal colic. The main reason for constant crying in infants will be due to abdominal colic, which can be subsided by these drugs mentioned in Table 2.

#### Table 2. Herbal drugs in the management of infantile colic

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Herbal drugs</th>
<th>Latin name (Family)</th>
<th>Part used</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sunthi (Dry ginger)</td>
<td>Zingiber officinale (Zingiberaceae)</td>
<td>Rhizome</td>
<td>Appetizer,23 laxative, stomachic, expectorant, carminative, emollient, thermogenic</td>
</tr>
<tr>
<td>2</td>
<td>Misreya (Fennel)</td>
<td>Foeniculum vulgare (Apiaceae)</td>
<td>Fruits</td>
<td>Digestive, stomachic, carminative, febrifuge, antihelminthic, antiemetic</td>
</tr>
<tr>
<td>3</td>
<td>Pippali (Long pepper)</td>
<td>Piper longum (Piperaceae)</td>
<td>Fruit, root</td>
<td>Appetizer, analgesic, rejuvenator, carminative, tonic, stimulant, antibacterial</td>
</tr>
<tr>
<td>4</td>
<td>Maricha (Black pepper)</td>
<td>Piper nigrum (Piperaceae)</td>
<td>Fruit</td>
<td>Appetizer, analgesic, diuretic, laxative, tonic, febrifuge, bacteriostatic</td>
</tr>
<tr>
<td>5</td>
<td>Jeeraka (Cumin)</td>
<td>Cuminum cyminum (Apiaceae)</td>
<td>Fruit</td>
<td>Appetizer, cooling, digestive, stomachic, carminative, stimulant, antihelminthic, anti-inflammatory</td>
</tr>
<tr>
<td>6</td>
<td>Dhanyaka (Coriander)</td>
<td>Coriandrum sativum (Apiaceae)</td>
<td>Fruit</td>
<td>Appetizer, digestive, stomachic, carminative, stimulant, anti-inflammatory</td>
</tr>
<tr>
<td>7</td>
<td>Ajamoda (Ajowan)</td>
<td>Trachyspermum roxburghianum (Apiaceae)</td>
<td>Fruit</td>
<td>Appetizer,24 antispasmodic, digestive, tonic, stimulant, carminative, antihelminthic</td>
</tr>
<tr>
<td>8</td>
<td>Ela (Cardamom)</td>
<td>Elettaria cardomomum (Zingiberaceae)</td>
<td>Seed</td>
<td>Appetizer, digestive, carminative, stomachic, stimulant, laxative, anti-inflammatory, antipyretic</td>
</tr>
<tr>
<td>9</td>
<td>Vacha (Sweet flag)</td>
<td>Acorus calamus (Araceae)</td>
<td>Rhizome</td>
<td>Carminative, sedative, tranquilsing, antispasmodic, stomachic, laxative, anti-inflammatory, antihelminthic</td>
</tr>
<tr>
<td>10</td>
<td>Shatapushpa (Indian dill)</td>
<td>Anethum graveolens (Apiaceae)</td>
<td>Fruit</td>
<td>Appetizer, carminative, stomachic, thermogenic, digestive, antispasmodic, anti-inflammatory.</td>
</tr>
</tbody>
</table>
Mechanism of effect of herbal medications in infantile colic are depicted in Figure 2.

**ROLE OF BONNISPAZ IN INFANTILE COLIC**

Bonnispaz, a polyherbal formulation developed by The Himalaya Drug Company, Bangalore, is used in the treatment of abdominal colic in infants.

Each ml of Bonnispaz Drops contains:

<table>
<thead>
<tr>
<th>Sanskrit Name</th>
<th>Botanical Name</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oils of Krishnajiraka</td>
<td>Carum carvi</td>
<td>0.69 mg</td>
</tr>
<tr>
<td>Sonthi</td>
<td>Zingiber officinale</td>
<td>0.46 mg</td>
</tr>
<tr>
<td>Yavani</td>
<td>Carum copticum</td>
<td>0.69 mg</td>
</tr>
</tbody>
</table>

The pharmacological properties of drugs of Bonnispaz are mentioned below in Table 3.

**Indications**: Bala Udarashoola (infantile colic), Admana (flatulence), Ajirna (indigestion), Dugdhasahatva (milk intolerance).

**Dosage**: Four drops initially followed by 2 drops twice or thrice daily for a period of 3 to 5 days. It is advisable not to exceed 8 drops per day.

In order to assess the effects of Bonnispaz, several clinical studies have been conducted of which two are given below:

**Clinical Trial 1**: Bonnispaz drops.

**Investigator**: Dr. S.P. Ghosh, Paediatrician, Heritage Hospital, Lanka, Varanasi, India.

**Aim**: This study was planned to evaluate the clinical efficacy and safety of Bonnispaz drops in abdominal colic in infants and children.

**Study Procedure**

The study was an open, non-randomised, and non-comparative, phase III clinical trial, conducted at Heritage Hospital, Lanka, Varanasi, India, as per the ethical guidelines of Declaration of Helsinki. The study protocol, case report forms (CRFs), regulatory clearance documents, product-related information, and informed consent forms (in English and Hindi) were submitted to the institutional ethics committee and were approved by the same.

The parents/guardians of the patients were informed about the study drug and its effects, the duration of the trial, and the overall plan of the study. The patients were included in the clinical study only after written informed consents were obtained from their parents/guardians, and a witness, independent of the clinical trial, signed the informed consent form.

The history of the patient’s illness was obtained by interviewing the parent/guardian. Thorough clinical examination and symptomatic evaluation were carried out and
the details were noted down in the CRF. Parents/guardians of the patients were advised to administer 4 drops of the drug initially, followed by 2 drops thrice daily for a period of 5 days.

All patients were followed-up at the end of the treatment on day 5 and symptomatic evaluation and clinical examination were conducted, along with recording the occurrence of any adverse event/s (either reported or observed).

**Results**

A total of 23 patients enrolled and completed the clinical trial. Of these enrolled patients, 23 had excessive crying problem, 20 had abdominal bloating, 13 had reduced food intake, 10 had abdominal tenderness, and 20 had uncleared bowels (Table 4).

After 5 days of treatment with Bonnispaz drops, a significant relief from the indications of excessive crying, abdominal bloating, reduced food intake, uncleared bowels, and abdominal tenderness was observed in all the patients. These results were significant at p<0.001 as tested by student ‘t’ test.

A significant reduction in the mean time of relief from 0.4174 ± 0.05944 to 1.157 ± 0.1809 hours (p<0.003) was observed after treatment with Bonnispaz drops in infants suffering from abdominal colic (Table 5).

A significant increase in the percentage of relief from 26.09 ± 5.325 to 53.39 ± 4.468 (p<0.0005) was seen in infants suffering from flatulence at the end of 5-day treatment with Bonnispaz drops (Table 5).

There were no clinically significant adverse events, either reported or observed, during the entire study period.

Although infantile colic is commonly reported and causes appreciable distress for both the parents and the pediatricians, its pathogenesis remains unclear despite 40 years of research. Available evidence suggests that this condition has multiple independent causes. Infantile colic has been attributed to infants’ difficult temperament, inadequate or inappropriate mother-infant interaction or mothers’ anxiety, abnormal gastrointestinal function, transient relative lactase deficiency, and allergic problems.

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**Table 4. Effect of bonnispaz drops on crying, bloating, food intake, abdominal tenderness, and uncleared bowels**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Pretreatment (No. of patients)</th>
<th>Posttreatment (No. of patients)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate</td>
<td>Reduced</td>
<td>Moderate</td>
</tr>
<tr>
<td>Excessive crying</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>20</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Food intake</td>
<td>13</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>10</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Uncleared bowels</td>
<td>20</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 5. Increase in the percentage and intensity of relief from flatulence with bonnispaz drops**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity of relief (minutes)</td>
<td>0.4174 ± 0.05944</td>
<td>1.157 ± 0.1809</td>
<td>p&lt;0.003, t = 4.315, df = 22, R² = 0.4583</td>
</tr>
<tr>
<td>Relief from flatulence (%)</td>
<td>26.09 ± 5.325</td>
<td>53.39 ± 4.468</td>
<td>p&lt;0.0005, t = 4.047, df = 22, R² = 0.4267</td>
</tr>
</tbody>
</table>
such as exposure to cow’s milk protein in formula or breast milk. Recent studies indicate that exposure of the child to tobacco smoking by the mother during pregnancy and after delivery, and smoking by the father were associated with excessive crying. Moreover, it is suggested that smoking is linked to increased plasma and intestinal motilin levels. Higher-than-average intestinal motilin and ghrelin levels seem to be related to elevated risk of infantile colic.

Results from the present clinical study with Bonnispaz drops showed a significant symptomatic relief from abdominal colic and flatulence in all the included patients. Relief from symptoms was observed in all the patients suffering from abdominal bloating and tenderness. There were no clinically significant adverse events, either reported or observed, during the entire study period.

In one of the experimental studies on Bonnispaz drops, a potent antispasmodic activity was observed. Bonnispaz drops inhibited the contractions produced by various spasmogens like acetylcholine, barium chloride, histamine, and oxytocin. Since these spasmogens have different modes of action, the antagonism elicited by Bonnispaz drops indicates that it might be acting at a common step in the contraction mechanism elicited by these agonists. The antagonism displayed was concentration dependent. Bonnispaz drops altered the effects of acetylcholine, histamine, oxytocin, and barium chloride, which indicated a nonspecific antagonist action. The study also revealed that Bonnispaz drops decreased gastric emptying and intestinal transit in a dose-dependent manner, which indicates the inhibition of gastrointestinal motility in vivo. All these findings suggest that Bonnispaz drops has a nonspecific antispasmodic activity.

Conclusion of the Trial
Abdominal colic in infants and children is a commonly encountered condition. Being a multifactorial syndrome complex, many therapeutic interventions have been studied. But, no clinically effective and safe medication is available in the management of abdominal colic. The present study was planned to evaluate the clinical efficacy and safety of Bonnispaz drops in abdominal colic of infants and children.

This clinical study observed a significant symptomatic relief from abdominal colic and flatulence in all the patients. Total relief was observed in all patients suffering from bloating and abdominal tenderness. There were no clinically significant adverse events, either reported or observed, during the entire study period. Therefore, it may be concluded that Bonnispaz drops is clinically safe and effective in the management of abdominal colic in infants and children.

Clinical trial 2: Evaluation and safety of Bonnispaz drops in abdominal colic infants and children

Aim: The present study was planned to evaluate the clinical efficacy and safety of Bonnispaz drops in abdominal colic in infants and children.

Investigator: Dr. Bharat J. Paramar, Assistant Professor of Pediatrics, B.J. Medical College, Civil Hospital, Ahmadabad, India.

Study procedure
The study was an open, non-randomised, and non-comparative, phase III clinical trial, conducted at B.J. Medical College, Civil Hospital, Ahmadabad, India, from August 2002 to April 2003 as per the ethical guidelines of Declaration of Helsinki. The study protocol, CRFs, regulatory clearance documents, product-related information, and informed consent forms (in English, Hindi, and Gujarati) were submitted to the Institutional Ethics Committee and were approved by the same.

The parents/guardians of the patients were informed about the study drug and its effects, the duration of the trial, and the overall plan of the study. The patients were included in the clinical study only after written informed consents were obtained from their parents/guardians, and a witness, independent of the clinical trial, signed the informed consent form.

The history of the patient’s illness was obtained by interviewing the parent/guardian. Thorough clinical examination and symptomatic evaluation were carried out and
the details were noted down in the CRF. Parents/guardians of the patients were advised to administer 4 drops of the drug initially, followed by 2 drops thrice daily for a period of 5 days.

All patients were followed-up at the end of the treatment on day 7 and symptomatic evaluation and clinical examination were conducted, along with recording the occurrence of any adverse event/s (either reported or observed).

**Statistical analysis**

Statistical analysis was done according to intention-to-treat principles. The changes in various parameters from pretreatment values to posttreatment values were analyzed by “Fisher’s Exact Test” and “Paired Student ‘t’ Test.” The minimum level of significance was fixed at 95% confidence limit and a 2-sided p value of <0.05 was considered significant.

### Results

A total of 105 patients enrolled and completed the clinical trial of which 103 patients had excessive crying problem and abdominal bloating; 105 patients had reduced food intake; and 67 patients were suffering from uncleared bowels (Table 6).

After 5 days of treatment with Bonnispaz drops, a significant relief from the indications of excessive crying, abdominal bloating, reduced food intake, uncleared bowels, and abdominal tenderness was observed in all the patients.

A significant reduction in the mean time of relief from 67.70 ± 31.02 to 23.29 ± 11.28 (p<0.0001) was observed after treatment with Bonnispaz drops in infants suffering from abdominal colic (Table 7).

A significant increase in the percentage of relief from 48.14 ± 1.306 to 84.86 ± 1.315 (p<0.0001) was observed in infants suffering from flatulence at the end of 5-day treatment with Bonnispaz drops (Table 7). These results were significant at p<0.0001 as tested by Student ‘t’ test.

There were no clinically significant adverse events, either reported or observed, during the entire study period. The cause of infantile colic remains unclear. Underlying causes of excessive crying must be considered during the evaluation. Organic causes account for less than 5% of infants presenting with excessive crying. Gastrointestinal, psychosocial, and neurodevelopmental disorders have been suggested as the cause of colic.

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### Table 6. Effect of bonnispaz drops on crying, bloating, food intake, abdominal tenderness, and uncleared bowels

<table>
<thead>
<tr>
<th>Indications</th>
<th>Pretreatment (No. of patients)</th>
<th>Posttreatment (No. of patients)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate</td>
<td>Reduced</td>
<td></td>
</tr>
<tr>
<td>Excessive crying</td>
<td>103</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>103</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Food intake</td>
<td>0</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>103</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Uncleared bowels</td>
<td>67</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

### Table 7. Effect of bonnispaz drops on the mean time of relief from abdominal colic and percentage of relief from flatulence

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean time of relief from abdominal colic</td>
<td>67.70 ± 31.02</td>
<td>23.29 ± 11.28</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>(minutes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relief from flatulence</td>
<td>48.14 ± 1.306</td>
<td>84.86 ± 1.315</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>
Conclusion of the Trial
The present study observed a significant symptomatic relief from abdominal colic and flatulence in all the patients included. Total relief was observed in all patients suffering from abdominal bloating and tenderness. There were no clinically significant adverse events, either reported or observed, during the entire study period.

Therefore, the observed clinical benefits of Bonnispaz drops might be due to the synergistic actions of its ingredients. It can be concluded that, abdominal colic in infants and children is a commonly encountered syndrome. Being a multifactorial syndrome complex, many therapeutic interventions have been studied. But, there is no clinically effective and safe medication that can be recommended in management of abdominal colic. This study was planned to evaluate the clinical efficacy and safety of Bonnispaz drops in abdominal colic of infants and children.

This clinical study observed a significant symptomatic relief from abdominal colic and flatulence in all the patients. Total relief was observed in all patients suffering from bloating and abdominal tenderness. There were no clinically significant adverse events, either reported or observed, during the entire study period. Therefore, it may be concluded that Bonnispaz drops is clinically safe and effective in the management of abdominal colic in infants and children.

MODE OF ACTION OF BONNISPAZ DROPS
For generations, parents have experienced the stress and frustration of increased, inconsolable crying in their infants in the first 3 to 5 months of life. Infantile colic is a distinct, although poorly defined, clinical entity. Whereas a general consensus regarding its cause is lacking, it is most likely multifactorial in genesis. Possible causative factors can be divided into two main groups: gastrointestinal and non-gastrointestinal. Food protein hypersensitivity or allergy is the leading contender in the former group, and disturbances in parental or maternal-child interactions in the latter. In all likelihood, the various factors act in tandem, leading to disturbances in infant gastrointestinal tract that manifests clinically as colic.

Abdominal discomfort, spasmodic pain, flatulence, infection, bloating of abdomen is the common problems related to gastrointestinal tract usually experienced by the infants.

PHARMACOLOGICAL ACTIONS OF INDIVIDUAL HERBS OF BONNISPAZ
The extracts of individual ingredients (Bonnispaz) of Carum carvi, Carum copticum, and Zingiber officinale were credited for their antispasmodic, analgesic, anti-inflammatory, and antioxidant activities.

- Carum carvi (seeds and essential oil) is used in food and medicine as carminative, and prescribed in flatulent colic and stomach derangement. The main components of Carum carvi oil (Caraway oil) are carvone, limonene, germacrene D, and trans-dihydrocarvone. Carvone is carminative in action. Carum carvi exhibits neurotropic antispasmodic activity.

- Carum copticum is much valued for its antispasmodic, stimulant, tonic, and carminative properties. The essential oil extracted from the seeds of Carum copticum have been studied for antibacterial activity. Carum copticum has antidyspeptic action, especially in non-ulcer dyspepsia. Carum copticum also possesses analgesic effect.

- The active ingredients of Zingiber officinale are gingerols and diarylheptanoids. Zingiber officinale is proven to be effective in inhibiting the intestinal, gastric, and colonic motility. The spasmolytic activity of Zingiber officinale might be attributed to gingerol that was found to inhibit prostaglandin (PG) biosynthesis and serotonergic activity. The antioxidant effect of Zingiber officinale extract was comparable to ascorbic acid as demonstrated by lowered lipid peroxidation, while maintaining the activities of other antioxidant enzymes (superoxide dismutase, catalase, and glutathione peroxidase).
• Anticholinergic drugs such as hyoscyamine and dicyclomine are generally used in the treatment of infantile colic. But side effects such as breathing difficulties, apnea, seizures, and muscular hypotonia are common. In their places, Bonnispaz can be used safely in all types of abdominal colic of varied etiology.

All the ingredients have appetite stimulant and digestive properties, thus promoting digestion and assimilation of infants.

CONCLUSION

The results from the clinical trials have provided the proof of significant efficacy of Bonnispaz in the management of infant abdominal colic. It is a polyherbal composition consisting of drugs having multi-pharmacological properties, and hence can be safely used in abdominal colic of infants of varied etiology.

The effects of Bonnispaz are due to the synergistic action of all the three herbs rather than a single herb alone. The constituents act in a synergistic, complementary manner to potentiate the therapeutic effects of Bonnispaz.

Bonnispaz is found to significantly reduce abdominal colic, bloating, flatulence and abdominal tenderness in infants with abdominal colic as reported in the above two clinical trials.

No adverse effects were reported during the use of Bonnispaz for treating abdominal colic. It is safe for long-term use and has no contraindications. Thus, Bonnispaz is a safe, effective, practical, and affordable therapeutic modality for infantile abdominal colic.

About the Authors

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