

# Screening for infantile colic and parents experiences of simethicone and probiotics: a quantitative, descriptive sub-study

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## Abstract

**Background** Colic affects at least 10% of newborns and parents seek help. The aim of this study was to present why infants whose parents sought help for colic, were not included in two colic trials and to describe the use and perceived effect of simethicone and probiotics amongst those infants who were included.

**Method** A quantitative, descriptive sub-study based on unpublished data collected in two RCTs, examining the effect of acupuncture in 228 infants with colic. In this sub-study, screening lists and background data from a questionnaire answered by the included infant's parents were analyzed.

**Results** 636 infants were screened for participation in the two trials. Of these, 389 were not included as they according to the diary cried < 3 hours per day and thereby did not fulfill the criteria for colic. Either parents had overestimated the crying, or the symptoms of colic were reduced when introducing a cow's milk free diet. Almost every included infant in the first trial (2010) and 76% in the second (2015) had been treated with simethicone but only 2.7% and 5.4% of the parents reported effect. The use of probiotics increased from 14,8% in the first trial to 86.3% in the second trial. Zero and 3.2% respectively reported effect.

**Conclusion** The use of a diary is valuable to assess the infants crying and can help nurses to adapt their advice and support to these families. Excluding cows milk protein helped many infants with excessive crying. Most parents had tried simethicone and probiotics without experiencing effect.

## Background

Infantile colic affects 10-17% of infants in the Western world (Canivet et al 2002; Lucassen, 2010). Colic is often defined as crying or fussing for at least three hours per day, three days per week in otherwise healthy infants under three months of age (Wessel et al 1954). Although infantile colic is a benign condition with spontaneous recovery it causes substantial distress to the parents as well as the infant, which can affect

essential early interaction and family relations. Excessive crying is associated with depression in mothers during the postpartum period (Howell et al 2009; Miller et al 1993; Murray et al 1996; Vik et al., 2009) and has been associated with an elevated risk of child abuse in multiple studies (Barr, 2014; Talvik et al 2008; Barr et al 2006; Reijneveld et al., 2004; van der Wal et al 1998). Infantile colic is a frequent cause of pediatric consultations at Child Health Centers (CHC). It is of great importance that health professionals do not dismiss the condition as harmless and temporary, but rather respond to the parents' mental and physical exhaustion with respect and proficiency. Nurses working at the CHC have therefor an important but difficult role to support these parents since there is still no known cure and several treatments are lacking scientific evidence (Landgren et al 2012).

## Pathogenesis

Although the etiology is unknown there have been multiple theories for the cause of infantile colic and unanimity

is still lacking in its treatment. Theories about inadequate interaction between the parents and the infant as a cause of colic have been considered controversial (Savino, 2007). Another possible explanation is intolerance to cows' milk protein. Approximately 5-20% of the infants are relieved of their symptoms when excluding cow's milk protein from the breastfeeding mother's diet and/or the infant's formula for five days (Iacovou et al 2012). A common theory has been the lack of normal gastrointestinal function due to the infants nervous or digestive system being immature. This theory has led to scientists studying the effect of simethicone to help reduce gas (Savino, 2007) and the effect of probiotics (*Lactobacillus Reuteri*) to help normalize the composition of the intestinal microbial environment (Savino et al., 2005; Lehtonen et al 1994). Complementary factors that could increase the risk

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Simethicone, Probiotics, Infantile colic, Acupuncture, Infant

for infantile colic might be associated with maternal smoking, infant being a firstborn, increased maternal age and atopic eczema (Savino, 2007).

### Treatments

Treatment is often recommended from parents’ subjective description of the infants’ behavior without measuring the infants crying, and advice given by the CHC nurse often lack structure and follow up (Landgren et al., 2012). Counseling parents by giving them specific instructions on how to adapt their interaction with the infant showed good results in two studies (Keefe et al 2005; Dihigo, 1998) while another study did not find that the infants crying reduced more than compared with evaluation and support from the CHC nurse and pediatrician alone (Parkin et al 1993). The use of herbal tea might have effect when treating colic but given the lack of standardization of components in the herbal products, unknown optimal dosage and the risk of interference with the infant’s normal food intake parents are advised to use these products with caution (Roberts et al 2004). Sugar solution can be used for its analgesic effect in infants and has therefore been suggested as a possible method to also reduce discomfort in infants with colic. Although there are limited studies conducted there have been some positive results when compared to placebo (Perry et al 2011). Spinal manipulations as treatment for colic are performed by chiropractors. This treatment has however shown varied results in studies conducted in Scandinavia (Wiberg & Wiberg, 2010; Olafsdottir et al 2001; Wiberg et al 1999). Acupuncture has a pain-inhibiting effect and has been proven to reduce crying and gastrointestinal symptoms in infants with colic according to Landgren et al (2010) and Reinthal et al., 2008. Skjeie et al (2013) however did not find any statistically significant effect of acupuncture as treatment for colic in infants. The anticholinergic drug dicyclomine showed significant improvement when used for treating colic (Lucassen et al., 1998) but was withdrawn from the Swedish market due to serious side effects.

### Simethicone and probiotics

The two most common recommendations for treating colic in Sweden are Minifom (simethicone) and Semper magdroppar (probiotics containing *Lactobacillus Reuteri*), both are available

over the counter. Several review articles found no evidence for treatment with simethicone in infantile colic (Savino et al 2014; Hall et al 2011; Lucassen, 2010). Three RCTs have compared simethicone with placebo; one showed a significant difference between the groups but was dismissed because of poor quality (Lucassen, 2010). The other two (Metcalf et al 1994; Danielsson & Hwang, 1985) found no significance that simethicone would have more effect than placebo in treating colic (Lucassen, 2010).

Probiotics are sold in pharmacies and are commonly used e.g. in Sweden for relieving symptoms of colic. It has shown promising results in three RCTs where colicky crying was significantly reduced compared to a placebo group (Szajewska et al 2013; Savino et al 2010; Savino et al 2007). The largest RCT on the prophylactic effect of probiotics containing *Lactobacillus Reuteri* in 589 infants showed a significant difference in symptoms of colic in the invention group compared to the placebo group (Indrio et al., 2014). However another RCT did not find any significant difference between probiotics and placebo (Sung et al., 2014). The majority of studies that found positive results when using probiotics for colic have been conducted on breastfed infants. There is still a lack of research on the effect of probiotics in formula fed infants with colic (Urbanska & Szajewska, 2014).

The aim of this study was to present why infants whose parents sought help for colic, were not included in two colic trials and to describe the use and perceived effect of simethicone and probiotics amongst those infants who were included. A further aim was to describe the possible associations between use of simethicone/probiotics and demographic background data and the difference in use of simethicone/probiotics over time. The results may help the CHC nurses to adapt their support for these families.

## Method

### Design

This study is a quantitative, descriptive sub-study based on unpublished data collected in two RCT’s examining the effect of acupuncture in colic (Landgren et al., 2010; Landgren et al., 2015). Screening lists for infants who were not included and background data for included infants from a questionnaire

were analyzed.

### Participant enrollment

For the first trial, data were collected from November 2005 to February 2007. This blinded RCT on acupuncture in infantile colic was conducted at a private acupuncture clinic in Sweden (Landgren et al., 2010). Consecutive sampling was used and parents who sought treatment for colic at their CHC, the pediatric clinic at the regional hospital or the acupuncture clinic and wanted to participate in the study were asked to exclude cows’ milk protein from the bottlefed infants diet and from the breastfeeding mothers diet for at least five days, and to register their infants crying in a diary.

The second trial, a multicenter RCT on acupuncture in infantile colic, called ACU-COL, collected data between January 2013 and May 2015. ACU-COL was conducted at four CHC in different regions in southern Sweden (Landgren et al., 2015). The study centers were chosen to provide a wide range of the population, incorporating both larger and smaller cities with cultural and socioeconomic differences. Consecutive sampling was used, and parents to infants with symptoms of colic who contacted one of the study centers or another CHC within an 80 kilometers range of each study center and wanted to participate were asked to exclude cows’ milk protein from the bottle-fed infants and from breastfeeding mothers diet for at least five days, and to register their infants’ crying in a diary. Parents had received information about the study from their ordinary CHC nurse, physician or from a website, [www.spädbarnskolik.se](http://www.spädbarnskolik.se).

### Participants

Inclusion criteria for both studies were healthy infants, not older than eight weeks, who according to a daily baseline registration fulfilled the criteria for colic: crying/fussing more than three hours/day at least three days per week. At least one of the parents had to speak Swedish. Exclusion criteria were infants born before gestational week 37, insufficient weight gain, having tried acupuncture or taking prescribed medication. Simethicone and/or probiotics were allowed.

In the first trial (Landgren et al., 2010) parents to 210 infants registered their infants crying and fussing in a diary during at least three days. Of these infants, 90

fulfilled the criteria for colic and were included. In the second trial, ACU-COL (Landgren et al., 2015), 426 infants were initially screened for participation in the study and after daily registration of crying and fussing in a diary during a baseline week, 152 infants met the criteria and were included in the study (Landgren & Hallström, in manuscript).

### Sample size

The power analysis for the first trial (Landgren et al., 2010) for detecting a significant difference in crying between the intervention and control group was calculated to 40 infants per group. For ACU-COL the sample size calculation, conducted by an independent statistician at the center for clinical research and development (R&D, Region Skåne), found that a total of 144 infants were needed to detect a significant difference in crying between infants who got acupuncture and infants who did not (Landgren et al., 2015).

### Outcomes

The primary outcome in the present sub-study was the reasons for which screened infants were not included in the two main trials. A secondary outcome was the frequencies of parents using simethicone and probiotics and their reported effect of the treatment. Other secondary outcomes were the association between treatment with simethicone and probiotics and background characteristics and the difference in frequency of treatment with simethicone and probiotics over time between the two main studies.

### Data collection and instruments

When a parent sought treatment for colic and wanted to participate in the study they were noted on a screening list and instructed to register the infant’s behavior in a diary. The project leader called the parents three to seven days later. Infants who according to the diary cried > 3 hours/day were then included. The project leader made a short note on the screening list for the rest of the infants on why they were not included; these notes were analyzed in this study. Data on the use of simethicone and probiotics and background data were collected from a structured questionnaire that parents had to answer at the first visit to the study center after inclusion. The questionnaire consisted of 43 questions, including 30 main topics and 13 follow-up

questions with different set of answers. One question regarding alternative treatments for colic were added to the questionnaire in the ACU-COL study. To describe the use and perceived effect of simethicone and probiotics two questions were analyzed in the present study. These questions asked whether parents treated, or had treated, their infant with simethicone or probiotics. If the answer was “yes” parents were asked if simethicone/probiotics had had effect. This question could be answered with “yes”, “no” or “some effect”. To investigate the possible associations between the use of simethicone/probiotics and demographic background data collected in the same questionnaire the associations between these variables were analyzed. This data included demographic information as well as information about the parents education, smoking, food intolerance, allergies, asthma, eczema or bowel diseases in the family, other family members having had infantile colic, complications during pregnancy or delivery and the mother’s intake of prescribed medication during pregnancy and after the delivery. It also contained information about the infants feeding, gas, vomiting, rashes, and the use of alternative treatment as herbal tea, sugar solution or chiropractic treatment.

### Statistical analysis

The statistical software package SPSS™ version 22 (SPSS Inc., Chicago, IL) was used for calculations. Initially the descriptive statistics were calculated. The Kolmogorov Smirnov’s test was used to determine if the variables were normally distributed. Since all the variables were not normally distributed the data were analyzed with a non-parametric Chi square test using crosstabs for significance testing and Phi for determining the strength of the correlations. Phi was chosen instead of Cramer’s V since the analysis only demanded a two-by-two contingency table, which was used to describe the association between the variables as well as the difference in use of simethicone and probiotics over time. P-values <0.05 were considered statistically significant. For determining the strength of the correlations between parents use of probiotics or simethicone and their reported experience of the infants appetite the Spearman rank correlation test were used since this variable contained more than two

available answers where the parents could rank appetite on a three level scale.

### Ethical considerations

There is a need for more research to find a safe and effective treatment for colic but research in infants requires special ethical consideration since these children are already vulnerable and cannot sign the form of consent themselves. To be able to analyze and present already collected but still unpublished data from earlier studies including infants with colic must therefore be considered a valuable addition to the research on methods for threatening infantile colic. Informed consent was received from all the parents, and participation in the study could be interrupted at any time. The first trial (Landgren et al., 2010) was approved by the Lund University Research Ethics Committee (Dnr 583/2005) and ACU-COL was approved by the Regional Ethical Review Board in Lund (Dnr 2012/620). The participants were not exposed to any additional interventions related to the present sub-study.

## Results

### Reasons for why screened infants were not included

Out of the 210 infants whose parents completed daily registrations in the diary in the first trial (Landgren et al., 2010) 90 were included and 120 were not. In the second trial, ACU-COL (Landgren & Hallström, submitted), 426 infants were screened for participation of which 157 were randomized and 269 were not included. Notes made by the project leader for the reasons why infants were not included were categorized (Table 1). For some infants more than one reason was listed (e.g. “Don’t want to be randomized” and “Is going to a private acupuncturist”) and for some infants in the first RCT the reason is missing. The category “Participation in the trial/registering in the diary requires more time/energy than I have” contains four families living on islands which required lengthy travelling times and several who remarked they were too stressed, among them one single mother with two more children. Two families also referred to issues with the mothers’ psychiatric health. In the category “Don’t want to participate” many referred to “Don’t want to be randomized”. One did not want to leave the child alone with the acupuncturist for five minutes.

**Table 1.** Reasons noted on the screening list for infants not being included after the baseline week (Landgren et al., 2010; Landgren & Hallström, submitted).

|                                                                                          | RCT 1              | RCT 2              |
|------------------------------------------------------------------------------------------|--------------------|--------------------|
|                                                                                          | Infants<br>(n=120) | Infants<br>(n=269) |
| Crying and fussing < 3 hours/day, n (%)                                                  | 63 (52,5)          | 119 (44,2)         |
| Did not want to participate, n (%)                                                       | 16 (13,3)          | 54 (20,0)          |
| Did not answer phone calls/email at the end of the baseline week, n (%)                  | 0 (0,0)            | 20 (7,4)           |
| Premature                                                                                | 1 (0,8)            | 8 (2,9)            |
| Parents chose to take the infant to a private acupuncturist                              | 3 (2,5)            | 17 (6,3)           |
| Parents chose to take the infant to a homeopath                                          | 1 (0,8)            | 0 (0,0)            |
| Parents chose to take the infant to a chiropractor                                       | 0 (0,0)            | 1 (0,3)            |
| Participation in the trial/registering in the diary required too much time/energy, n (%) | 6 (5,0)            | 17 (6,3)           |
| Symptoms improved when formula was introduced, n (%)                                     | 2 (1,6)            | 0 (0,0)            |
| Spontaneous remission or remission due to cows milk free diet, n (%)                     | 8 (6,6)            | 26 (9,6)           |
| Treated with dicyclomine                                                                 | 6 (5,0)            | 0 (0,0)            |
| The father did not want the infant to participate                                        | 1 (0,8)            | 2 (0,7)            |
| The infant was hospitalized                                                              | 1 (0,8)            | 0 (0,0)            |
| The mother was hospitalized                                                              | 0 (0,0)            | 1 (0,3)            |
| The breastfeeding mother could not manage a cow's milk protein free diet for 5 days      | 0 (0,0)            | 1 (0,3)            |
| The infant fulfilled the criteria but no acupuncturist was available at the study center | 0 (0,0)            | 3 (1,1)            |
| Missing                                                                                  | 13 (10,8)          | 0 (0,0)            |

**Table 2.** Treatment with simethicone and probiotics in the first (Landren et al., 2010) and the second (Landgren & Hallström., submitted) RCT.

|                                                             | RCT 1             |                  | RCT 2              |                  |
|-------------------------------------------------------------|-------------------|------------------|--------------------|------------------|
| Frequency and effect of treatments                          | Infants<br>(n=81) | Missing<br>n (%) | Infants<br>(n=147) | Missing<br>(n %) |
| <b>Simethicone</b>                                          |                   |                  |                    |                  |
| Treated with simethicone, n (%)                             | 75 (92,6)         | -                | 111<br>(76,0)      | 1 (0,7)          |
| Reported "effect" of treatment with simethicone, n (%)      | 2 (2,7)           | -                | 6 (5,4)            | -                |
| Reported "some effect" of treatment with simethicone, n (%) | 25 (33,3)         | -                | 29 (26,1)          | -                |
| Reported "no effect " of treatment with simethicone, n (%)  | 48 (64)           | -                | 76 (68,5)          | -                |
| <b>Probiotics</b>                                           |                   |                  |                    |                  |
| Treated with probiotics, n (%)                              | 12 (14,8)         | -                | 126<br>(86,3)      | 1 (0,7)          |
| Reported "effect" of treatment with probiotics, n (%)       | 0 (0)             | -                | 4 (3,2)            | -                |
| Reported "some effect" of treatment with probiotics, n (%)  | 2 (16,7)          | -                | 28 (22,2)          | -                |
| Reported "no effect " of treatment with probiotics, n (%)   | 10 (83,3)         | -                | 94 (74,6)          | -                |

**Drop outs**  
Three out of the 90 infants that were included in the first trial was later excluded due to the discovery of a miscalculation of the daily registration of crying which meant these infants had not fulfilled the criteria before the trial started. One of the infant's parents changed their mind about participating and chose to get treatment at a private acupuncture clinic instead. There were also five drop outs during the trial; four started treatment with dicyclomine and one went to a private acupuncture clinic. In the second trial three of the 157 included infants were excluded due to virus related illnesses. Seven more were unable to participate for different reasons; one lost a family member, three others changed their mind about participating in the study and three were not able to participate because no acupuncturist was available at the study center.

**Frequency of treatments and effect**  
Almost every infant in the first trial (Landgren et al., 2010) had been treated with simethicone and even though the frequency decreased from 93 to 76% in the second trial (Landgren et al., submitted) the majority of infants still got treated with simethicone. Only a few reported "effect" and about one third reported "some effect" in both trials. The use of probiotics increased significantly between the two trials but despite the remarkable increase there were still 83.3% in the first trial and 74.6% in the second trial who reported "no effect" from the treatment (Table 2).

**Association with background characteristics**  
Descriptive data and background characteristics from both RCT's (Landgren et al., 2010, Landgren & Hallström, submitted) are reported in table 3.

There was a significant association between the use of simethicone and parents having more than one child (p=0.018) as well as treatment with simethicone and previous experience of colic in the family (p=0.013). There was also a difference in the reported use of simethicone after having had a normal or a complicated delivery (p=0.015), where the majority of infants being treated with simethicone had been delivered without complications. The use of probiotics had a significant association with reported food allergies and/or food intolerances amongst

siblings and/or parents (p=0.019). There was also a significant association between higher frequency of complications during the pregnancy and a more frequent use of probiotics (p=0.002) as well as having tried probiotics and exclusive breastfeeding (p=0.031). The results also indicate an association between higher use of probiotics in families where parents and/or siblings had fewer problems with eczema (p=0.049) as well as having tried probiotics and the infant having less problems with skin rashes (p=0.035). All background characteristics were analyzed for association between the frequency of treatment with simethicone and use of probiotics. There were no other significant associations found amongst the remaining background characteristics.

**Treatment over time**  
There was a statistically significant difference in the frequency of treatment with simethicone between the two RCTs (p=0.002). The use of simethicone in the first RCT was 93%, which had reduced to 76% in the second RCT. The use of probiotics however had increased significantly between the two studies (p=0.000), from 15% that had tried treatment with probiotics in the first RCT to 86% in the second RCT (Table 4).

**DISCUSSION**  
There were two main reasons for infants who were screened for participation in the two trials not to be included. When the crying was actually measured in a diary, about half of the infants were reported to cry < 3 hours per day and therefore did not fulfill the criteria for colic. Besides, several infants reduced their symptoms of colic spontaneously when introducing a cows' milk protein free diet. It is interesting that so many parents who claimed their infant had colic reported normal crying when they used a diary. This indicates that the diary is a valuable tool for nurses working at CHCs when discussing normal crying and fussing with this group of parents. All parents who had not already tried a period of five days where the infant was not exposed to cows' milk protein neither via breast milk nor formula was instructed to try this intervention during baseline. Thus there might be a substantial overlap between the categories "Crying and fussing < 3 hours/day" and "Spontaneous remission or remission due to cows' milk free diet". It is noteworthy that so many of the infants

with excessive crying calmed down to normal crying when they were no longer exposed to cows' milk protein. As five days was enough to normalize the crying in a large group of infants, this seems to be a safe, inexpensive and simple intervention that nurses could encourage parents to try as an early intervention. In these trials where more than 600 parents were instructed to try this diet only one mother was reported not to manage a cows' milk protein free diet for five days.

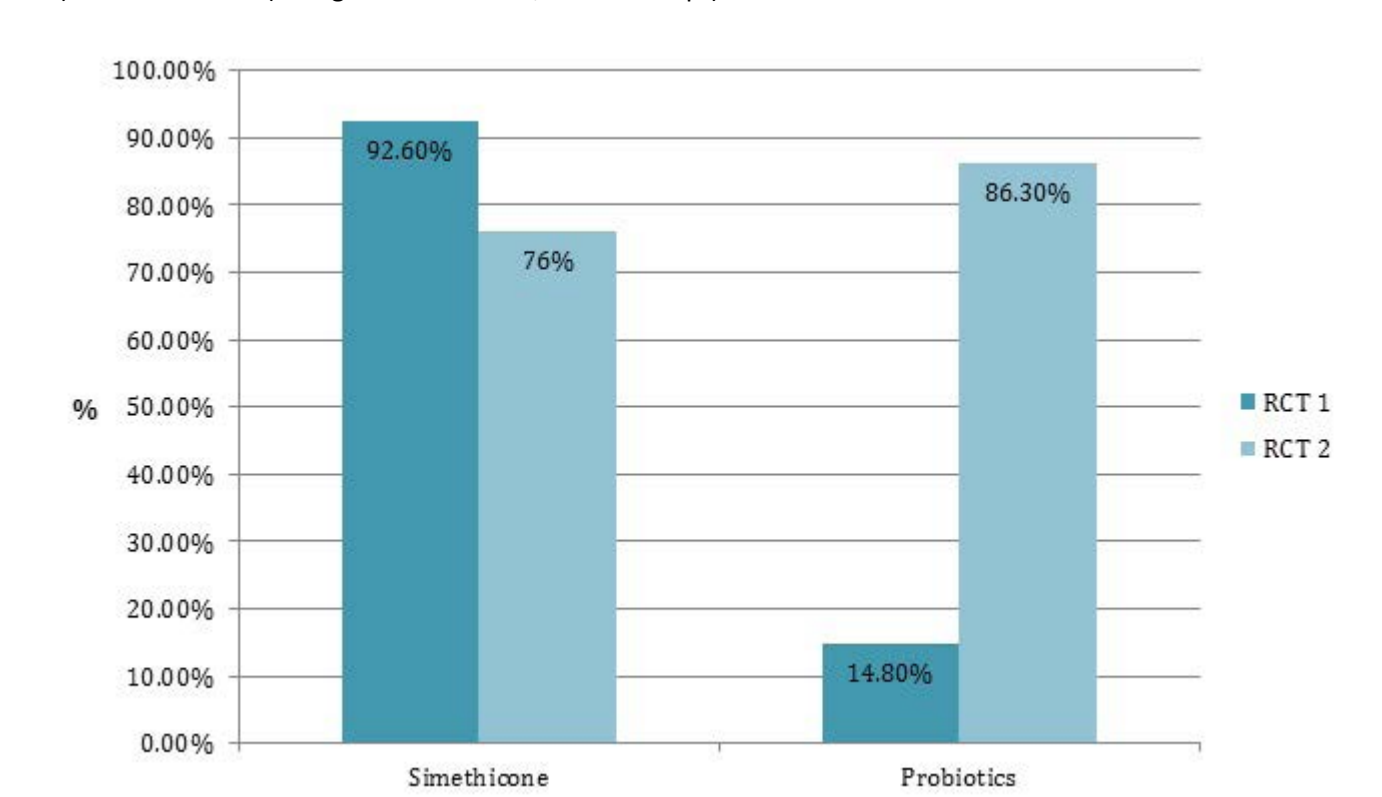
The result also showed a difference in the use of the anticholinergic drug dicyclomine between the two trials. In the first trial, collecting data 2005 – 2007, six infants started with dicyclomine during baseline, and four more dropped out as parents started to give the infant dicyclomine (Landgren et al., 2010). In the ACU-COL trial conducted eight years later the use of dicyclomine had been reduced to zero. This reflects changed recommendations from the authorities due to reported side effects from this medication. Another difference is that more parents in the second trial chose to take the infant to an acupuncturist outside the study center to avoid being randomized to the control group. This choice was possible during ACU-COL's data collection period since acupuncture for colic at that time was available in more clinics.

Even though almost every infant in the first trial had been treated with simethicone only 2.7% of the parents reported effect. The number of infants being treated with simethicone had decreased in the second trial where 5.4% reported having effect of the treatment. Probiotics were introduced on the market while the first trial was being conducted which can explain the increased use of probiotics from only 14.8% in the first trial to 86.3% in the second trial. While no one reported perceived effect of probiotics in the first trial, only 3.2% reported effect in the second trial despite the excessive increase. It is noteworthy that despite the lack of research that supports the use of simethicone when treating infantile colic (Lucassen, 2010; Hall et al., 2011; Savino et al., 2014) it is still one of the most common recommended treatments in Sweden (Landgren et al., 2012). The use of simethicone reduced between the two trials but more than three quarters of the infants was still given simethicone. About one third of these reported "effect" or "some effect" of treatment with

**Table 3.** Descriptive data from the first (Landgren et al., 2010) and the second (Landgren & Hallström, in manuscript) RCT.

|                                                                                                        | RCT 1             |                  | RCT 2              |                  |
|--------------------------------------------------------------------------------------------------------|-------------------|------------------|--------------------|------------------|
|                                                                                                        | Infants<br>(n=81) | Missing<br>n (%) | Infants<br>(n=147) | Missing<br>n (%) |
| <b>Background characteristics</b>                                                                      |                   |                  |                    |                  |
| <b>Family</b>                                                                                          |                   |                  |                    |                  |
| Born in Sweden, mother, n (%)                                                                          | 76 (93,8)         | -                | 125 (85)           | -                |
| Born in Sweden, father, n (%)                                                                          | 72 (88,9)         | -                | 125 (85)           | -                |
| University education, both parents, n (%)                                                              | 26 (32,1)         | -                | 52 (35,4)          | 2 (1,4)          |
| University education, one parent, n (%)                                                                | 33 (40,7)         | -                | 50 (34,5)          | 2 (1,4)          |
| Smoking, mother, n (%)                                                                                 | 6 (7,4)           | -                | 3 (2,1)            | 1 (0,7)          |
| Smoking, father, n (%)                                                                                 | 5 (6,2)           | -                | 15 (10,3)          | 2 (1,4)          |
| Parent and/or sibling with food intolerance/allergy, n (%)                                             | 60 (74,1)         | -                | 77 (52,7)          | 1 (0,7)          |
| Parent and/or sibling who had asthma, n (%)                                                            | 16 (19,8)         | -                | 34 (23,3)          | 1 (0,7)          |
| Parent and/or sibling who had eczema, n (%)                                                            | 25 (30,9)         | -                | 35 (24,0)          | 1 (0,7)          |
| Parent and/or sibling who had a bowel disease, n (%)                                                   | 22 (27,2)         | -                | 29 (19,9)          | 1 (0,7)          |
| Parent and/or sibling who had had infantile colic, n (%)                                               | 45 (55,6)         | -                | 81 (55,5)          | 1 (0,7)          |
| Parent and/or sibling had infantile colic; “don’t know”, n (%)                                         | 3 (3,7)           | -                | 14 (9,6)           | 1 (0,7)          |
| <b>Pregnancy and delivery</b>                                                                          |                   |                  |                    |                  |
| Pregnancy was overall free from complications, n (%)                                                   | 35 (43,2)         | -                | 106 (72,1)         | -                |
| Pregnancy was overall a positive experience, n (%)                                                     | 63 (77,8)         | -                | 114 (77,6)         | -                |
| Prescription drugs were used during or after pregnancy, n (%)                                          | 44 (54,3)         | -                | 84 (57,5)          | 1 (0,7)          |
| Normal delivery, n (%)                                                                                 | 48 (59,3)         | -                | 103 (70,5)         | 1 (0,7)          |
| <b>Infant</b>                                                                                          |                   |                  |                    |                  |
| Firstborn, n (%)                                                                                       | 42 (52,5)         | 1 (1,2)          | 57 (38,8)          | -                |
| Infants gender, male, n (%)                                                                            | 41 (50,6)         | -                | 80 (54,4)          | -                |
| Healthy appetite, n (%)                                                                                | 79 (97,5)         | -                | 142 (97,3)         | 1 (0,7)          |
| Exclusive breastfeeding, n (%)                                                                         | 57 (70,4)         | -                | 85 (58,2)          | 1 (0,7)          |
| Excessive gastrointestinal gas, n (%)                                                                  | 76 (93,8)         | -                | 136 (93,8)         | 2 (1,4)          |
| Repeated vomiting, n (%)                                                                               | 43 (53,1)         | -                | 65 (44,5)          | 1 (0,7)          |
| Skin rash, n (%)                                                                                       | 47 (58)           | -                | 52 (36,4)          | 4 (2,7)          |
| <b>Alternative treatment for colic</b>                                                                 |                   |                  |                    |                  |
| Treatment with alternative options; herbal tea, suger solution, chiropractor or other treatment, n (%) | -                 | -                | 30 (20,6)          | 1 (0,7)          |
| Effect of alternative treatment, n (%)                                                                 | -                 | -                | 10 (34,5)          | 1 (0,7)          |
| Some effect of alternative treatment, n (%)                                                            | -                 | -                | 8 (27,6)           | 1 (0,7)          |
| No effect of alternative treatment, n (%)                                                              | -                 | -                | 11 (37,9)          | 1 (0,7)          |

**Table 4.** Differences in frequency of treatment with simethicone and probiotics between the first (Landgren et al., 2010) and the second (Landgren & Hallström, in manuscript) RCT.



simethicone which is comparable to using placebo (Metcalf et al., 1994) and the infants still fulfilled the criteria for colic in spite of the medication. While the use of simethicone was significantly reduced, the treatment with probiotics increased remarkably which could be a reflection of both the introduction of the product on the market during the first trail and the increasing research on treatment with probiotics that are showing positive results. These studies have however mainly been conducted on infants that are being exclusively breastfed which still leaves a need for research on infants being fed with formula before probiotics can be recommended to the general population (Urbanska & Szajewska, 2014). This might also explain the association between the use of probiotics and exclusive breastfeeding.

There was no significant difference in the frequency of treatment with simethicone or probiotics depending on the parents’ demographic background which is in alliance with Lucassen et al. (2001) who found no association between colic and socioeconomic class, parental smoking, history of atopic syndrome in the family, type of feeding or the gender of the infant. The association between treatment with simethicone and having more than one child in the present study might be

related to the association with having earlier experience of colic in the family due to siblings also having had colic, leading to a search for treatment. These families might therefore be more familiar to using simethicone after already having treated their older children. In the general population 10-17% have had infantile colic (Canivet et al., 2002, Lucassen, 2010). However this study showed that 55% of the infant’s had parents and/or siblings reported also to having had colic as infants. This indicates that infantile colic might have a hereditary factor and that infants in families with previous experience of colic therefor could be exposed to a higher risk than infants in the general population.

**Strength and limitations**

The strength of this study was the possibility to analyze unpublished data from two different RCT’s, which allowed a comparison over time and a greater sample size. Furthermore, data from all the infants with symptoms of colic that were screened for participation in the study but were not included could be categorized which gave a valuable and unusual insight to how these parents and infants may be helped by using a diary for both registration of crying and for evaluating the effects of given advice and

treatments. It is also a strength that this study used data from two different trials where the location of the study centers were chosen to provide a wide range of the population, incorporating both larger and smaller cities with cultural and socio-economic differences. The participants should therefore be reasonably representative of the general population. All the infants in the two trials that had been treated with simethicone or probiotics still fulfilled the criteria for colic at inclusion. This is a limitation as there might be infants who received the same medication with sufficient effect and therefore never applied for participation. Although this is a risk for both treatments it is however unlikely for simethicone since there is a lack of positive results in earlier RCTs that where specifically designed to evaluate the effect of simethicone when treating colic (Lucassen, 2010).

**Conclusion**

It is valuable for pediatricians and nurses working at the CHC to know that the majority of parents treat their infant with simethicone and/or probiotics despite weak evidence to support this in infantile colic. The CHC nurse is the primary contact between these parents and the health care system and they are required

to base their recommendations on scientific evidence or methods that has been well proven to have effect from years of experience. This foundation helps built trust between the parents seeking advice and their CHC nurse and ensures the safety and quality of care. Since there is no scientific evidence for the effect of simethicone in infantile colic, simethicone should not be recommended by the CHC nurse when giving advice on treating colic in infants. There is a need for more RCTs that could compare the effect of probi-

otics to placebo when treating infantile colic before CHC nurses can recommend probiotics based on scientific evidence. Parents also wish that advice given by their CHC nurse are more structured and systematically evaluated. The CHC nurse has therefore a great responsibility to not only give advice based on up-to-date scientific evidence but to also adapt how the advice is being given and evaluated. By using a diary where parents report the infants crying both the parents and the CHC nurse get valuable information about

how much the infant is actually crying. The diary can therefore be a valuable tool in the clinical practice of the CHC nurse when trying to help infants with colic and their families by discussing normal crying and evaluating the effect of given advice. Excluding cows' milk protein completely from both the mothers' and the infants' diet during five days helped many infants with excessive crying and can therefore be recommended by the CHC nurse as an early intervention combined with the diary for evaluating the intervention.

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