

# Dietary treatment of infant colic: a double-blind study

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**SUMMARY.** *The possible role of cows milk intolerance in the aetiology of infant colic was evaluated in 19 babies presenting to their health visitor or general practitioner in one town. Over a three week period a standard modified cows milk formula was compared with a soya milk formula on a double blind basis. The duration of colic symptoms was significantly reduced during the week on soya milk ( $P < 0.01$ ), with 11 out of 19 babies fulfilling the diagnostic criteria for cows milk intolerance. Four babies whose symptoms failed to improve either spontaneously or with soya milk were given a hydrolysed protein milk with a positive response in two, confirmed by challenge testing. Thus in 13 out of 19 babies (68%) the symptoms of infant colic resolved almost completely with dietary change.*

## Introduction

INFANT colic is a common condition, affecting 15–40% of babies;<sup>1,4</sup> it usually starts in the second or third week of life and subsides spontaneously within three to four months.<sup>1</sup> It is a condition which is difficult to define precisely, but may be regarded as 'paroxysms of unexplained irritability, fussing or crying during the first three months of life, lasting more than three hours per day on more than three days per week in a healthy infant with normal weight gain'.<sup>5</sup> The diagnosis thus requires an arbitrary decision as to when crying becomes excessive, and the exclusion of other causes of crying or irritability.

Over the years many suggestions have been made as to the cause of infant colic. It has been linked with 'autonomic hyper-reactivity',<sup>6,7</sup> progesterone deficiency,<sup>5,8</sup> and events during labour.<sup>9,10</sup> Crying is a baby's principal means of communication, and several authors see colic as a behavioural problem.<sup>11-14</sup> However, with such a vague symptom it is unlikely that there is one single cause.

Allergy was suggested as a cause of infant colic as early as 1927.<sup>15</sup> More recently a Swedish study<sup>16</sup> looking at 60 babies with colic severe enough to warrant hospital referral found 43 had complete remission of symptoms when their diet was changed from a cows milk based formula to either soya milk or a hydrolysed protein milk. The remaining 17 got better spontaneously. These impressive results prompted us to look at a less highly selected population by repeating this study in a general practice setting.

## Method

The town of Livingston in West Lothian has a population of about 40 000 served by 46 general practitioners, trainees and health visitors working from four health centres. These doctors and health visitors agreed to refer any bottle-fed baby whom they considered to have infant colic (defined as above) for inclusion in the study. There are about 650 births per annum in

Livingston, and over the two-year study period there were 41 referrals.

## Selection of study group

All the babies were seen at home and underwent an initial assessment, including physical examination. The baby's feeding was unchanged in the first week of the study in order to obtain a baseline measurement of the degree of colic.

Eight of the 41 babies were excluded at initial assessment, and a further 14 after the baseline observation week. The majority were excluded for failing to meet the inclusion criteria, mostly because the severity of colic symptoms had improved spontaneously. Because infant colic is a condition with a high rate of spontaneous remission a large drop-out rate is to be expected. Of the 19 babies who entered the cross-over trial 11 were males and eight were females. Four babies were the first born, seven were second born and eight were third to sixth born. Colic had started at one week old for eight babies, at two weeks for four, at three weeks for six and at four weeks for one baby. The mean age at entry to the study was seven weeks (range three to 14 weeks) and the mean age of the mother was 28 years (range 21–40 years). There was an atopic family history in 11 of the babies (58%).

## Study

On the basis of random assignment 10 babies were given soya milk (Cow and Gate Formula S) for one week followed by standard modified cows milk formula (Cow and Gate Premium) in the following week, and nine had standard milk followed by soya milk. The milks were packaged in identical coded tins and the code for each pair of milks was not broken until the end of the three week period so that the observations would be double-blind. Those babies whose symptoms resolved while taking soya milk were then challenged with standard infant formula. The absence of symptoms on soya milk with return of symptoms when given cows milk formula was regarded as diagnostic of cows milk intolerance.

Babies who failed to improve either with soya milk or spontaneously were then given a milk free of whole protein (Cow and Gate Peptalac). This is a milk based on hydrolysed lactalbumin containing mostly short-chain peptides with 15–20% free amino acids.<sup>17</sup> No attempt was made to give this milk on a double-blind basis as its appearance is obviously different from standard milk, and any placebo effect was likely to have become manifest in the first phase of the study. Babies whose symptoms resolved with this milk were again challenged with a standard milk to establish whether true intolerance existed to both cows milk and soya milk.

Babies who demonstrated cows milk intolerance were continued on either soya milk or peptide milk, and were given further challenge tests at three month intervals. In addition mothers received dietary advice on cows milk exclusion before weaning.

## Measurement of symptoms

Mothers kept a record sheet noting the amount of time the baby had colic symptoms each day. The record sheets were scored by totalling all the periods of colic, to the nearest half hour, for six days of each week of the study. The first day of each week was excluded to allow transition time between different milks.

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**Results**

The results were analysed in two ways — first, a quantitative analysis by scoring the duration of symptoms in each of the two periods, and secondly, a ‘binary’ analysis noting how many subjects fulfilled the criteria for cows milk tolerance.

*Quantitative analysis*

Figure 1 shows the distribution of symptom scores for the two six-day periods on standard milk and soya milk, irrespective of the order of the periods. This shows a wide scatter of scores, with a median value of 20 hours of colic on standard milk compared with a median of five hours on soya milk.

Table 1 gives the symptom scores with the associated descriptive statistics. Allowing for the small numbers and any period effect, the results confirmed a significant reduction in symptoms associated with soya milk ( $P<0.01$ ). The anticipated period effect due to spontaneous remission did not reach significance.<sup>18</sup>

Because of the skewed distribution of scores the data were further analysed using the Wilcoxon signed rank test. The result ( $T+ = 149$ ) was above the critical value of 105 ( $n=18$ ), again indicating a significant difference between scores on standard milk and soya milk ( $P<0.01$ ).<sup>19</sup>

*Binary analysis*

Of the 19 babies who entered the crossover trial, 11 had a marked reduction in symptoms while on soya milk, and prompt return of symptoms when subsequently given cows milk formula. Four babies had improved spontaneously on soya milk as they had no symptoms when challenged with cows milk formula. Four babies continued to have significant symptoms on soya milk; they were given Peptalac for a further week, during which three were significantly improved but one continued to have symptoms. Again, the three who showed improvement were given a challenge test with a positive reaction in two. On the basis of challenge testing the results for the 19 babies can be summarized as follows: 11 (58%) intolerance of cows milk; two (11%) in-

tolerance of cows milk and soya milk; five (26%) symptoms resolved spontaneously; one (5%) failure of dietary treatment.

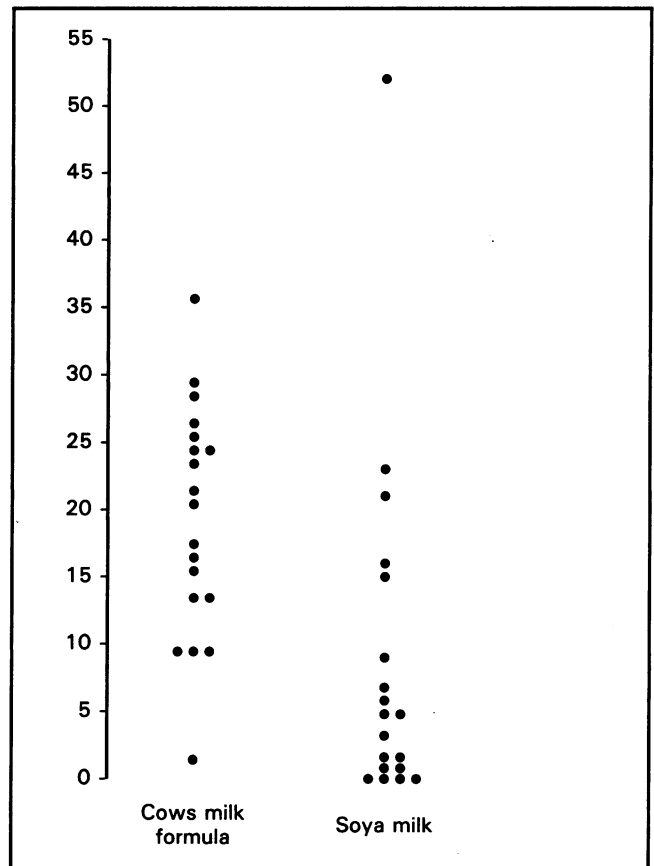


Figure 1. Distribution of symptom scores for the two six-day periods on standard milk and soya milk.

Table 1. Duration of colic symptoms for each subject during cross-over weeks, with analysis of differences.

Baby	Duration of colic symptoms (hours)					
	Week A soya milk	Week B standard milk	B minus A	Week A standard milk	Week B soya milk	A minus B
1	0.0	26.0	26.0			
2	0.0	20.0	20.0			
3				28.0	5.0	23.0
4				13.0	0.5	12.5
5				9.0	16.0	-7.0
6	0.5	9.0	8.5			
7				13.0	0.0	13.0
8	21.0	29.0	8.0			
9				23.0	3.0	20.0
10	9.0	1.0	-8.0			
11	5.0	17.0	12.0			
12	23.0	35.0	12.0			
13				24.0	0.0	24.0
14				9.0	1.0	8.0
15				16.0	6.0	10.0
16	52.0	25.0	-27.0			
17	15.0	15.0	0.0			
18	1.0	24.0	23.0			
19				21.0	7.0	14.0
Mean (SD)	12.7 (16.4)	20.1 (10.0)	7.5 (15.9)	17.3 (6.9)	4.3 (5.1)	13.1 (9.4)

Difference in treatment effects = 10.3 hours, 95% confidence interval = 4.3 to 16.2 hours, treatment effect significant ( $P<0.01$ ). Difference due to period effect (2.9 hours) not significant at 10% level.

Only 11 out of the 13 babies with cows milk intolerance could be contacted after three months at which time eight still had a positive challenge test, indicating continuing intolerance of cows milk. At six months no babies reacted on challenge testing.

### Discussion

With no clear idea about the cause of infant colic, treatment has tended to be empirical, and numerous approaches have been tried.<sup>1,6,7,20,21</sup> The existing evidence for the possible role of allergy in infant colic is slender.<sup>22,23</sup> In one study of jejunal biopsies in babies with colic<sup>24</sup> the IgE plasma cell count was higher than a control group, suggesting an allergic basis, but this study had limitations<sup>25</sup> as the control group was not normal, and the 14% acceptance rate for biopsy might have introduced bias.

The large-scale use of cows milk in infant feeding is less than 100 years old, and a large number of adverse effects have been described.<sup>26</sup> One adverse effect might be infant colic. Whether cows milk intolerance is due to lactose or protein intolerance is not clear and no attempt was made in this study to determine which component of milk was responsible for the intolerance (both soya and peptide milks are also lactose-free). Indeed the two conditions cannot be entirely separated as cows milk protein has been shown to affect lactose absorption,<sup>27</sup> and cases have been described of cows milk allergy and lactose intolerance coexisting.<sup>28</sup>

Colic also occurs in breast-fed babies and seems to be as common. This fact does not exclude diet as a possible cause of infant colic — several maternal foods can cause reactions in breast-fed infants, and cows milk is the commonest.<sup>29</sup> In one study 12 out of 18 breast-fed babies with colic were rendered symptom-free by elimination of cows milk from the mother's diet.<sup>30</sup> This study was criticized, however, because of the placebo effect of treatment, and the lack of difference in the presence of antigen in the mother's milk in responders and non-responders.<sup>31</sup> In addition, a similar but double-blind study failed to show any significant difference in the rate of colic.<sup>32</sup>

Breast milk has been compared with cows milk, both treated and untreated with lactase, in a double-blind crossover study on 10 infants.<sup>33</sup> There was no difference in the duration or severity of colic on the different milks, but as the subjects were weaned and had a mean age of 12 weeks, they cannot be regarded as typical babies with colic.

The diagnosis of cows milk intolerance is traditionally made using Goldman's criteria<sup>34</sup> which state that: (a) symptoms must subside after milk elimination, (b) they must recur within 48 hours after trial feeding of milk, (c) three such challenges must be positive and have similar features, and (d) symptoms must subside after each challenge reaction. In this study a single positive challenge test was considered sufficient — the parents' relief after the disappearance of colic symptoms was such that their cooperation with more than one test would have been difficult to achieve.

In this study 13 out of 19 babies (68%) presenting with colic to the primary health care team had evidence of cows milk intolerance as a cause of their colic. Only one baby still had colic symptoms at the end of the study period. Statistical analysis of the symptom scores showed a significant reduction in colic symptoms with soya milk. The subjects studied represented most of the babies in a defined population with significant and persistent symptoms whose mothers sought medical help. The 41 referrals represent an incidence of infant colic of only 3%, which is low, even allowing for the exclusion of breast-fed babies, and either reflects a true low incidence or a low referral rate. However, medical advice is not always sought for every baby with colic,

and thus the incidence rate of those who complain to health workers is likely to be lower than that from direct population surveys. Our study confirms the results obtained by Lothe and colleagues<sup>16</sup> on a selected clinic-based population by demonstrating that a significant number of bottle-fed babies with infant colic have cows milk intolerance, and can achieve complete freedom from symptoms with a change in diet.

Not all babies with cows milk intolerance will respond to soya milk — there is some evidence that soya milk is at least as antigenic as cows milk.<sup>35</sup> Those babies who react to both cows milk and soya milk may be helped by a hydrolysed protein milk. It has been suggested that babies who are otherwise thriving should not have their diet changed,<sup>36</sup> but the distress caused by colic should be taken into account. Soya milk for infant feeding is widely available and nutritionally complete, but it is more costly and may have other disadvantages (such as the bioavailability of minerals). Its ease of use may lead to the overdiagnosis of cows milk intolerance and the possibility of other diagnoses being missed. However, the safety of soya milk is supported by the approval of the Department of Health and Social Security advisory committee on borderline substances. In addition, the soya milk used in this study complies with DHSS guidelines for infant formulae,<sup>37</sup> and has been shown to support a healthy growth rate.<sup>38</sup>

Suggested guidelines for the use of soya milk in infant colic are as follows:

1. Parent to keep diary of symptoms for one week.
2. Trial of soya milk for one week (two tins).  
If symptoms have resolved:
3. Challenge baby with standard milk.  
If symptoms return:
4. Continue with soya milk and repeat challenge tests at monthly intervals.

Any treatment should take account of the high spontaneous remission rate, and hence the need for regular assessment. Great care is required both with the initial diagnosis of colic and any subsequent diagnosis of cows milk intolerance. However, the safety and apparent efficacy of dietary treatment is such that it should be considered in the treatment of bottle-fed babies with significant and persistent symptoms of infant colic.

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