Infantile colic: exploring the potential role of maternal acupuncture

Yusuf Ozgur Cakmak

Abstract
Lack of knowledge about the pathophysiology of infantile colic limits the development of effective drugs and treatment modalities including acupuncture. Acupuncture research has targeted the baby without considering the mother. However, the pathophysiological clues indicate that infantile colic is a shared pathology between the mother and the baby, especially in the case of breastfeeding mothers. A new theory proposed in this paper involves levels of the cytokine tumour necrosis factor α (TNFα) in the mother’s milk and its influences on melatonin and serotonin metabolism in the baby as major components of the pathophysiology of infantile colic. These can be normalised by applying acupuncture to the breastfeeding mother alone or also to the baby.

INTRODUCTION
The development of infantile colic in infants is a complex process and the underlying pathophysiology is still uncertain. This lack of knowledge limits the production of effective drugs. Moreover, drugs and alternative therapies including acupuncture target the baby without considering the mother. However, the pathophysiological clues indicate that infantile colic in babies of breastfeeding mothers is a shared pathology between the mother and baby.

The identification in 1980 of prostaglandins E and F in human milk led to the hypothesis that these prostaglandins were probably a cause of irregular gut motility in the infant. However, the samples were not taken selectively from the mothers of babies with colic. Based on this theory, in 1981 Butler reported a trial in 22 breastfeeding mothers whose infants had colic and who were given 900–1800 mg aspirin (acetylsalicylic acid) a day in divided doses. Eighteen reported a definite improvement in the infant’s symptoms. Although these results are consistent with the prostaglandin theory, they are not direct evidence. Subsequently, Beckmann et al reported that prostaglandin E2 levels are increased in blood samples after aspirin intake, which is contrary to the prostaglandin theory. Furthermore, one effect of the ingestion of low-dose aspirin was overlooked—namely, a reduction in the cytokine tumour necrosis factor α (TNFα) releasing capacity of activated leucocytes. This is observed after ingestion of low-dose aspirin, independent of changes in prostanoid biosynthesis. The improvements in the infantile colic symptoms seen with acetylsalicylic acid ingestion might therefore be attributed to the TNFα-based pathway. A new theory proposed in this paper is that TNFα in the mother’s milk might influence the metabolism of melatonin and serotonin in the infant, and that these are major components in the pathophysiology of infantile colic.

EXPLORING THE MOTHER FACTOR: TNFα
Melatonin is involved in the regulation of gastrointestinal motility and sensation while serotonin, which is found mostly in the gastrointestinal tract, has a muscular contraction action within the bowel. It is worth noting that melatonin can reduce abdominal and rectal pain. Levels of 5-hydroxy-3-indole acetic acid (5-OH IAA), a metabolite of serotonin, were studied in infants with infantile colic in order to investigate the aetiology of infantile colic: urinary 5-OH IAA levels in infants with colic were found to be higher than those in the control group. Peak serotonin levels cause intestinal cramps associated with colic because serotonin increases intestinal smooth muscle contractions. Intestinal cramps caused by serotonin are unopposed by melatonin during the first 3 months of life because only serotonin circadian rhythms are present at birth and melatonin circadian rhythms do not appear until the age of 3 months, the time at which colicky cramps disappear.

Although the potential roles of delayed normalisation of melatonin circadian rhythms and high levels of serotonin metabolites have been studied in the pathophysiology of infantile colic, the role of TNFα still needs to be investigated because of its influence on melatonin and serotonin levels. Babies who had been or were being breast fed are significantly more likely to have colic. Moreover, there is also a significant trend for breast fed babies to have a longer reported duration of colic than bottle-fed babies. It can therefore be hypothesised that mother’s milk might contain a factor that increases colic. Elevated TNFα levels in the mother’s milk are a likely factor for increasing colic because it has been shown that an increase in circulating TNFα results in the suppression of nocturnal melatonin production as well as an increase in serotonin levels by decreasing the serotonin reuptake transporter function. In accordance with these data, TNFα that is repeatedly passed to the baby by breast feeding can potentially downregulate the production of melatonin and upregulate serotonin levels in the baby, so it may be the major maternal factor for increasing or triggering infantile colic.

It is interesting to compare the effects of diet on the level of TNFα in mother’s milk and on infantile colic. It has been shown that, when the mother’s diet includes more cheese and tomato, the incidence of infantile colic is decreased. Interestingly, it has also been shown by different research groups that TNFα levels can be decreased by cheese and tomato consumption. Furthermore, when mothers are restricted from cow’s milk, wheat and egg, their infants...
have less infantile colic.\textsuperscript{18} It has also been shown that cow’s milk, wheat and egg consumption results in the elevation of TNFα levels.\textsuperscript{19, 20} In addition to clues relating TNFα in the mother’s diet to infantile colic symptoms, postpartum depression is also closely related to infantile colic\textsuperscript{21} and it has been shown that TNFα levels are elevated in postpartum depression.\textsuperscript{21}

Furthermore, one of the most significant factors related to infantile colic is maternal tobacco smoking and, again, high levels of TNFα have been shown in the serum of smokers\textsuperscript{22} (figure 1).

The nocturnal melatonin surge observed 3 days after vaginal delivery is absent in the colostrum after caesarean section and synchronised with elevated levels of TNFα in the colostrum.\textsuperscript{12} Although caesarean section can increase TNFα levels and suppress melatonin levels, it is not a risk factor for infantile colic.\textsuperscript{12, 15} In fact, this is not contrary to the TNFα theory because TNFα levels are increased for only 3–10 days after caesarean section whereas infantile colic occurs later, up to 3 months.\textsuperscript{12, 15} The cytokine theory proposed in this paper is that infantile colic is caused by repeated transmission of elevated TNFα levels to the baby as a result of maternal sleep disturbances, smoking and diet.

### POSSIBLE EFFECTS OF ACUPUNCTURE IN BREASTFEEDING INFANTS

It has been shown that the application of acupuncture to infants with infantile colic results in a decrease in symptoms.\textsuperscript{1} It should be noted that the increase in circulating TNFα results in the suppression of nocturnal melatonin production and also a decrease in the production of interleukin 2 (IL-2).\textsuperscript{12} A longitudinal evaluation of the correlation between melatonin and IL-2 showed that recovery of the nocturnal melatonin surge was always followed by an increase in IL-2 secretion.\textsuperscript{12} Acupuncture can reduce pathologically increased TNFα levels\textsuperscript{23–24} and can also increase nocturnal melatonin and IL-2 levels.\textsuperscript{25–26} The increase in IL-2 levels with acupuncture is also proof of the normalising effect of acupuncture on melatonin, in addition to the proposed TNFα pathway.

Acupuncture may also potentially normalise infant serotonin levels by decreasing TNFα, thus normalising the inhibitory effect of TNFα on serotonin reuptake.\textsuperscript{13} Furthermore, it has been shown that acupuncture can modulate the availability of serotonin to restore the balance between serotonin synthesis and removal, and thereby it can attenuate stress-induced defecation in rats with chronic visceral hypersensitivity via the serotonergic pathway.\textsuperscript{27} According to this model it can therefore be assumed that acupuncture directly targets the pathophysiology of infantile colic.

On the other hand, if we consider the clues from pathophysiological, nutritional and psychological research summarised above, infantile colic is clearly a shared pathology between the mother and the baby, so the breastfeeding maternal factor—elevated TNFα—should not be excluded from the target of research designs for acupuncture treatment of infantile colic. Applying acupuncture to the breastfeeding mother may result in decreased levels of TNFα which may help to overcome the suppression of melatonin secretion in the infant in addition to its potentially normalising effect on elevated serotonin levels by overcoming the inhibitory effect of TNFα on the serotonin reuptake transporter (figure 1).

The sleep of the mother and infantile colic is also an important area where melatonin and the pathophysiology of infantile colic intersect. It has been reported that sleep disturbance is greatest in mothers during the first postpartum month, particularly for first-time mothers, and by the third month postpartum—at which time infantile colic tends to cease—there is an improvement in the maternal sleep pattern.\textsuperscript{28} The finding that first-born infants have a higher rate of colic is in accordance with these data.\textsuperscript{29} It has been shown that acute total sleep deprivation is sufficient to induce secretion of proinflammatory cytokines such as TNFα, a marker described in chronic sleep restriction or deprivation and as mediators of excessive sleepiness in humans in pathological conditions.\textsuperscript{26} The relationship between maternal sleep disturbance and infantile colic can therefore be explained by the decrease in maternal melatonin levels during the first postpartum month and the increase in TNFα in the mother’s milk, and thereby elevation of serotonin levels. All these irregularities can potentially be normalised by applying acupuncture to the mother (figure 1).\textsuperscript{25–26} In addition, the TNFα secretory factors of maternal

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**Figure 1** Diagram of TNFα hypothesis of infantile colic. The numbers represents the corresponding references. IL-2, interleukin 2; SERT, serotonin reuptake transporter.
depression and maternal diet including cow’s milk, wheat and egg might also be normalised by maternal acupuncture. 15,18–21,23–26

In addition to the transfer of elevated TNFα to the baby, the suppressive effects of elevated TNFα may result in a low level of melatonin transfer to the baby as a secondary phenomenon. It is therefore possible that there is a high suppressive effect (high TNFα transfer) and low suppressive effect (low melatonin transfer) for the baby as maternal factors in the pathophysiology of infantile colic. It is known that acupuncture can normalise both factors in the mother. 23–26

It is worth noting the psychology of the mother during the first acupuncture session of their babies. Although there have been no studies of the anxiety levels of mothers during acupuncture of their babies, we have observed that mothers are concerned that their babies will feel pain during the acupuncture procedure. Needling the mothers before their babies reassures them about how their babies will feel during the acupuncture session and may help to calm them, in addition to the potential beneficial effects on the infantile colic.

**CONCLUSIONS**

The treatment of a disease should be based on knowledge of its pathophysiology. The pathophysiology of infantile colic still needs to be investigated further but factors in the breastfeeding mother should be included. After consideration of factors that have not received adequate attention, medical acupuncture might achieve better results. Further studies of maternal acupuncture are needed to clarify the changes in TNFα, melatonin and serotonin levels in the mother’s milk and the baby and to correlate them with the symptoms of infantile colic. An appropriate acupuncture research design and treatment algorithm for infantile colic should include needling breastfeeding mothers as the first step or in addition to acupuncture of the baby. Moreover, acupuncture may also be advised for the prevention of infantile colic, especially in first-time mothers who are considering breast feeding.

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