

Do Newborn Infants of Ethiopian Origin Spit Up More than Other Newborn Infants?

Vered Nir MD, Erez Nadir MD, Mulunesh Mekonen RN and Michael Feldman MD

Department of Neonatology, Hillel Yaffe Medical Center, Hadera, Israel

ABSTRACT: **Background:** Ethnic differences in the incidence of spitting up have not been reported. The nursing team at our well-baby nursery observed that newborn infants of Ethiopian origin appeared to spit up more than the others. **Objective:** To determine whether there are such ethnic differences and what, if anything, is their clinical relevance. **Methods:** Of the 3663 enrolled infants born at the Hillel Yaffe Medical Center during the 12 month study period, 55 were of Ethiopian origin and their medical records were retrospectively surveyed. The retrieved data were compared with those of 167 randomly selected non-Ethiopian newborns (controls). Exclusion criteria were preterm delivery, admission to the neonatal intensive care unit, and congenital birth defects. **Results:** Newborn infants of Ethiopian origin spit up 57% more than control infants. The difference in the number of spit ups was more obvious when only the infants who spit up were compared (2.3 ± 1.7 Ethiopian newborns vs. 1.5 ± 0.9 controls, $P = 0.002$), although the percentage of infants who spit up was the same in the two groups. There was no difference in weight gain, days of hospitalization, bilirubin levels or nutrition type between the groups. **Conclusions:** Infants of Ethiopian origin spit up more than the control newborn infants of non-Ethiopian origin, while other clinical parameters were similar. In the absence of other pathological signs, spitting up is a non-relevant clinical condition.

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Data on how often healthy newborn infants spit up during the first 48 hours of life (the usual length of stay in a well-baby nursery) are sparse. Barak et al. [1] reported an incidence of 0–8 spit ups in 58% of healthy newborn infants during the first 48 hours. In contrast, Hegar and co-authors [2] reported that 96% of newborn infants in their well-baby nursery did not spit up at all. Daily spit ups are common among healthy infants during the first month of life and were reported to occur in 50–73% of all newborn infants, although less frequently among those who were being breastfed [3,4].

The prevalence of breastfeeding among Ethiopian mothers is very high, reaching almost 100% during the first days of life [5]. Breastfeeding in this population is also longer than in other African populations, lasting up to 25–30 months [6]. Ethiopia is one of the poorest countries in the world and there is a high prevalence of malnutrition among mothers and infants in that country. The incidence of low birth weight (i.e., less than 2500 g) is about 11–22% of all newborn infants in Ethiopia [7-9]. Breastfeeding protects infants up to 6 months of age from starving and enables them to grow within the normal range [5]. Mothers in Ethiopia are recommended not to stop breastfeeding or provide replacement nourishment to their infants under the age of 6 months [10,11]. Indeed, the most common reason for stopping breastfeeding is suspected deficiency of breast milk [10,11].

Since 1984 about 100,000 people have emigrated from Ethiopia to Israel. Rubin et al. [12] found that the breastfeeding rate has declined somewhat among Ethiopian born mothers after immigration to Israel.

Since maternal nutrition during pregnancy and breastfeeding is essential for the infant's ability to thrive and develop, there is a tendency to over-supply food additives to mothers during this period [13]. A continuous state of starvation prevails in Ethiopia and this influences the traditions of the Ethiopian people, even though people of Ethiopian origin who live in Israel are no longer exposed to the threat of a lack of food.

Interviewing the nurses of Ethiopian origin who work in the well-baby nursery at Hillel Yaffe Medical Center revealed a unique tradition practiced by pregnant women in their community during the last months of pregnancy and after delivery. It appears that they supplement their diet with muck porridge, which is made of teff flour, derived from a species of lovegrass native to the northern Ethiopian highlands, to which they add water, minced flax, olive oil, honey and salt. According to tradition, the porridge assists in post-delivery recovery and improves the production of breast milk. The nurses in our unit observed that newborn infants of Ethiopian origin seemed to spit up more frequently than other infants. We designed this study to determine whether newborn infants born to mothers of Ethiopian origin spit up more often than other newborns and, if they did, whether the rate of spitting up has any clinical significance.

SUBJECTS AND METHODS

All files of infants born to mothers of Ethiopian origin over a 12 month period (January 2009 to December 2009) at the Hillel Yaffe Medical Center were retrospectively surveyed. The files of the newborns in the control group were randomly selected from all the files of newborn infants born to mothers of non-Ethiopian origin at the medical center during the same period, using a table of random numbers. Exclusion criteria were preterm delivery (less than 37 weeks of gestation), congenital defects, and transfer to the neonatal intensive care unit. The following data were retrieved and analyzed: duration of pregnancy (weeks), type of delivery, birth weight, nutrition type during hospitalization (breast milk, formula, or both), total number of spit ups that were reported by mothers or nurses during the entire hospitalization, any defecation difficulties, length of stay, minimal weight during hospital stay, and weight at discharge.

Since breastfeeding jaundice is a common cause of neonatal hyperbilirubinemia, we also retrieved the number of times bilirubin was measured and the maximal total bilirubin level.

The *t*-test for unpaired samples was used for parametric data comparison, and the chi-square test was used for non-parametric data comparison. A difference of < 0.05 was considered significant. Data were evaluated by SPSS software for Windows version 13.0 (SPSS Inc., Chicago, IL, USA). The study was approved by the institutional Ethics Committee on Human Research at the Hillel Yaffe Medical Center and registered in ClinicalTrials (ID NCT01185327).

RESULTS

Of the 4221 infants who were born in the Hillel Yaffe Medical Center during 2009, 354 were premature, 385 were transferred to the NICU, and 2 had congenital defects. This left 3663 newborns for inclusion into the current study: 55 of them were born to mothers of Ethiopian origin (study group) and 167 were chosen randomly to serve as the control group [Table 1]. The data that were retrieved from hospital records included maternal age, birth number, pregnancy length, delivery mode, Apgar score, birth weight and gender. Table 2 presents the data that were collected during the infant's stay in the well-baby nursery of the hospital.

The only significant difference between the two groups was an increase in the average number of spit ups (1.1 ± 1.6 for the study group vs. 0.7 ± 0.9 for the controls, $P = 0.045$). The difference was more obvious when only the infants who spit up in each group were analyzed (2.3 ± 1.7 Ethiopian newborns vs. 1.5 ± 0.9 controls, $P = 0.002$), although the percentage of spitting-up infants was similar within the two groups (45% vs. 47%, $P = 0.872$). Nutrition, weight loss, bilirubin levels,

NICU = neonatal intensive care unit

Table 1. Maternal and neonatal data

		Study group (n=55)	Control group (n=167)	P
Maternal age (yrs)		29.8 ± 4.6	28.6 ± 5.1	0.105
Birth number		2.6 ± 1.6	2.4 ± 1.5	0.524
Pregnancy length (wks)		39.3 ± 1.4	39.3 ± 1.3	0.896
Delivery type	Vaginal	67%	75%	0.122
	Cesarean	22%	20%	
Apgar score at 1 min		8.9 ± 1.0	9.1 ± 0.5	0.024
Apgar score at 5 min		9.9 ± 0.1	9.9 ± 0.2	0.335
Birth weight (g)		3233 ± 507	3268 ± 430	0.617
Gender	Male	56%	55%	0.876
	Female	44%	45%	

Values are mean ± SD

Table 2. Neonatal nutritional and laboratory data

		Study group (n=55)	Control group (n=167)	P
Nutrition type	Breast milk	9%	17%	0.343
	Formula	82%	77%	
	Both	9%	6%	
Minimal weight during hospitalization (g)		3035 ± 485	3068 ± 411	0.616
Maximal weight loss (g)		6.2 ± 1.9 %	6.1 ± 3.7 %	0.656
Discharge weight (g)		3050 ± 488	3090 ± 406	0.548
Weight loss at discharge (g)		5.7 ± 2.2 %	5.4 ± 3.2 %	0.823
Bilirubin level measurement rate		69%	77%	0.285
Bilirubin level (mg/dl)		6.9 ± 3.2	7.9 ± 2.8	0.051
Length of stay (days)		2.9 ± 1.2	2.6 ± 1.1	0.090
Average number of spit ups during hospitalization		1.1 ± 1.6	0.7 ± 0.9	0.045
Percentage of infants who spit up		45%	47%	0.872
Number of spit ups in spitting-up infants during hospitalization		2.3 ± 1.7	1.5 ± 0.9	0.002

Values are mean ± SD

number of bilirubin measurements and length of hospital stay were also similar.

Next, we looked for a possible explanation for the increased spitting-up rate. Within the control group we checked the parameters listed in Tables 1 and 2 and compared the infants who spit up with those who did not [Table 3]. The only statistically significant difference was the higher rate of bilirubin measurements performed in the spitting-up infants subgroup (83% of spitting-up infants vs. 69% of non-spitting-up infants, $P = 0.023$), although no difference was found in the mean bilirubin levels (7.9 ± 2.7 mg/dl for spitting-up infants vs. 8.0 ± 2.8 mg/dl for non-spitting-up infants, $P = 0.709$).

Table 3. Comparisons between the newborn infants who spit up and those who do not in the control group

		Spitting up newborns (n=89)	Non-spitting up newborns (n=78)	P
Maternal age (yrs)		28.4 ± 5.4	28.8 ± 4.8	0.699
Birth number		2.4 ± 1.5	2.5 ± 1.5	0.648
Pregnancy length (wks)		39.1 ± 1.4	39.5 ± 1.2	0.071
Delivery type	Vaginal	74%	77%	0.207
	Cesarean	19%	22%	
Apgar score at 1 min		9.1 ± 0.5	9.1 ± 0.5	0.810
Apgar score at 5 min		9.9 ± 0.2	9.6 ± 0.2	0.849
Birth weight (g)		3234 ± 395	3307 ± 467	0.271
Gender	Male	54%	55%	0.877
	Female	46%	45%	
Nutrition type	Breast milk	18%	15%	0.340
	Formula	73%	81%	
	Both	9%	4%	
Minimal weight during hospitalization (g)		3051 ± 371	3087 ± 454	0.579
Maximal weight loss (g)		5.5±3.7 %	5.8±2.1 %	0.057
Discharge weight (g)		3069 ± 372	3113 ± 442	0.488
Weight loss at discharge		5.5 ± 3.7 %	6.7 ± 3.7 %	0.081
Bilirubin level measurement rate		83%	69%	0.023
Maximal bilirubin level (mg/dl)		7.9 ± 2.7	8.0 ± 2.8	0.709
Length of stay (days)		2.6 ± 1.2	2.6 ± 1.0	0.951

Values are mean ± SD

DISCUSSION

The nurses in our well-baby nursery observed that newborns of mothers of Ethiopian origin seemed to spit up more often than the newborns of other mothers. One possible explanation for this difference could be that the Ethiopian mothers produce more breast milk than the other mothers, possibly due to the muck porridge supplement to their diet, and that the overfed babies spit up more. However, this explanation was ruled out by our finding that only 18% of the newborns in the study group were fed with breast milk. A second possible explanation was based on the Ethiopian tradition of providing an especially rich diet to pregnant Ethiopian women and their infants. It is plausible that those newborns were fed more formula than the others and that they spit up the excess. We also considered that there might be an anatomical difference at the lower esophageal sphincter that could be responsible for the increased number of regurgitations.

Although breastfeeding is the optimal food for infants, if mothers wish to feed their infants with formula, we cooperate with them. Most infants are hospitalized for 2 to 3 days after birth. Some mothers room-in, yet they usually report

their infants' spit ups immediately. One could argue that there might be a difference in the number of spit ups during hospitalization because not all infants were hospitalized at exactly the same time, but there was no statistically significant difference in length of stay between groups.

We found no statistically significant differences between the study and control groups during their hospital stay in the following variables: minimal weight, the proportion of maximal weight loss, the weight at the time of discharge, or the proportion of total weight loss until the infants went home. Although nurses measure bilirubin levels only when they suspect jaundice, there was no significant difference between the groups in the rate of bilirubin measurements or the maximal bilirubin levels. Also, there was no significant group difference in the length of hospital stay. These data support the explanation that the excess spitting up among the infants of Ethiopian origin is more likely to be a result of overfeeding than anything anatomical or pathological.

Within the control group we found no statistically significant difference between the newborns who spit up and those who did not. Although the former required more bilirubin level measurements than the latter, there was no difference in the maximal bilirubin levels between these two subgroups. These findings serve to support the position that spitting up in the absence of any sign of illness is probably a clinically non-relevant condition.

In conclusion, we found that newborns of mothers of Ethiopian origin do spit up slightly more than newborns of other mothers in our well-baby nursery. A prospective study with meticulous data collection on maternal diet prior to delivery in both arms and a good recording of spit ups and their timing may help explain these findings of ethnic differences. The Ethiopian origin mothers in the current study represent the first and second generation of relatively segregated Ethiopian communities in Israel. It can be expected that the traditional African attitudes towards unreliable food supply and the fear of starvation will dissipate with the acceptance of the reality that food is in plentiful supply in Israel. This should remove the differences in spitting up behaviors between the Ethiopian and newborns of other origins.

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Corresponding author:

Dr. E. Nadir

Dept. of Neonatology, Hillel Yaffe Medical Center, 38100 Hadera, Israel

Phone: (972-4) 630-4379

Fax: (972-4) 630-4399

email: erezn@hy.health.gov.il

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Capsule

Black mamba venom peptides target acid-sensing ion channels to abolish pain

Polypeptide toxins have played a central part in understanding physiological and physiopathological functions of ion channels. In the field of pain, they led to important advances in basic research and even to clinical applications. Acid-sensing ion channels (ASICs) are generally considered principal players in the pain pathway, including in humans. A snake toxin activating peripheral ASICs in nociceptive neurons has been recently shown to evoke pain. Diocho et al. show that a new class of three-finger peptides from another snake, the black mamba, is able to abolish pain through inhibition of ASICs expressed either in central or peripheral neurons. These peptides, called mambalgins, are not toxic in mice but show a potent analgesic effect upon central and

peripheral injection that can be as strong as morphine. This effect is, however, resistant to naloxone, and mambalgins cause much less tolerance than morphine and no respiratory distress. Pharmacological inhibition by mambalgins combined with the use of knockdown and knockout animals indicates that blockade of heteromeric channels made of ASIC1a and ASIC2a subunits in central neurons and of ASIC1b-containing channels in nociceptors is involved in the analgesic effect of mambalgins. These findings identify new potential therapeutic targets for pain and introduce natural peptides that block them to produce a potent analgesia.

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Eitan Israeli

Capsule

Melanomas resist T cell therapy through inflammation-induced reversible dedifferentiation

Adoptive cell transfer therapies (ACTs) with cytotoxic T cells that target melanocytic antigens can achieve remissions in patients with metastatic melanomas, but tumors frequently relapse. Hypotheses explaining the acquired resistance to ACTs include the selection of antigen-deficient tumor cell variants and the induction of T cell tolerance. However, the lack of appropriate experimental melanoma models has so far impeded clear insights into the underlying mechanisms. Landsberg et al. establish an effective ACT protocol in a genetically engineered mouse melanoma model that recapitulates tumor regression, remission and relapse as seen in patients. They report the unexpected observation that melanomas acquire ACT resistance through an inflammation-induced reversible loss of melanocytic antigens. In serial transplantation experiments, melanoma cells switch between a differentiated and a dedifferentiated phenotype in response to T cell-driven inflammatory stimuli. The authors identified the pro-inflammatory cytokine tumor

necrosis factor-alpha (TNF α) as a crucial factor that directly caused reversible dedifferentiation of mouse and human melanoma cells. Tumor cells exposed to TNF α were poorly recognized by T cells specific for melanocytic antigens, whereas recognition by T cells specific for non-melanocytic antigens was unaffected or even increased. Our results demonstrate that the phenotypic plasticity of melanoma cells in an inflammatory microenvironment contributes to tumor relapse after initially successful T cell immunotherapy. On the basis of our work, they propose that future ACT protocols should simultaneously target melanocytic and non-melanocytic antigens to ensure broad recognition of both differentiated and dedifferentiated melanoma cells, and include strategies to sustain T cell effector functions by blocking immune-inhibitory mechanisms in the tumor microenvironment.

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Eitan Israeli