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Exclusively Breastfeeding and Hypernatremic Dehydration

MK Çağlar, FŞ Altugan, I Özer

Dept. of Pediatrics, Faculty of Medicine, Gaziosmanpaşa University, Tokat, Turkey

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Abstract

There is no doubt that breast-feeding is the best and safest way of feeding infants. Physiological weight loss occurs in the first two or three days of life, and the achievement of birth weight is expected towards the end of the first week. Hypernatremic dehydration may occur in exclusively breast-fed infants if milk supply is low during these first few days. It is not because of the high sodium content in breast milk; it is because of insufficient lactation. That is, the main cause of hypernatremic dehydration is water deprivation. There are many causes for low milk intake. Since most causes are preventable or able to be improved, mothers, particularly first time mothers, should receive more reassurance and practical advice in the technique of breast-feeding. Before their discharge from the hospital, they should be educated about the associated features of unsuccessful breast-feeding, such as going to the breast infrequently or for short times, infrequent passage of urine and stool, jaundice, lethargy, irritability and fever. Late diagnosis may cause catastrophic outcomes, such as a variety of palsies, apnea, bradycardia, seizures, hypertension, disseminated intravascular coagulation, necrotising enterocolitis after establishing full oral feeds, amputation of an extremity secondary to arterial thrombus, multiple cerebral infarctions, intracranial hemorrhages, massive intra ventricular hemorrhage, multiple dural thromboses. If babies are weighed on the day of the Guthrie test, those in the early onset of a disease and those who could not achieve their birth weight can be easily identified. The latter should be closely followed.

Keywords: *Breast milk, Hypernatremia, Dehydration, Electrolyte imbalance, Breastfeeding*

Introduction

It is a reality that breast-feeding is increasing day by day, not only in the developing world, but also in developed countries (1, 2). There is no doubt that breast-feeding is the best and safest way of feeding infants (3).

In the past, hypernatremia occurred most often when artificial feeds of too high a sodium concentration were fed to babies (4). This was more common in infants who were fed powdered milk, especially if the mother added extra spoons of powder to less water in the mixture. Education of the community and the production of proprietary milks in liquid form have helped to solve this problem due to incorrect formula preparation.

Unfortunately, in the last two decades there are increasingly appearing reports about excess weight loss and hypernatremia in exclusively breast-fed infants (EBFI) (5-16). The infant's plasma sodium concentration is raised predominantly because of loss of extra-cellular water. Not uncommonly, this can result in catastrophic outcomes for EBFI. Both anecdotal reports (5-9) and recent retrospective (10-14) and prospective (15, 16) studies indicate an increase in the frequency and severity of outcomes of hypernatremia.

However, the question must be asked as to whether hypernatremia is really increasing or we are beginning to more clearly identify an old unrecognized condition? It is possible that hypernatremic dehydration (HD) has always been a problem in breast-fed infants and has been inadequately published in the medical literature. Therefore, we would like to bring

***Corresponding author:** GSM: 0 505 319 60 08, Fax: 0 356 212 80 31, E-mail: mkc@ttnet.net.tr

attention the condition of HD due to excessive weight loss in EBFI.

The Importance of Breast-Feeding and Human Milk Extensive research documents enormous advantages of breast-feeding and the use of human milk for infant feeding not just to infants, but also to mothers, families, and society, including health, nutritional, immunologic, developmental, psychological, social, economic, and environmental benefits.

Epidemiologic research shows that human milk and breast-feeding of infants provide advantages not only with regard to general health, growth, and development, but also significantly decrease the risk of contracting a large number of acute and chronic diseases. Research in many developed countries, among predominantly middle-class populations, provides strong evidence that human milk feeding decreases the incidence and/or severity of diarrhea (17, 18), lower respiratory infection (19, 20), otitis media (18, 21), bacteremia (22, 23), bacterial meningitis (22), urinary tract infection (24), and necrotizing enterocolitis (25). In addition, there are possible protective effects of feeding with human milk against sudden infant death syndrome (26), insulin-dependent diabetes mellitus (27), inflamatory bowel diseases (28), cancer (29) and allergic diseases (30). Here, the relation of breast-feeding to possible enhancement of cognitive development (31) should also be emphasized.

Physiological Weight Loss Weight loss in the first few days of the lives of newborns is a well-known clinical entity. Mean weight loss is approximately 6% of birth weight in healthy babies during the first three days (32-34). In a recent report (35), the median and 95th percentiles for weight loss have been defined as 6.6% and 11.8%, respectively, in EBFI. Weight loss up to an acceptable degree (<10%) is a physiological event unless a negative imbalance occurs between weight loss and milk production.

Most infants start to gain weight when they are 3 d old (34). A progressive decrease in body weight as a percentage of birth weight occurs, reaching its maximum decrease (5.7%± 1.7%) at 1 to 2 d, after which the infant starts to regain weight.

The recovery of birth weight in breast-fed and formula-fed infants has been assessed a median of 8.3 and 6.5 d, with the 95th percentile at 18.7 and 14.5 d (35). The time taken to regain birth weight correlates with both the degree and timing of initial weight loss for all groups.

The glomerular filtration rate of infants is low *in utero*, but increases rapidly in the few hours immediately after delivery as a result of increasing renal blood flow (36). A high urine output of 7-8 ml/kg/h is seen immediately in the first 6-8 h after birth. Then, a physiological oliguria (urine output less than 1 ml/kg/d) occurs, which lasts until the end of first day, because of a high elevation of vasopressin. Later, plasma vasopressin levels begin to decrease throughout the next 2 d (34) and atrial natriuretic peptide becomes more active (37). Therefore, all babies undergo a diuresis (4 ml/kg/h) after delivery that is characterized by a natriuresis (38), resulting in physiological weight loss.

Infants with body weight reduction exceeding 10% exhibit a further elevation of the serum sodium level and serum osmolality, and the plasma vasopressin level is two-fold higher compared with corresponding levels in infants with less weight reduction (34). When the reduction of body weight exceeds 10%, the newborn infant releases vasopressin in response to fluid hypertonicity. This state affects feeding behavior, perhaps as an expression of thirst. These infants show a need for a reduced interval between two subsequent feedings.

Lactogenesis At birth, a girl's breast consists of a nipple, a few small ductal elements and an underlying fat pad. With the onset of puberty and the secretion of estrogen, the gland initiates a complex developmental process (39). With the onset of menses, alveolar structures begin to sprout from the sides of the duct stimulated by progesterone and also probably prolactin. The mature breast resembles a flowering tree in

springtime with lobular alveolar complexes, called terminal duct lobular units (40). The breast reaches a stagnant stage marked by some increasing and decreasing of the terminal duct lobular units provided by the hormonal changes of the menstrual cycle (40-42). Breast development continues in pregnancy. Along with the rising of progesterone, prolactin and placental lactogen levels, the terminal duct lobular units show a remarkable expansion so that each lobule begins to look like a large bunch of grapes. During mid-pregnancy, secretory differentiation begins with a rise in mRNA for many milk proteins and enzymes important in milk production. Fat droplets enlarge in size in the mammary cells throughout pregnancy. This secretory differentiation switch is called stage I lactogenesis (43, 44). The gland remains stagnant due to high levels of circulating progesterone. However, it is preparing to initiate copious milk secretion around the time of the delivery of the child. When this hormone is released around the time of birth, stage II lactogenesis, or the onset of copious milk secretion, begins. As long as prolactin secretion is maintained and milk is removed from the gland, milk secretion is maintained. After weaning, the terminal duct lobular units involute and return to a mature stagnant state (45).

It has been estimated that infants get a volume of less than 100 mL/d of breast milk on the first postpartum day. On the second day, milk production begins to increase and levels off at an average of 500 mL/d at around the fourth day (46, 47). Milk composition also changes dramatically during this period, with a fall in the sodium and chloride concentrations and an increase in the lactose concentration that starts immediately after birth and are largely complete by 72 h postpartum (48).

A delay in the onset of lactogenesis has been reported as a result of poorly controlled diabetes (46, 49), stress during parturition (50) and obesity (51). High breast milk sodium concentrations on or before day 3 are observed in clinical situations in which the infant fails to latch on properly (52, 53). A normal drop in sodium is highly predictive of successful lactation, although a prolonged elevation of sodium signifies impaired lactogenesis with a high risk of failure (53). Formula feeding before lactogenesis is associated with a delay in the perception of lactogenesis (54). Furthermore, the time of first feeding and the breast-feeding frequency on day 2 postpartum have been positively correlated with milk volume on day 5 postpartum (55), suggesting that milk removal at early times after birth increases the milk secretion.

The problem of failed lactogenesis can be conceptualized as pre-glandular, glandular or post-glandular (53). An example of the pre-glandular type would be hormonal causes, such as retained placenta or lack of pituitary prolactin. Glandular causes might be surgical procedures, such as reduction mamoplasty or, possibly, insufficient mammary tissue. Post-glandular types would be any cause for ineffective or infrequent milk removal.

Hypernatremic Dehydration

Epidemiology Hypernatremia was previously thought to be unusual in breast-fed babies. Nevertheless, in the last two decades a great many reports associated with HD have appeared in the literature (5-16). The incidence of hypernatremia and dehydration in exclusively breast-fed newborn babies is quite difficult to determine. An increase in the number of breast-fed infants reported to have hypernatraemic dehydration might coincide with the fact that breast-feeding rates have reaching their highest levels ever in the last half century.

It has been reported (56) that over a period of 18 months, 13 of almost 9,000 infants born were admitted to the neonatal unit with HD at less than 3 weeks of age whose plasma sodium concentrations ranged from 150 to 173 mmol/l. All were breast-fed. Seven infants were readmitted having already been discharged home,

but six were diagnosed on the post-natal wards before discharge.

As part of a population-based regional review of all neo-natal re-admissions, the incidence of dehydration with hypernatraemia in EBFI was estimated to be 2.5 per 10,000 live births (11). Serum sodium at re-admission varied from 150 to 175 mmol/l. One infant had convulsions. In all cases, the sole explanation for hypernatremia was unsuccessful breast-feeding.

Five infants, whose the average presenting sodium was 186± 19 mmol/l, were admitted to a children's hospital in a 1.7 million population metropolitan area over a 5-month period with severe breast-feeding malnutrition and hypernatremia (10). Three of these five infants suffered significant complications. From 1990 to 1994, a statistically significant annual increase in the number of infants admitted with breast-feeding malnutrition and hypernatremia has been shown.

In a recent prospective study from Italy (15), the infants were weighed on a daily basis from birth until discharge to determine those babies whose weight loss was greater than 10%. Of 686 neonates over a six month period, 53 had a weight loss of greater than 10% and 19 had a plasma sodium concentration greater than 149 mmol/l (range 150–160 mmol/l).

According to a retrospective study of 51,383 newborns weighing 2000g or more, with a gestational age of 36 weeks or more born during 1995 and 1996,110 infants were re-hospitalized within 15 d of discharge because of either 12% or greater weight loss or a serum sodium level of 150 mmol/l or greater (10). The re-hospitalization rate for dehydration was in 2.1 per 1000 live births.

Causes The sodium content of breast milk at birth is high and declines rapidly over subsequent days. In 1949, it has been established that the mean (SD) sodium content of colostrum in the first five days is 22 (±12) mmol/l, and of transitional milk from day five to ten is 13 (±3) mmol/l, and of mature milk after 15 d is 7 (±2) mmol/l (57). It has been well documented that women who failed to establish good breast-feeding did not experience the normal physiological decrease in breast milk sodium concentration compared with those who experienced establishing a good milk flow (52). It is therefore not surprising that there have been attempts to establish that the cause of HD in breast-fed babies is unusually high sodium content of maternal breast milk.

However, the most common cause of excessive weight loss and hypernatremia must be inadequate breast milk intake, since it is not possible for a poorly-fed infant to get high sodium content from a low volume of breast milk. Hypernatremia occurs primarily because of water deprivation and secondarily because of an accumulation of sodium in an attempt to maintain a proper circulating volume. The infant becomes dehydrated while the kidneys are mature enough to retain sodium ions. Water loss occurs predominantly through the skin and from the lungs. The poor urine output and poor stool output of the infants also suggest that the problem is water deprivation.

A case with oesophageal atresia that lost 20% of her birth weight within 6 d and had a serum sodium concentration of 158 mmol/l supports this hypothesis since the infant was not able to receive any amount of breast milk into its stomach (12).

Other cases also support this hypothesis. For example, a breast-fed baby with serum sodium of 192 mmol/l had lost 36% of birth weight in 15 d (58). The mother’s breast milk had a sodium content of 31 mmol/l. It is tempting to conclude that the high sodium content of the milk was the cause of the problem, but the infant was feeding for only five minutes every four hours. It seems unlikely that such a limited intake of high sodium content milk was sufficient to raise the child’s plasma sodium concentration to such a degree. It is more probable that poor suckling by the infant caused the elevated milk sodium concentration. Today the evidence suggests that the most common cause of HD is low volume intake of breast milk.

How and why do the babies get insufficient volume of breast milk? Primary insufficient lactation is a rare condition. As the levels of gestational hormones rise, both structural and functional changes occur in the breasts during gestation, which can be observed by an increase in size of the breasts (39). In some cases, these kinds of changes do not happen, resulting in insufficient milk production. Unfortunately in some, glandular tissues are destroyed or obstructed by surgical procedures, such as reduction mamoplasty. Milk production of these breasts never reaches high enough levels to meet the amount that can sustain normal growth.

Inadequate milk production is usually due to secondary insufficient lactation, caused by poor milk removal from the breast. Anatomical breast problems with breast-feeding difficulties such as flat, inverted or big nipples are the major causes of huge engorged breasts, which also results in poor milk removal from the breast. In such a situation as this, the child may tire and fail to stimulate further lactogenesis. Preterm infants or those small for their gestational age are more prone to suckle less powerfully than appropriately sized gestational age term infants (39). Consequently, these mothers fail to feed their babies properly, although their breasts are capable of producing sufficient milk.

Previous reports have demonstrated the importance of early commencement of breast-feeding post delivery for successful lactation (59-61). Formula feeding before lactogenesis was associated with a delay in the perception of lactogenesis (54). Furthermore, the time of first feeding and the breast-feeding frequency on second postpartum day were positively correlated with milk volume on fifth postpartum day (55), suggesting that milk removal at early times after birth increases the efficiency of milk secretion.

Diagnosis Approximately 6% of birth weight loss occurs in healthy babies during the first three days (32-34). Most infants start to gain weight when they are 3 d old, along with an increase in milk production (34). A progressive decrease in body weight continues if milk production fails to meet daily needs for growth.

The clinical presentation of HD, therefore, is usually seen between 7-10 d, but depends on the rate of meeting the infant's daily water and electrolytes needs via breast-feeding. Parents may not think that the infant is ill since most of them are alert, hungry and look apparently well. Signs may be non-specific, including lethargy, irritability, fussiness, low amounts of stool and low urination. Occasionally an acute deterioration happens, which results in taking the baby to hospital. Convulsion, coma, and anuria are fortunately rare. Jaundice and pyrexia (62) are seen more frequently than healthy infants.

Signs of hypovolemia do not develop early in hypernatremic patients since the intra-cellular water moves towards extra-cellular space because of hyperosmolality in the serum. During acute isonatremic or hyponatremic dehydration, sunken eyes and depressed anterior fontanelle are reliable signs of total body water loss, but this is not so in HD and fullness of the anterior fontanelle may mask an underlying dehydration. Clinical examination of these infants at presentation is very variable.

For a long time there has been an accepted approach that healthy term infants may lose up to 10% of their birth weight. There is no doubt that infants can lose more than this amount and be entirely healthy, but it is also of concern that there is a report in the literature of a child with symptomatic hypernatremia who had apparently lost only 8% of birth weight (14).

Weighing all infants on the same day that the Guthrie test is carried out seems to be appropriate for diagnosing early dehydrated and hypernatremic newborns. The baby should be weighed while undressed. If the Guthrie screening test is carried out on day 5 or 7, some infants with very early onset disease and those who could not achieve the birth weight could be easily identified. It will be valuable to follow up the latter for the development of HD.

Morbidity and Mortality What we know about morbidity and mortality is sourced from acute conditions and there are no studies in the literature describing a long-term follow up of breast-fed infants who have suffered from HD.

A temporary right sided facial palsy case with 180 mmol/l (63); an apnea and bradycardia case with 174 mmol/l (64); a seizures, hypertension, and disseminated intravascular coagulation case with 206 mmol/l (64); a necrotising enterocolitis case with 176 mmol/l after establishing full oral feeds (65); an amputation of the left leg secondary to an iliac artery thrombus, decreased facial movement, electroencephalography slowing, multiple cerebral infarctions, and seizures (11); cerebral edema, intra-cranial hemorrhages, hemorrhagic infarcts, and thromboses identified in babies by using magnetic resonance imaging (66); a seizures, massive intra-ventricular hemorrhage, and multiple dural thromboses case with 191 mmol/l (67); a multiple area intra-ventricular, peri-ventricular, and cortical hemorrhage case with 180 mmol/l (66) have been reported related to HD. A few of these cases died (67).

Treatment Seizures are the most common complication of treatment (68, 69). Therefore, re-hydration should be accomplished very slowly in order to prevent cerebral edema, which can occur due to severe osmotic changes. Oral re-hydration is first choice for treatment since most of the hypernatremic babies can be fed via an oral route. It is important to express breast milk for re-lactation even though it has high content of sodium. It is well known that sodium concentration in breast milk decreases with a sustained increase in milk production (53). In one study (70), an adoptive mother and six mothers who could not initiate or maintain lactation ten to 150 d after delivery for a variety of reasons attempted re-lactation. The adoptive mother and one other failed to provide a significant amount of milk. Shorter post-partum intervals and less post-partum breast involution correlated with the likelihood of successful re-lactation and the rapidity of the onset of lactation. It has been shown in other reports that patients with HD, severe wasting and pre-renal failure experienced excellent catch-up growth during follow-up, while exclusive breast-feeding was maintained (8,71). These reports point out that early initiation to express breast milk could provide a baby to nurse exclusively or partially by breast milk thereafter. If an infant appears well, then slow re-hydration can be carried out using expressed breast milk or proprietary milk or a combination of both.

If the child looks like unwell, re-hydration with 100 ml/kg/d should be done intravenously (56). There are no enough publications on recommended regimens for intravenous re-hydration of such a child. In one report (72), infants re-hydrated at a rate of 150 ml/kg/d was more likely to develop convulsions and peripheral edema than those infants whose fluid intake was restricted to 100 ml/kg/d. Serum sodium concentration should be decreased not more than 10-15 mmol/l/d. Daily body weight increment is preferred less than 5%.

20 ml/kg colloid or 0.9% saline is infused over half an hour to be resuscitated initially if there is a collapsed situation. Then re-hydration may be started intravenously using a fluid of 0.9% NaCl in 5-10% dextrose at 100 ml/kg/d provided that the plasma glucose concentration remains greater than 2.5 mmol/l (56). Plasma urea and electrolyte concentrations should be measured 6 hourly. It has been stated that it is not uncommon to see plasma urea concentrations quickly fall in the first 24 h, but little change is seen in the plasma sodium concentration. After 24 h, re-hydration is recommended at the same rate, but using 0.45% saline in 5–10% dextrose. The patient should be put on breast or bottle- or both- with cautious increases in volume rates in the subsequent days whenever the health condition becomes suitable for oral intake.

Discussion

It is obvious that hypernatremia is not the result of high sodium content of breast milk. Rather,

high sodium content is the result of insufficient milk production (52, 53). It has been well documented that women who failed to establish good breast-feeding do not experience a normal physiological decrease in breast milk sodium concentration compared with those who experienced in establishing a good milk flow (53). On the contrary, if sodium concentration in insufficient amount of milk did not increase, it would be most probably expected that those infants fed with a low volume of milk could not keep on their extra-cellular volume for a long time when compared to babies fed with low volume milk that contained a normal sodium concentration. Renal sodium handling in newborn babies is generally not as mature as in older children (36). They still lose more sodium in the event of less sodium intake when compared to older children. High sodium concentration in insufficient milk production is probably aimed at meeting daily sodium loss for babies fed with a lesser volume of milk, in order to keep on extra-cellular volume in normal.

Less than expected milk volume intake is the main cause of HD. There are many causes for less milk intake, such as less milk production (obesity, diabetes mellitus, stress during labor), breast-feeding technique errors, and problems related to both mother (flat or inverted or huge nipple, abuse) and child (depressed, cleft lip and palate, small chin, pre-maturity, small for gestational age). Most of these are preventable or improvable problems. Therefore, mothers, particularly first time mothers, should receive more reassurance and practical advice in the technique of breast-feeding. In the hospital, those who wish to breast-feed should receive intensive support and such mothers should be trained how to correctly position a child, appropriately attach it to the breast and observe that suckling is successful.

Associated features of unsuccessfully breast-feeding include the infant going to the breast infrequently or for short times, infrequent passage of urine (<6 times/d) and stool (<4 times/d), delayed passage of yellow seedy stools (after 4 d), jaundice, lethargy, irritability and fever. Verbal discussions could give the mother the knowledge that she can recognize the infant's needs.

Unfortunately, because of economic reasons when the mean length of stay of newborns in hospital was gradually reduced (11, 73, 74) re-admission rates rose, and the risk of re-admission for dehydration, jaundice and feeding problems, and poor weight gain was particularly high. HD is mostly seen in term infants. On the other hand, pre-term and small for gestational age infants who have poor suckling capabilities are also at particular risk. Therefore, special attention should also be given to them.

Secondary reasons for insufficient milk supply are more likely to be found in the dehydrated infants' mothers. Therefore, these mothers could be identified ante-natally (for the nipple conditions) and post-natally (for the breast engorgement), and additional support for breast-feeding should be provided.

Previous reports have demonstrated the importance of an early commencement of breast-feeding post delivery for successful lactation (59-61). Prompt initiation of breast-feeding after delivery and prompt intervention, if problems occur with breast-feeding (in particular poor breast attachment, breast engorgement, delayed breast milk "coming in" and nipple problems), will help promote successful breast-feeding. Therefore, mothers should be helped and supported to breast-feed their infants as soon as possible after delivery. Unnecessary system delays, particularly after caesarean section, should be minimized.

It has been reported that environmental factors could also be a factor in the formation of dehydration because of increased insensible water loss (5). Environmental factors in the home, such as extra heater usage, could exacerbate dehydration increasing insensible water loss.

Fever (13, 62) and hypernatremia (5, 8, 11-13, 15, 62) are often found in neonates with excessive weight loss. In low-risk full-term infants, fever with no other symptoms during the first days of life is primarily related to dehydration

and breast-feeding, and the infection is the least common explanation (62).

Conclusion

Cases with HD are essentially likely to be an iatrogenic problem, due to an inadequate understanding of the normal physiological process of breast-feeding by health professionals and those mothers who relied on their care. These babies are described as being exclusively breast-fed: it is likely that, although put to the breast, they never actually effectively breast-fed and this was not recognized by their mothers or by the staff. It is also possible that a few mothers may have insufficient milk for any number of reasons. Therefore, the problem does not lie with breast-feeding, but with a lack of effective feeding. This needs to be assessed very early by skilled personnel, taught and shown to the new parents who should continue to assess the course of breast-feeding over the next few days. As stated in a recent report (35), the median time of maximum weight loss and recovery have been determined as being 2.7 and 8.3 days, respectively. Therefore, it is expected that the recovery of weight loss must be accomplished by the end of an infant's first week. Weighing all infants on the same day that the Guthrie test is carried out seems to be an appropriate method of diagnosing early dehydrated and hypernatremic newborns. If the Guthrie screening test is carried out on day 5 or 7, some infants with very early onset of the disease and those who could not achieve the birth weight will be easily identified. It would also be valuable to follow up the latter for the development of HD.

References

1. Ryan AS, Wenjun Z, Acosta A (2002). Breastfeeding continues to increase into the new millennium. *Pediatrics,* 110: 1103- 9.
2. Tappin DM, Mackenzie JM, Brown AJ, Girdwood RW, Britten J, Broadfoot M, Warren J (2001). Breastfeeding rates are increasing in Scotland. *Health Bull (Edinb),* 59:102-13.
3. American Academy of Pediatrics (1997). Breastfeeding and the use of human milk. Work Group on Breastfeeding. *Pediatrics,* 100: 1035-39.
4. Chambers TL, Steel AE (1975). Concentrated milk feeds and their relation to hypernatraemic dehydration in infants. *Arch Dis Child,* 50: 610-15.
5. Sofer S, Ben-Ezer D, Dagan R (1993). Early severe dehydration in young breast - fed newborn infants. *Isr J Med Sci,* 29: 85-9.
6. Smith RG (1998). Severe hypernatremic dehydration in a newborn infant. *Pediatr Child Health,* 3: 413-15.
7. Pascale JA, Brittian L, Lenfestey CC, Jarrett-Pulliam C (1996). Breastfeeding, dehydration, and shorter maternity stays. *Neonatal Netw*, 15: 37-43.
8. Paul AC, Ranjini K, Muthulakshmi RA, Kirubakaran C (2000). Malnutrition and hypernatremia in breastfed babies. *Ann Trop Paediatr*, 20: 179-83.
9. Harding D, Cairns P, Gupta S, Cowan F (2001). Hypernatremia: why bother weighing breast fed babies? *Arch Dis Child Fetal Neonatal Ed*, 85: F145.
10. Escobar GJ, Gonzales VM, Armstrong MA, Folck BF, Xiong B, Newman T (2002). Rehospitalization for neonatal dehydration: a nested case-control study. *Arch Pediatr Adolesc Med*, 156:155-61.
11. Cooper WO, Atherton HD, Kahana M, Kotagal UR (1995). Increased incidence of severe breastfeeding malnutrition and hypernatremia in a metropolitan area. *Pediatrics*, 96: 957-60.
12. Oddie S, Richmond S, Coulthard M (2001). Hypernatraemic dehydration and breast feeding: a population study. *Arch Dis Child*, 85: 318-20.
13. Zachariassen G, Juvonen P (2002). Neonatal dehydration (dehydration fever) in

newborn infants. *Ugeskr Laeger*, 164: 4930-34.
14. Livingstone VH, Willis CE, Abdel-Wareth LO, Thiessen P, Lockitch G (2000). Neonatal hypernatremic dehydration associated with breast-feeding malnutrition: a retrospective survey. *CMAJ*, 162: 647-52.
15. Manganaro R, Mamí C, Marrone T, Marseglia L (2001). Incidence of dehydration and hypernatremia in exclusively breastfed infants. *J Pediatr*, 139: 673-5.
16. Dewey KG, Nommsen-Rivers LA, Heinig MJ, Cohen RJ (2003). Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. *Pediatrics*, 112: 607-19.
17. Beaudry M, Dufour R, Marcoux S (1995). Relation between infant feeding and infections during the first six months of life. *J Pediatr*, 126: 191-7.
18. Kovar MG, Serdula MK, Marks JS (1984). Review of the epidemiologic evidence for an association between infant feeding and infant health. *Pediatrics*, 74: S615-S38.
19. Wright AI, Holberg CJ, Martinez F (1989). Breast feeding and lower respiratory tract illness in the first year of life. *Br Med J*, 299: 945-9.
20. Wright AL, Holberg CJ, Taussig L (1995). Relationship of infant feeding to recurrent wheezing at age 6 years. *Arch Pediatr Adolesc Med*, 149: 758-63.
21. Aniansson G, Alm B, Andersson B (1994). A prospective cohort study on breastfeeding and otitis media in Swedish infants. Pediatr *Infect Dis J*, 13:183-8.
22. Cochi SL, Fleming DW, Hightower AW (1986). Primary invasive Haemophilus influenzae type b disease: a population-based assessment of risk factors. *J Pediatr*, 108: 887-96.
23. Takala AK, Eskola J, Palmgren J (1989). Risk factors of invasive Haemophilus influenzae type b disease among children in Finland. *J Pediatr*, 115:694-701.
24. Pisacane A, Graziano L, Mazzarella G (1992). Breast-feeding and urinary tract infection. *J Pediatr*, 120:87-9.
25. Covert RF, Barman N, Domanico R (1995). Prior enteral nutrition with human milk protects against intestinal perforation in infants who develop necrotizing enterocolitis. *Pediatr Res*, 37: 305A.
26. Ford RPK, Taylor BJ, Mitchell EA (1993). Breastfeeding and the risk of sudden infant death syndrome. *Int J Epidemiol*, 22: 885-90.
27. Gerstein HC (1994). Cow's milk exposure and type I diabetes mellitus. A critical overview of the clinical literature. *Diabetes Care*, 17: 13-9.
28. Rigas A, Rigas B, Glassman M (1993). Breast-feeding and maternal smoking in the etiology of Crohn's disease and ulcerative colitis in childhood. *Ann Epidemiol*, 3: 387-92.
29. Shu X-O, Clemens J, Zheng W (1995). Infant breastfeeding and the risk of childhood lymphoma and leukaemia. *Int J Epidemiol*, 24:27-32.
30. Saarinen UM, Kajosaari M (1995). Breastfeeding as prophylaxis against atopic disease: prospective follow-up study until 17 years old. *Lancet*, 346:1065-69.
31. Morrow-Tlucak M, Haude RH, Ernhart CB (1988). Breastfeeding and cognitive development in the first 2 years of life. *Soc Sci Med*, 26: 635-9.
32. Maisels MJ, Gifford K (1983). Breast feeding, weight loss and jaundice. *J Pediatr*, 102: 117-8.
33. Maisels MJ, Gifford K, Antle CE, Leib GR (1988). Jaundice in the healthy newborn infant: a new approach to an old problem. *Pediatrics*, 81:505-11.
34. Marchini G, Stock S (1997). Thirst and vasopressin secretion counteract dehydration in newborn infants. *J Pediatr*, 130: 736-9.

35. Macdonald PD, Ross SRM, Grant L, Young D (2003). Neonatal weight loss in breast and formula fed infants. *Arch Dis Child Fetal Neonatal Ed*, 88: F472-6.
36. Robillard JE, Weismann DN, Herin P (1981). Glomerular filtration rate in prenatal lambs. *Pediatr Res*, 15:1248–55.
37. Modi N, Betremieux P, Midgley J, Hartnoll G (2000). Postnatal weight loss and contraction of the extracellular compartment is triggered by atrial natriuretic peptide. *Early Hum Dev*, 59: 201-8.
38. Modi N, Hutton JL (1990). The influence of postnatal respiratory adaptation on sodium handling in preterm neonates. *Early Hum Dev*, 21:11–20.
39. Neville MC, Morton J (2001). Physiology and endocrine changes underlying human lactogenesis II. *J Nutr*, 131: 3005S-8S.
40. Bartow SA (1998). Use of the autopsy to study ontogeny and expression of the estrogen receptor gene in human breast. *J Mammary Gland Biol Neoplasia*, 3:37-48.
41. Anderson E, Clarke R, Howell A (1998). Estrogen responsiveness and control of normal human breast proliferation. *J Mammary Gland Biol Neoplasia*, 3:23-35.
42. Andres AC, Strange R (1999). Apoptosis in the estrous and menstrual cycles.*J Mammary Gland Biol Neoplasia*, 4:221-8.
43. Hartmann PE (1973). Changes in the composition and yield of the mammary secretion of cows during the initiation of lactation. *J Endocrinol*, 59:231-47.
44. Neville MC, Morton JA, Umemora S (2001). Lactogenesis: the transition between pregnancy and lactation. *Pediatr Clin North Am*, 48:35-52.
45. Furth PA (1999). Mammary gland involution and apoptosis of mammary epithelial cells. *J Mammary Gland Biol Neoplasia*, 4:123-7.
46. Neville MC, Keller RP, Seacat J, Lutes V, Neifert M, Casey CE, Allen JC, Archer P (1988). Studies in human lactation: milk volumes in lactating women during the onset of lactation and full lactation. *Am J Clin Nutr*, 48: 1375-86.
47. Saint L, Smith M, Hartmann PE (1984). The yield and nutrient content of colostrum and milk of women from giving birth to one month postpartum. *Br J Nutr*, 52: 87-95.
48. Neville MC, Allen JC, Archer P, Seacat J, Casey C, Lutes V, Rasbach J, Neifert M (1991). Studies in human lactation: milk volume and nutrient composition during weaning and lactogenesis. *Am J Clin Nutr*, 54: 81-93.
49. Hartmann P, Cregan M (2001). Lactogenesis and the effects of insulin-dependent diabetes mellitus and prematurity. *J Nutr*, 131: 3016S-20S.
50. Grajeda R, Perez-Escamilla R (2002).Stress during labor and delivery is associated with delayed onset of lactation among urban Guatemalan women. *J Nutr*, 132: 3055-60.
51. Rasmussen KM, Hilson JA, Kjolhede CL (2001). Obesity may impair lactogenesis II. *J Nutr*, 131: 3009S-11S.
52. Aperia A, Broberger O, Herin P, Zetterstroem R (1979). Salt content in human breast milk during the first three weeks after delivery. *Acta Paediatr Scand*, 68: 441-2.
53. Morton JA (1994). The clinical usefulness of breast milk sodium in the assessment of lactogenesis. *Pediatrics*, 93:802-6.
54. Chapman DJ, Perez-Escamilla R (1999). Identification of risk factors for delayed onset of lactation. *J Am Diet Assoc*, 99: 450- 54.
55. Chen DC, Nommsen-Rivers L, Dewey KG, Lonnerdal B (1998). Stress during labor and delivery and early lactation performance. *Am J Clin Nutr*, 68: 335-44.

56. Laing IA, Wong CM (2002). Hypernatraemia in the first few days: is the incidence rising? *Arch Dis Child Fetal Neonatal Ed*, 87: F158-62.
57. Macy IG (1949). Composition of human colostrum and milk. *Am J Dis Child*, 78: 589-603.
58. Anand SK, Sandborg C, Robinson RG, Lieberman E (1980). Neonatal hypernatremia associated with elevated sodium concentration of breast milk. *J Pediatr*, 96: 66–8.
59. Salariya E, Easton P, Cater J (1978). Duration of breastfeeding after early initiation and frequent feeding. *Lancet*, 2: 1141-43.
60. Chapman DJ, Pérez-Escamilla R (2000). Maternal perception of the onset of lactation is a valid, public health indicator of lactogenesis Stage II. *J Nutr*, 130: 2972-80.
61. Sozmen M (1992). Effects of early suckling of caesarean-born babies on lactation. *Bio Neonate*, 62: 67-8.
62. Maayan-Metzger A, Mazkereth R, Kuint J (2003). Fever in healthy asymptomatic newborns during the first days of life. *Arch Dis Child Fetal Neonatal Ed*, 88: F312-4.
63. Arboit JM, Gildengers E (1980). Breastfeeding and hypernatremia. *J Pediatr*, 97: 335-36.
64. Rowland TW, Zori RT, Lafleur WR, Reiter EO (1982). Malnutrition and hypernatremic dehydration in breast-fed infants. *JAMA*, 247: 1016-17.
65. Clarke AJ, Sibert JR (1985). Hypernatraemic dehydration and necrotizing enterocolitis. *Postgrad Med J*, 61: 65–6.
66. Korkmaz A, Yigit S, Firat M, Oran O (2000). Cranial MRI in neonatal hypernatraemic dehydration. *Pediatr Radiol*, 30: 323-25.
67. Kaplan JA, Siegler RW, Schmunk GA (1998). Fatal hypernatremic dehydration in exclusively breast-fed newborn infants due to maternal lactation failure. *Am J Forensic Med Pathol*, 19: 19-22.
68. Roddey OF Jr, Martin ES, Swetenburg RL (1981). Critical weight loss and malnutrition in breast-fed infants. *Am J Dis Child*, 135: 597–99.
69. Ernst JA, Wynn RJ, Schreiner RL (1981). Starvation with hypernatremic dehydration in two breast-fed infants. *J Am Diet Assoc*, 79: 126–30.
70. Bose CL, D'Ercole AJ, Lester AG, Hunter RS, Barrett JR (1981). Relactation by mothers of sick and premature infants. *Pediatrics*, 67: 565-69.
71. Thullen JD (1988). Management of hypernatremic dehydration due to insufficient lactation. *Clin Pediatr*, 27:370–72.
72. Banister A, Matin-Siddiqi SA, Hatcher GW (1975). Treatment of hypernatraemic dehydration in infancy. *Arch Dis Child*, 50: 179–86.
73. Liu S, Wen SW, McMillan D, Trouton K, Fowler D, McCourt C (2000). Increased neonatal readmission rate associated with decreased length of hospital stay at birth in Canada. *Can J Public Health*, 91: 46–50.
74. Pascale JA, Brittian L, Lenfestey CC, Jarrett-Pulliam C (1996). Breastfeeding, dehydration, and shorter maternity stays. *Neonatal Netw*, 15: 37-43.