BREASTFEEDING MEDICINE
Volume 9, Number 2, 2014

DOI: 10.1089/bfm.2013.0084

Taste of Milk from Inflamed Breasts of Breastfeeding Mothers with Mastitis Evaluated Using a Taste Sensor

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Abstract

Background: The refusal of infants to suckle from a breast that is inflamed with mastitis suggests that the taste of the milk has changed. However, the taste of milk from a breast with mastitis has never been empirically determined. The present study compares the taste of milk from breastfeeding mothers with or without mastitis and identifies specific changes in the taste of milk from mothers with mastitis.

Subjects and Methods: The intensity of four basic tastes (sourness, saltiness, bitterness, and *umami*) of breastmilk from 24 healthy mothers at 3–5 days and at 2–3, 4–5, and 8–10 weeks postpartum and from 14 mothers with mastitis was determined objectively using a taste sensor. The intensity of each basic taste and the concentrations of main taste substances in milk were compared between the inflamed breasts and the normal breasts of control mothers or the contralateral asymptomatic breast of mothers with unilateral mastitis.

Results: The transition from colostrum to mature milk was accompanied by changes in the taste of the milk, such as decreased saltiness and *umami* and increased bitterness and sourness. *Umami* and saltiness increased in milk from inflamed breasts. Contents of sodium, glutamate, and guanosine monophosphate increased in milk from inflamed breasts.

Conclusions: Tastes that were specifically associated with inflamed breasts appeared to include an increase in *umami* and saltiness, which might have resulted from an increased content in factors associated with *umami* and sodium.

Introduction

Mastitis, which frequently develops in breastfeeding women during the first 3 months postpartum,[1,2] is usually conservatively managed, and continued breastfeeding is recommended to prevent breast engorgement.[3,4] However, infants sometimes suddenly refuse to suckle from a breast with mastitis.[5]

Why infants avoid suckling from a breast with mastitis has not been defined, but it might be associated with the taste of the milk. Mastitis alters the biochemical composition of milk because of increased breast permeability[6,7] and reduced milk synthesis.[7] Increased sodium and chloride[7–11] and decreased lactose[7,10,11] concentrations are specific changes in milk composition that occur during mastitis. Thus, milk might become saltier during mastitis as a result of increased sodium content.[5] However, descriptions from mothers with mastitis who have tasted their own breastmilk do not agree with respect to increases in saltiness, bitterness, or sourness, and the taste of milk during mastitis has never been empirically investigated.

A major technical hurdle to identifying specific tastes of milk during mastitis has been objective evaluation. Taste sensations are produced when chemicals in foodstuffs react with membrane receptors on taste buds, and at least five basic tastes, including sourness, saltiness, sweetness, bitterness, and *umami* are associated with taste sensation.[12] However, because an abundance of factors is associated with the taste of foodstuffs, detection of specific factors is almost impossible. However, a taste-sensing system based on a unique concept has been developed.[13–16] The sensor does not detect factors associated with taste in foodstuffs, but rather estimates the intensity of each basic taste by integrating electric signals through lipid/polymer membranes, which mimic the membrane receptors of human taste buds.[13] The sensor has been applied to several clinical studies, including evaluations of the palatability of bottled nutritive drinks[14] and of bitterness for the development of new drugs.[15,16] Therefore,

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specific milk tastes during mastitis could be quantified and identified.

The present study objectively evaluates the taste of milk during early lactation using a test sensor to identify changes during mastitis. We also estimated correlations between some factors associated with taste and the basic taste of milk, which might explain why infants sometimes refuse to suckle from a breast that is inflamed because of mastitis.

Materials and Methods

Participants and sample collections

We determined reference ranges of each basic taste in milk during early lactation in mothers who delivered normally at a private prenatal clinic (controls). The eligibility criteria included the full-term delivery of a singleton without obstetric, medical, or psychiatric complications. Mothers who consumed alcohol and/or smoked were excluded. Thus, 12 primiparous and 12 multiparous mothers with a mean age of 29.8 (range, 23–36) years participated in this study. The mothers donated milk from both breasts with the help of a midwife at a clinic on 3–5 days postpartum and, thereafter, collected milk at home between 2 to 3, 4 to 5, and 8 to 10 weeks postpartum. The mothers reported any breast symptoms that were present at each sampling time. Foremilk (> 10 mL) samples were separately collected from each breast and immediately frozen at the hospital or at home for subsequent transportation on dry ice to our laboratory, where they were stored at −80°C.

Breastmilk samples were similarly collected during the same study period from mothers who attended the clinic for treatment of lactation mastitis within 3 months postpartum. Mastitis was diagnosed as local breast redness, warmth, swelling, and pain observed by midwives at the clinic. Eight primiparous and six multiparous mothers (mean age, 28.7 years; range, 22–35 years) with mastitis donated milk for this study. The mean interval from delivery to attending the clinic due to mastitis was 6.8 (range, 1–12) weeks. The symptoms were unilateral and bilateral in 11 and three mothers, respectively. At the time of attending the clinic, all mothers had elevated body temperatures, including three with temperatures >38.0°C. The infants of 11 (78.6%) mothers with mastitis (eight mothers with unilateral mastitis and three mothers with bilateral mastitis) refused to suckle. Two infants of mothers with unilateral mastitis refused to suckle the inflamed breast only, and the other infants refused to suckle both breasts.

The Ethics Committee of Akita University Graduate School of Medicine approved the study protocol. All of the women who received written and verbal explanations about the nature of the study and ethical considerations provided written, informed consent to participate. The mothers received a few packs of disposable diapers as a token of appreciation for their participation.

Evaluation of milk taste by a taste sensor

The intensity of each basic taste from the milk samples was evaluated using a taste sensing system model SA402B test sensor (Intelligent Sensor Technology, Inc., Atsugi, Japan). We evaluated the intensity of four of the five basic tastes because the sensor could not evaluate sweetness during the study period. The principles of the sensor have been described in detail.[13–16] In brief, transducers of the sensor comprise several lipid/polymer membranes. Immersing the transducers in sample solutions alters the electrical potential of each membrane. Appropriate membranes detect patterns in potential changes generated by chemical substances that produce different tastes, whereas similar patterns are generated by chemicals producing the same taste. Patterns in potential changes obtained from samples are then converted to information about taste quality and intensity using Rev5 version 1.0.0.4 software (Intelligent Sensor Technology Inc.). The performance of the test sensing system has been validated based on ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) guideline Q2.[17]

Because the intensity of the basic tastes is expressed as relative values, we used a single brand of commercial bovine milk (Megamilk; Nippon Milk Community Co. Ltd., Tokyo, Japan) as the standard. Thus, negative values for basic taste mean that the intensity of the basic taste was weaker for human than for bovine milk.

The bovine standard was whole milk, in which the contents of fat and nonfat solids were within the ranges of 3.7–4.0% and 8.5–8.8%, respectively. All samples were assayed in triplicate, and inter- and intra-assay coefficients of variability in each taste measurement were < 15% and < 10%, respectively.

Biochemical analysis of factors associated with taste

The major factors, called taste substances, that produce each basic taste have been identified.[12] Saltiness is primarily produced by sodium ions, but other alkali metal ions also taste weakly salty. Sourness is produced by acids containing protons (H^+).[18] Sweetness in breastmilk is usually produced by sugars and other substances, but mostly by lactose. *Umami* is most frequently produced by free amino acids, including glutamate, and/or 5′-ribonucleotides such as 5′-guanosine monophosphate (5′-GMP) and 5′-inosine monophosphate,[19] but 5′-inosine monophosphate is apparently undetectable in human milk.[20] Many substances, including quinine sulfate, urea, and some metal ions, are associated with bitterness, but major contributors to bitterness in breastmilk have not been identified.

We determined the concentration of several main taste substances in groups of milk samples. The substances measured were glutamate and 5′-GMP for *umami*, sodium for saltiness, calcium and urea for bitterness, lactose for sweetness, and pH for sourness. We also determined concentrations of ammonia, which might not affect taste but has a very powerful and distinctive odor.

The concentrations of free amino acids, including glutamate, urea, and ammonia were determined using an amino acid analyzer (model L-8800; Hitachi, Tokyo) according to the manufacturer's instructions. The analyzer separates amino acids using ion-exchange chromatography and then detects them using a post-column ninhydrin reaction detection system. Nucleotides or sugars in milk were separated and quantified using an ion-pair, high-performance liquid chromatography system (Nihon Waters K.K., Tokyo) as described.[21] The content of sodium or calcium in milk was determined using an inductively coupled plasma emission spectrophotometer (model iCAP 6300; Thermo Fisher

Scientific K.K., Yokohama, Japan), according to the manufacturer's instructions. The pH of milk samples was determined using a pH meter with a glass electrode (model D-53; HORIBA Instruments, Kyoto, Japan). The pH of samples was immediately measured after thawing to avoid the influence of air.

Statistics

Results are expressed as mean ± SD values. The distribution of intensity of each basic taste of the milk samples was assumed to be normal according to the Kolmogorov–Smirnov test; thus we performed parametric tests. Overall differences in the means of each basic taste at different stages of lactation were assessed using the one-way repeated-measures analysis of variance. Intra-individual variability in each basic taste was assessed using interclass correlation coefficients (ICCs) between milk samples from normal breasts at 4–5 and at 8–10 weeks postpartum using a two-way mixed model.[22] Differences in the intensity of each basic taste and the main taste substances between milk from the inflamed breasts of mothers with mastitis and from the normal breasts of control mothers were examined using an analysis of covariance, adjusted for lactation stage (week postpartum), primiparous or not, age, and body mass index. Correlations between the concentrations of the main taste substances and the intensity of each basic taste in mature milk samples were evaluated using partial correlation analysis controlled for characteristics of the mothers. Differences in the intensity of basic tastes and concentrations of main taste substances in milk between the inflamed and contralateral asymptomatic breasts of mothers with unilateral mastitis were examined using a paired Student's t test. All data with two-sided P values were statistically analyzed using the software Statistical Package for the Biosciences (Nankodo, Tokyo). A value of $p < 0.05$ was considered to indicate statistical significance.

Results

Table 1 shows the intensity of each basic taste of milk from normal breasts at various lactation stages. Two of the 24 mothers developed mastitis after donating milk postpartum, but samples from these mothers were included in this analysis because their symptoms were relieved by the next sampling period. Because the colinearity of the intensity of basic tastes in milk from both breasts of the same mother was very high (correlation coefficients, 0.70–0.96; $p < 0.001$), only data obtained from left breasts are presented. The intensity of saltiness and *umami* significantly decreased, whereas that of sourness and bitterness significantly increased as the lactation stage progressed. Compared with values at 3–5 days postpartum (colostrum), saltiness, bitterness, and *umami* significantly changed at 2–3 weeks postpartum (transitional milk), whereas sourness significantly changed at 8–10 weeks postpartum (mature milk). The calculated ICCs for each basic taste were 0.976, 0.966, 0.630, and 0.978 for sourness, saltiness, bitterness, and *umami*, respectively, at both 4–5 and 8–10 weeks postpartum.

Mean intensities of basic tastes and mean concentrations of main taste substances were compared between milk samples from inflamed and normal breasts (Table 2). This comparison comprised mature milk samples from mothers with mastitis (samples within 4 weeks postpartum were excluded, and 11 samples remained for analysis) and from healthy mothers (either 4–5 or 8–10 weeks postpartum, $n = 24$). The intensity of *umami* significantly increased in milk from inflamed breasts. Furthermore, the concentrations of taste substances in milk including glutamate, 5′-GMP, sodium, calcium, urea, and ammonia significantly differed between the inflamed and normal breasts.

Table 3 shows correlations between the intensity of each basic taste and the concentration of main taste substances in samples of mature milk determined as described above. Significant correlations were identified between sourness and lactose, between saltiness and lactose or calcium, and between bitterness and calcium (negative), urea, or pH (negative).

Table 4 compares the intensity of each basic taste and the concentrations of main taste substances in milk between the inflamed and contralateral asymptomatic breast of mothers with unilateral mastitis ($n = 11$). The intensity of *umami* and saltiness was significantly increased in milk from inflamed breasts. Concentrations of glutamate, 5′-GMP, and sodium significantly increased, whereas calcium concentrations significantly decreased, in milk from the inflamed breasts. The direction of changes in these substances appeared consistent with the taste changes that occurred in the inflamed breasts.

Discussion

This study showed that transitions in breastmilk from colostrum to mature milk were accompanied by changes in the

Table 1. Intensity of Basic Taste of Milk from Normal Breasts at Different Stages of Lactation ($n = 24$)

	Postpartum				
	4–5 days	*2–3 weeks*	*4–5 weeks*	*8–10 weeks*	F (p)[a]
Sourness	2.36 ± 3.02[b]	2.84 ± 3.15	3.11 ± 3.50	3.31 ± 3.47	4.05 (0.005)
Saltiness	−6.44 ± 2.53[c]	−7.71 ± 2.36	−8.07 ± 2.48	−8.09 ± 2.44	14.41 (0.000)
Bitterness	1.22 ± 1.28[c]	3.17 ± 1.59	3.39 ± 1.49	2.32 ± 1.25[e]	19.84 (0.000)
Umami	−0.47 ± 1.28[d]	−0.79 ± 1.720	−0.99 ± 1.35	−0.87 ± 1.44	10.25 (0.000)

Data are mean ± SD values.
[a]By one-way repeated-measures analysis of variance. Group differences were evaluated by Bonferroni's multiple comparison test.
[b]$p < 0.05$ versus 8–10 weeks.
[c]$p < 0.01$ versus 2–3, 4–5, and 8–10 weeks.
[d]$p < 0.05$ versus 2–3 weeks; $p < 0.01$ versus 4–5 and 8–10 weeks.
[e]$p < 0.05$ versus 2–3 weeks; $p < 0.01$ versus 4–5 weeks.

Table 2. Comparisons of Mean Intensities of Basic Tastes and Mean Concentrations of Main Taste Substances in Milk from Breasts Inflamed Because of Mastitis and Normal Breasts of Control Mothers

	Inflamed breasts (n = *11*)	*Normal control breasts* (n = *24*)	p[a]
Intensity of basic tastes			
Sourness	4.19 ± 1.87	3.26 ± 3.27	0.424
Saltiness	−7.93 ± 1.29	−8.09 ± 2.44	0.784
Bitterness	2.17 ± 1.01	2.32 ± 1.25	0.676
Umami	0.42 ± 0.87	−0.87 ± 1.44	0.012[b]
Concentrations of main taste substances			
Lactose (mmol/L)	140 ± 19	152 ± 20	0.268
Glutamate (μmol/L)	23.7 ± 11.2	16.1 ± 4.5	0.012[b]
5′-GMP (μmol/L)	10.1 ± 5.0	5.1 ± 5.4	0.025[b]
Sodium (μmol/L)	11.5 ± 8.5	5.8 ± 2.6	0.007[c]
Calcium (μmol/L)	6.2 ± 1.0	7.5 ± 1.0	0.012[b]
Urea (μmol/L)	59.0 ± 17.8	43.6 ± 12.1	0.010[c]
Ammonia (μmol/L)	4.3 ± 2.9	1.8 ± 1.0	0.001[c]
pH	6.69 ± 0.21	6.56 ± 0.23	0.146

Data are mean ± SD values.
[a]Analysis of covariance, adjusted for stage of lactation (weeks postpartum), primiparous or not, age, and body mass index.
[b]$p < 0.05$, [c]$p < 0.01$.
5′-GMP, 5′-guanosine monophosphate.

Table 4. Comparisons of Intensity of Basic Tastes and Concentrations of Main Taste Substances in Milk from Inflamed and Contralateral Asymptomatic Breasts of Mothers with Unilateral Mastitis ($n = 11$)

	Inflamed breasts	*Asymptomatic breasts*	p[a]
Intensity of basic tastes			
Sourness	3.98 ± 1.88	4.43 ± 2.43	0.071
Saltiness	−7.84 ± 1.18	−8.34 ± 1.07	0.016[b]
Bitterness	2.43 ± 0.84	2.21 ± 0.99	0.451
Umami	0.45 ± 0.88	0.26 ± 0.82	0.002[c]
Main taste substances			
Lactose (mmol/L)	140 ± 19	149 ± 22	0.124
Glutamate (μmol/L)	27.1 ± 6.7	21.9 ± 9.1	0.025[b]
5′-GMP (μmol/L)	9.6 ± 5.6	5.3 ± 5.1	0.040[b]
Sodium (mmol/L)	10.7 ± 6.3	6.1 ± 2.9	0.010[b]
Calcium (mmol/L)	6.5 ± 1.3	7.0 ± 1.3	0.038[b]
Urea (μmol/L)	66.6 ± 20.3	63.9 ± 15.5	0.388
Ammonia (μmol/L)	4.9 ± 2.2	3.8 ± 1.7	0.251
pH	6.63 ± 0.20	6.61 ± 0.21	0.298

Data are mean ± SD values.
[a]By paired Student's *t* test.
[b]$p < 0.05$, [c]$p < 0.01$.
5′-GMP, 5′-guanosine monophosphate.

taste of milk, in which saltiness and *umami* decreased and bitterness and sourness increased. These changes in basic tastes are thought to result from changes in composition as colostrum progresses to mature milk.[23,24] Furthermore, the taste of milk is somewhat affected by flavors derived from individual dietary preferences before lactation[25] and might be influenced by demographic factors because parity and the body mass index of breastfeeding mothers reportedly influenced the composition of milk.[26] However, although the intensity of each basic taste varied widely among breastfeeding mothers, day-to-day variations in sourness, saltiness, and *umami* were considerably smaller in milk from one mother, compared with inter-mother variations, according to the remarkably high ICCs of successive values for these tastes in each mother (> 0.95). Bitterness was the exception, as it had a relatively low ICC and might have a relatively changeable nature. These findings indicated that the taste of breastmilk from breastfeeding mothers is unique and distinctive.

Table 3. Correlations Between Concentrations of Main Taste Substances and Intensity of Each Basic Taste in Samples of Mature Milk ($n = 35$)

	Sourness	*Saltiness*	*Bitterness*	Umami
Lactose	0.556[b]	0.376[a]	−0.338	0.032
Glutamate	0.024	0.276	−0.04	0.157
5′-GMP	0.269	0.029	−0.017	0.076
Sodium	0.121	−0.205	−0.152	−0.108
Calcium	0.065	0.518[b]	−0.391[a]	0.127
Urea	0.258	0.044	0.364[a]	−0.275
pH	0.08	−0.046	−0.476[b]	−0.041

Values are partial correlation coefficients controlled for mastitis, stage of lactation (weeks postpartum), primiparous or not, age, and body mass index.
[a]$p < 0.05$, [b]$p < 0.01$.
5′-GMP, 5′-guanosine monophosphate.

We initially compared the taste of milk between the normal breasts of control mothers and the inflamed breasts of mothers with mastitis to identify specific milk tastes in the latter. We found that *umami* was increased in milk from inflamed breasts. We then compared the taste of milk between the inflamed and contralateral asymptomatic breasts of mothers with unilateral mastitis. Although the asymptomatic breasts of mothers with unilateral mastitis might not be completely healthy because of the presence of subclinical inflammation,[27,28] their inclusion helped to control for the influences of confounding factors. Saltiness and *umami* increased in the inflammatory breasts. Therefore, the insignificant finding of saltiness in the former comparison was probably due to a relatively wide distribution of the intensity of saltiness in milk among breastfeeding women. Therefore, we concluded that the intensity of both *umami* and saltiness significantly increased in milk from the inflamed breasts of mothers with mastitis.

The concentrations of several taste substances were altered in milk from inflamed breasts and were probably linked to reduced secretory activities of mammary cells and increased breast tissue permeability during mastitis.[6,7,29] The concentration of sodium in milk is about $1/10^{th}$ of that in serum, and thus increased breast tissue permeability elicits the transudation of serum sodium into the milk spaces.[6] Reduced secretory activities result in a decline in lactose synthesis, and lactose is the osmotically dominant component in human milk. Thus, a decline in lactose content would cause a lower volume of milk, which might lead to other substances such as glutamate, 5′-GMP, urea, and ammonia becoming more concentrated in the milk space. In contrast, calcium concentrations significantly decreased in milk from inflamed breasts. The concentration of total calcium is much higher in milk than that in serum, and if the amount of diffusible calcium is also higher in milk, it is likely to pass through the blood–milk barrier. Furthermore, as most calcium in milk is associated with milk proteins, including casein, reduced synthesis of milk protein due to mastitis could explain the decreased calcium content.[29] Loss of lactose is one major change that reportedly occurs in the composition of milk during mastitis.[7,10,11] However, we only detected a trend for a decline in the lactose content of milk from inflamed breasts. A decline in lactose synthesis will result in a lower volume of milk rather than a lower concentration of lactose in the milk. Furthermore, a relatively wide interindividual distribution and a small reduction rate in lactose ($<10\%$ of total content) due to mastitis[10,11] might mask a significant difference.

Increases in the factors that cause *umami* (glutamate and 5′-GMP) or sodium content were probably associated with an increase in *umami* or saltiness of milk from inflamed breasts, respectively. However, such correlations were not found in mature milk samples. Furthermore, several significant relationships somewhat differed from our expectations. For example, saltiness correlated with lactose and calcium and not with sodium content. The intensity of saltiness in milk might principally depend on the sodium content but might also be somewhat affected by other substances, including lactose. However, the concentration and distribution of lactose were much higher and wider than those of sodium, and thus the influence of lactose on saltiness was easily detected in milk samples from different mothers.

Human infants are thought to have very keen taste abilities,[30] and they are probably very sensitive to subtle changes in the taste of breastmilk. Infants could be aware of an increase in saltiness in milk, but this might not be the main reason why they refuse to suckle because they have a relatively wide tolerance of saltiness.[31] Taste changes in milk might be more complicated during mastitis because both *umami* and saltiness seem to increase. *Umami* is basically an agreeable taste, and adding glutamate to bovine milk formula for feeding infants increases the degree of satisfaction.[32] However, *umami* is agreeable only within a relatively narrow concentration range,[33] and infants might dislike milk with an intensity of *umami* taste that exceeds their tolerance range. However, an unusual taste of milk during mastitis might not be the main reason for refusing the breast because infants often refuse to suckle both the inflamed and asymptomatic breasts of mothers with unilateral mastitis. One infant was reported to readily accept expressed breastmilk after refusing the breast of a mother with a herpes zoster infection in the T4 dermatome, and the authors speculated that a change in odor or skin texture of the breasts might have been the main cause.[34] We suggest that the ammonia content significantly increases in breasts with inflammation due to mastitis, and infants might be sensitive to a change in the odor of milk during mastitis. The perception of an ammonia odor in milk seems a reasonable explanation for refusing to suckle.

Finally, several limitations of the present study warrant discussion. First, because of the wide interindividual variations in most variables, the sample size was too small to reach accurate conclusions. Second, we could not determine overall milk tastes because we could not evaluate sweetness. Third, we only predicted specific milk tastes during mastitis. A prospective study is needed to confirm that the taste of milk is altered by mastitis. Fourth, our discussion was based on the hypothesis that the intensity of each basic taste evaluated by the sensor is absolutely correct. However, that the measured intensities of each basic taste actually correspond with the actual taste sensation experienced by infants is not absolutely guaranteed, and thus our discussions can only be speculative.

To our knowledge, this is the first study to objectively compare the taste of milk from breastfeeding mothers with or without mastitis. The results suggested an increase in *umami* and saltiness in milk from inflamed breasts, which might have resulted from an increased content in factors associated with *umami* and sodium. These specific taste changes might be associated with infants refusing to suckle from breasts with mastitis. However, a prospective study should validate our conclusions and include an evaluation of sweetness. A better understanding of specific tastes of milk from breastfeeding mothers with mastitis might help to predict infant suckling behavior and thus provide a benefit for such women.

Acknowledgments

This study was supported by Grant-in-Aid for Scientific Research number 23792633 from the Japan Society for the Promotion of Science. The authors thank Ito Toshihiko at the Department of Biological Resource Sciences, Akita Prefectural University, for measuring concentrations of free amino acids and nucleotides in milk.

Disclosure Statement

No competing financial interests exist.

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