Acta Clin Croat **2026**, vol. **65**, no. **1**: 128-138

Concentrations of Free Sphingosine and Sphinganine in the Breast Milk of Healthy Women and Women with Type 1 Diabetes

Slavica Potočki[1], Ana Mesić[2], Zrinka Šakić[3], Armin Atić[4], Ana Kulić[5] and Nikolina Bašić Jukić[4]

[1] Department of Chemistry and Biochemistry, School of Medicine, University of Zagreb, Zagreb, Croatia;
[2] Polyclinic Artemeda, Zagreb, Croatia;
[3] Vuk Vrhovac University Clinic for Diabetes, Endocrinology and Metabolic Diseases, Merkur University Hospital, Zagreb, Croatia;
[4] Department of Nephrology, Arterial Hypertension, Dialysis and Transplantation, University Hospital Centre Zagreb, Zagreb, Croatia;
[5] Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia

CORRESPONDENCE TO Slavica Potočki, Department of Chemistry and Biochemistry, School of Medicine, University of Zagreb, Šalata 2, 10000 Zagreb, Croatia
spotocki@mef.hr

RECEIVED October 21, 2024
ACCEPTED November 27, 2024

DOI 10.20471/acc.2026.65.01.12

SUMMARY

Sphingoid bases form the backbone of sphingolipids and there are indications that the sphingolipid metabolism is altered in diseases.

The purpose of this study was to determine the concentrations of free sphingosine (SO) and sphinganine (SA) in the breast milk (BM) of healthy women and women with type 1 diabetes (T1D) during lactation. After sphingolipid extraction, base hydrolysis was performed to obtain free SO and SA, which were then analyzed by means of high-performance liquid chromatography.

In the BM of healthy women, SO and SA concentrations decrease during lactation. Concentrations of SO and SA in BM from women with T1D decline until day 7 and rise starting on day 14 of lactation. Both healthy women and women with T1D showed significant differences in SO and SA concentrations by days of lactation. By comparing the concentrations of free SO in the BM of healthy women and women with T1D, a statistically significant difference was observed on the 5th and 14th day of lactation. A statistically significant difference was observed by comparing the concentrations of free SA in the BM of healthy women and women with T1D on days 14 and 42.

Our study is the first to provide insight into sphingoid base concentration in BM.

KEYWORDS

Sphingosine; *Sphinganine*; *Breast milk*; *Type 1 diabetes*

Introduction

Sphingolipids are one of the main classes of lipids present in all mammalian cells[1]. They are complex molecules, which contain the backbone of sphingoid bases. Sphingoid bases are a class of long-chain amino alcohols that are *N*-acylated with several fatty acids to form ceramide; a central molecule of the sphingolipid metabolism. Both *de novo* and salvage pathways are capable of synthesizing ceramide[2,3] (Figure 1). It is synthesized *de novo* from serine and palmitoyl-CoA in the endoplasmic reticulum. Sphinganine (SA) is the key intermediate in this pathway. Ceramide is essential for the production of complex sphingolipids, including glycosphingolipids and sphingomyelin. At the lumenal leaflet of the Golgi apparatus, phosphorylcholine is transferred from phosphatidylcholine to ceramide in order to produce sphingomyelin. Ceramide glycosylation, which occurs on the cytosolic leaflet of the Golgi apparatus, results in the structurally most complex group of sphingolipids, known as glycosphingolipids. Ceramide-1-phosphate (C1P) is the product of ceramide phosphorylation. After sugar residues of glycosphingolipids have been cut away by lysosomal glycosidases, the remaining fatty acids and sphingoid bases are degraded or recycled by the salvage pathway. Sphingomyelin is degraded by the enzyme sphingomyelinase in a reversible reaction to produce ceramide and phosphocholine. Ceramidase is an enzyme that catalyzes the conversion of ceramide to sphingosine (SO). SO can be further phosphorylated to form sphingosine-1-phosphate (S1P) with the enzymes sphingosine kinase 1 and 2. Because of their extensive bioactivity and ubiquity, dysregulation and

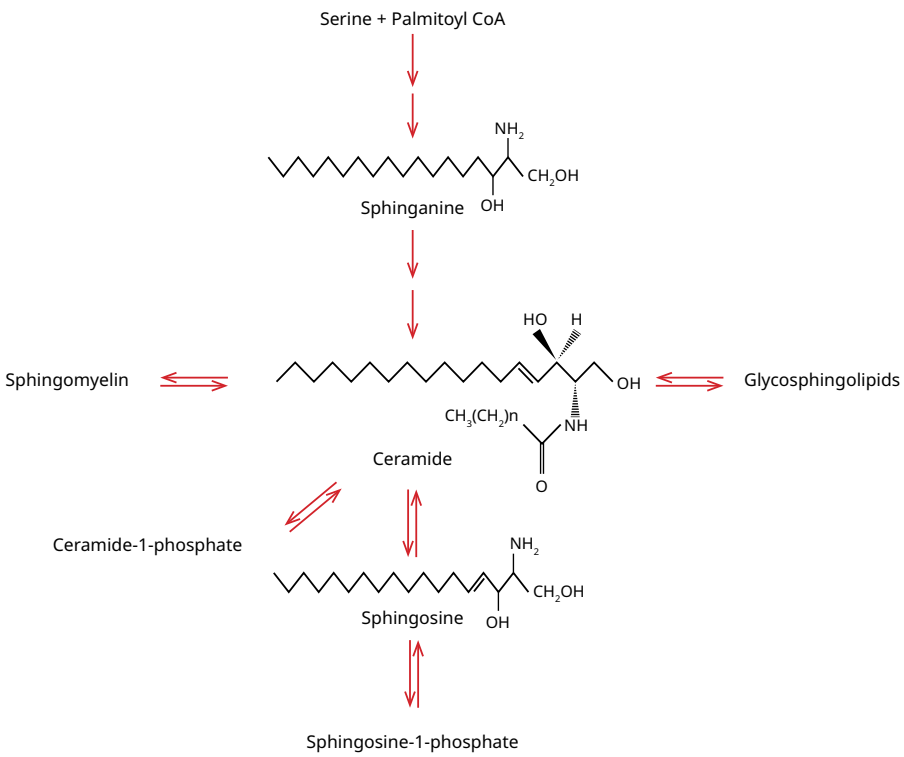

FIGURE 1 Synthesis and degradation pathways of sphingolipids

abnormalities in the sphingolipid metabolism have been suggested as possible causes of a number of pathological diseases, including diabetes mellitus and its related complications. Over the last twenty years, research has shown the significant functions played by a number of sphingolipids, particularly ceramide, SO, S1P and C1P[4,5]. These molecules are thought to modulate physiological and pathophysiological processes, including inflammatory responses, apoptosis and cell growth regulation. Thus, these bioactive substances have significance for both the development of disease and normal cell function. It has been suggested that sphingolipids may serve as biomarkers for a number of diseases, including heart failure, asthma, type 1 diabetes (T1D) and coronary artery disease[6,7]. According to evidence, sphingolipids may play a part in glucose homeostasis and metabolic diseases[8].

Because they are bioactive compounds, sphingoid bases have been an increasingly important subject of biomedical research in recent years. The 18-carbon dihydroxy amino alkene SO and its saturated precursor SA are the most basic and prevalent sphingoid bases found in mammals. In addition to being a component of sphingolipid composition, a small fraction is also present as free long-chain bases and is therefore associated with a number of biological activities[9]. By interacting with biological targets and preventing platelet aggregation and growth factor action, SO — a bioactive lipid — functions as a second messenger in cell membranes[10-12]. It has been connected to several diseases. Additionally, the prevention of disease and/or its associated consequences may benefit from SO. Sphingoid bases have been shown to have a protective antibacterial effect against infection[13]. According to mounting data, type 2 diabetes (T2D) is characterized by a dysregulated sphingolipid metabolism and substantial alterations in the serum metabolome prior to T1D development[14-16]. Diabetes mellitus is a chronic condition in which there is an insufficient or absent supply of the hormone insulin, resulting in increased blood glucose levels. There are several known types of diabetes. Insulin-dependent diabetes mellitus, or T1D, is primarily seen in young individuals. It is characterized by the pancreas producing very little or no insulin as a result of β-cells being destroyed, usually by an autoimmune process[17]. An abnormally elevated blood glucose level is the end result. Such people need insulin replacement therapy for the rest of their lives. T2D, also known as non-insulin-dependent diabetes mellitus, is the most prevalent type of the disease. Usually, it begins with insulin resistance, a condition in which cells do not react to insulin secretion appropriately. Numerous investigations have indicated that different sphingolipids may control the secretory function of β-cells[18]. Thus far, descriptions of the stimulatory effects of extracellular S1P and the inhibitory effects of ceramide on insulin secretion have been provided[19,20]. Diabetes has been linked to a number of short- and long-term consequences for both mothers and newborns, and it has been established that this disease can delay the start of lactogenesis II and change the content of human milk[21,22].

It is known that metabolic diseases can affect lipid content and quality, as well as milk synthesis. Consequently, alterations in the amounts of insulin in plasma can influence the kind and amount of lipids in milk. This would imply that the hormonal state could also have an impact on SO and SA concentrations in milk.

Thus, the purpose of this study was to determine the concentrations of free SO and SA in breast milk (BM) produced during lactation by both healthy and T1D mothers.

Methods

Patients

BM samples were collected from 15 women with T1D aged 29 ± 5.4 years on the 3rd, 5th, 7th, 14th and 42nd day of lactation. Ten healthy women (aged 31 ± 4.8 years) provided the control BM samples, which were collected on the same days of lactation as the cohort samples. Milk samples were collected at University Hospital Centre Zagreb, Croatia. After discharge from hospital, the mothers collected BM at home. The study was approved by the Ethics Committee of the School of Medicine, University of Zagreb and the Ethics Committee of University Hospital Centre Zagreb. The study was conducted in accordance with the Declaration of Helsinki.

Chemicals

The extraction solvents (CH_3OH and $CHCl_3$) and the solvents used for liquid chromatography (CH_3OH and H_2O) were both supplied by Riedel de Hähn AG, Seelze, Germany. Standards of sphingoid bases (C18 D-sphingosine and C18-dL-erythro-dihydrosphingosine), ortho-phthaldialdehyde (OPA) and 2-mercaptoethanol were purchased from Sigma Aldrich Chemie GmbH (Steinheim, Germany). All others chemicals were purchased from Kemika (Zagreb, Croatia).

Sphingolipid extraction

Sphingolipids were extracted from BM and then subjected to base hydrolysis according to the method used by Riley et al.[23] with minor modifications[24]. The aim of base hydrolysis is the splitting of acylglycerolipids and the hydrolysis of lysosphingolipids (free sphingoid bases modified on the SA or SO C1 atom hydroxyl group) in order to release free SA and SO. The phospholipids (phosphatidylethanolamine and phosphatidylserine) that may react with the OPA reagent for sphingoid base derivation are effectively removed by the base treatment. This process does not release sphingoid bases from complex sphingolipids.

Quantification of sphingoid bases

The sphingoid bases were analyzed using high-performance liquid chromatography (HPLC). HPLC was performed using the following Perkin–Elmer (Norwalk, CT, USA) equipment: isocratic pump, fluorescence detector, interface, column oven, auto sampler and software for chromatography (Turbochrom4.1.2). The analytical column (Radial-Pak™ cartridge, Nova-Pak™ C_{18}, 10x0.8 cm, 4 mm), column module and holder with pre-column filter (Guard-Pak assembly, Nova-Pak C_{18}, 4 mm) were purchased from the Waters Corporation (Milford, MS, USA).

Before the sphingoid bases were applied to the column, the OPA reagent was used to derivatize them by reaction via their amino group. Sample preparation and liquid chromatography conditions were carried out according to Ribar et al[24].

Statistics

Statistical analysis was performed using SAS© Ver. 9.4 (Cary, NC). All continuous variables were expressed as mean and standard deviations (SD) (as shown in Figure 2 and Figure 3). The following tests were used: independent sample t-test and paired t-test. All *P* values below 0.05 were considered statistically significant.

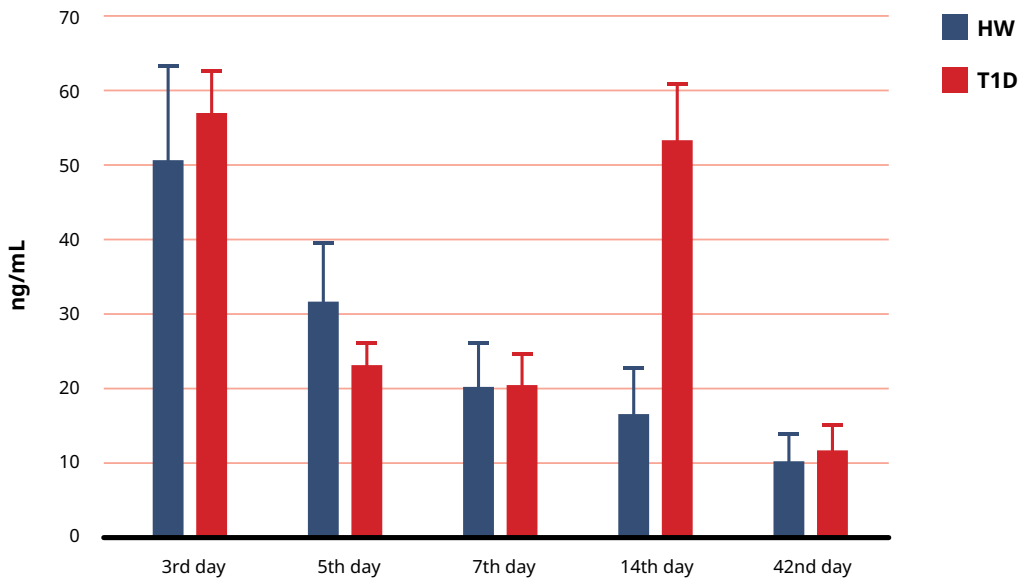

FIGURE 2 Concentrations of free sphingosine (SO) in the breast milk of healthy women (HW) and women with type 1 diabetes (T1D)
HW = healthy women; T1D = type 1 diabetes

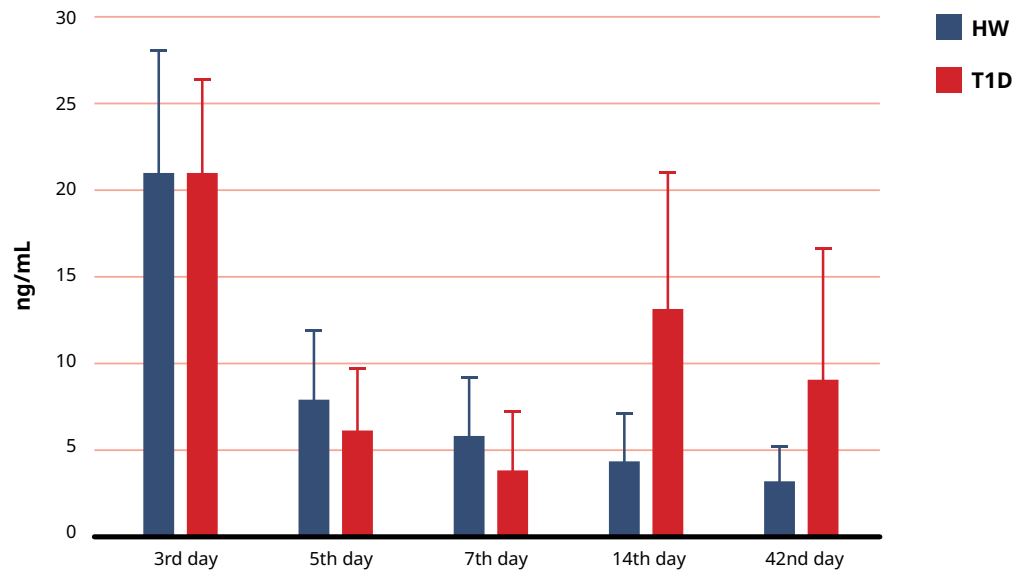

FIGURE 3 Concentrations of free sphinganine (SA) in the breast milk of healthy women (HW) and women with type 1 diabetes (T1D)
HW = healthy women; T1D = type 1 diabetes

Results

In this study, the concentrations of free SO and SA in the BM of healthy women and women diagnosed with T1D were determined during lactation (3rd, 5th, 7th, 14th and 42nd day). All participants were lactating mothers who vaginally delivered singletons. Mothers who suffered from acute mastitis or febrile illness, as well as those who underwent medical or plastic breast surgery, were excluded from the study. The mean age of healthy women was 31 ± 4.8 years and of T1D women 29 ± 5.4.

Sphingolipid extraction was used to treat BM samples from 10 healthy women and 15 women with T1D. After the extraction of sphingolipids from BM samples, base hydrolysis was performed to obtain free SO and SA. The concentrations of free SA and SO were determined by means of HPLC.

In the milk samples of healthy women, the concentrations of free SO and SA were the highest on the 3rd day of lactation and the lowest on the 42nd day. These results are shown in Figure 2 and Figure 3 as mean and standard deviations (SD). Statistically significant differences were found for free SO and SA concentrations when comparing by day within the control group. These results are shown in Table 1. Until now, the concentrations of free sphingoid bases in BM have not been discussed in the literature.

The concentration of free SO in the milk of T1D women was the highest on the 3rd day and the lowest on the 42nd day of lactation (Figure 2). The concentration of free SA in the milk of T1D women was the highest on the 3rd day as well, but the lowest concentration was registered on the 7th day of lactation (Figure 3). Statistically significant differences were found for free SO and SA concentrations when comparing by day within the T1D group (Table 2). The literature has not yet addressed the concentrations of free sphingoid bases in the BM of women with T1D.

TABLE 1 Statistically significant differences in the concentrations of free sphingosine (SO) and sphinganine (SA) by days of lactation

HEALTHY WOMEN	
SO	**SA**
3rd vs 5th	3rd vs 5th
3rd vs 7th	3rd vs 7th
3rd vs 14th	3rd vs 14th
3rd vs 42nd	3rd vs 42nd
5th vs 7th	5th vs 7th
5th vs 14th	5th vs 14th
5th vs 42nd	5th vs 42nd
14th vs 42nd	7th vs 14th

SO = sphingosine; SA = sphinganine

TABLE 2 Statistically significant differences in the concentrations of free sphingosine (SO) and sphinganine (SA) by days of lactation

TYPE 1 DIABETES	
SO	**SA**
3rd vs 5th	3rd vs 5th
3rd vs 7th	3rd vs 7th
3rd vs 14th	3rd vs 14th
3rd vs 42nd	3rd vs 42nd
5th vs 7th	5th vs 14th
5th vs 14th	7th vs 14th
5th vs 42nd	14th vs 42nd
7th vs 14th	
7th vs 42nd	

SO = sphingosine; SA = sphinganine

By comparing the concentrations of free SO in the BM of healthy women and women with T1D, a statistically significant difference was observed on days 5 and 14 of lactation ($P = 0.0112$; $P < 0.0001$) (Figure 2). As for SA, a statistically significant difference was observed in the concentration of free SA in the BM of healthy women and women with T1D on days 14 and 42 ($P = 0.0010$; $P = 0.0142$) (Figure 3).

Discussion

Breast milk (BM) is a special kind of food that is thought to include biological components that have both immediate and long-term health benefits. It is a biologically active fluid that is species-specific and differs greatly between women. Throughout lactation, BM continually modifies to meet the developing infant's physiological needs. In addition to providing the newborn with essential nutrients for their growth and development, BM also plays a role in protecting against infections and inflammation. It also plays a role in immune maturation, early microbial colonization and organ development[25]. According to certain theories, there are suggestions that early postnatal dietary signals could influence metabolic developmental pathways and cause long-lasting modifications to the vulnerability to metabolic diseases[26]. Research findings indicate that the consumption of BM may offer a preventive effect against T2D and obesity in later life[27]. According to some studies, immunological and nutritional alterations in the composition of BM might result from chronic diseases like diabetes[28]. BM has been the focus of several studies, but the impact of chronic diseases on its nutritional content has not yet been thoroughly understood and the findings vary, which is why it continues to be the subject of many studies. The amount and quality of BM can be directly influenced by inadequate levels of insulin in diabetes[21,22]. According to evidence, sphingolipids may be involved in glucose homeostasis and metabolic diseases[8]. Several studies have shown that various sphingolipids can affect the secretory ability of β-cells[18]. It is well known that ceramide and its analogs suppress the production and release of insulin[19]. Extracellular S1P, in contrast to ceramide, is a strong inducer of insulin production[29].

When an individual progresses from obesity to prediabetes and then into overt diabetes, both T1D and T2D, there is a progressive rise in glucose levels, and lipid and sphingolipid abnormalities that worsen inflammation and oxidative stress. It is widely acknowledged that sphingolipids play a role in the development of inflammatory and autoimmune diseases. Though the exact processes underlying this are still unknown, several researchers have recently proposed that dietary fats and changes in lipid metabolism, particularly sphingolipid metabolism, may be responsible for initiating or promoting the autoimmune onset of T1D[30]. Adipose sphingolipid accumulation was observed in diabetic patients compared to non-diabetic persons with a comparable body mass index[31]. Although lipids in BM function similarly to hormones in promoting the growth and development of infants, little research has been done on how the composition of lipids in BM varies, particularly when T1D is involved.

Dritsakou et al.[32] identified higher levels of fat in the milk of diabetic women.

Opposite to that finding, Jackson et al.[33] and Morceli et al.[22] observed that the amount of fat in the BM of diabetic women was lower compared to the control group. Despite their results' unanimity, the two studies used different methods to evaluate the nutritional composition of BM. Fujimori et al.[34] and Dritsakou et al.[32] found higher levels of fat and energy in the BM of overweight women.

Hormones are one of the several factors known to affect sphingolipid metabolism. Comparing T1D patients to non-diabetic controls, recent lipidomic studies of serum and blood cells from these patients have revealed changes in sphingolipid profiles[15,35]. The concentrations of SO, SA and several sphingolipid species were found to be significantly elevated in plasma samples from T2D patients compared to healthy control subjects[36], suggesting that the rate of cellular ceramide generation in T2D patients is likely elevated.

The purpose of this study was to determine the concentrations of free SO and SA in the BM of healthy and T1D mothers, as there is no information in the literature on this topic.

In this study, the concentrations of free SO and SA in the BM of 15 T1D patients and 10 healthy women were measured during lactation (3rd, 5th, 7th, 14th and 42nd day postpartum). The obtained results show that the concentrations of free SO and SA significantly decreased in healthy individuals during lactation (Figure 2 and Figure 3). However, in the BM of women with T1D, they decreased from day 3 to day 7 and increased on day 14 (Figure 2 and Figure 3).

Statistically significant differences in SO and SA concentrations by days of lactation were observed in both healthy women and women with T1D. By comparing the concentrations of free SO in the BM of healthy women and T1D women, a statistically significant difference was observed on the 5th and 14th day of lactation (Figure 2). A statistically significant difference was observed by comparing the concentrations of free SA in the milk of healthy women and T1D women on days 14 and 42 (Figure 3). Therefore, according to the obtained results, in the BM of women with T1D, a significantly higher concentration of SO was observed on day 14, and significantly higher concentrations of SA were observed on days 14 and 42 of lactation.

This may be partly explained by the abnormal lipid metabolism in diabetics, which is marked by an elevation of lipoprotein lipase and lipolysis. Irregularities in the concentration of plasma insulin may influence the type and amount of lipids in BM by influencing the activities of enzymes involved in the desaturation and elongation of fatty acids, as well as the transmembrane passage of glucose in mammary gland cells and lipids (via lipoprotein lipase activity). In the mammary gland, insulin can influence lipogenesis in several ways. A lack of insulin causes the mammary glands' phosphofructokinase activity to reduce, which decreases glucose metabolism. Since glucose serves as a substrate for fat synthesis, modifications in the metabolism of carbohydrates can alter the composition of BM. It could be assumed that there is an increased concentration of available fatty acids for the synthesis of complex sphingolipids, which are metabolized and broken down to sphingoid bases, which may result in a slightly higher concentration of sphingoid bases.

Despite its limitations, our study is still relevant because it provides insight into T1D-induced changes in BM sphingolipid metabolism.

More research needs to be done using a larger number of subjects and incorporating more biochemical parameters.

Conclusions

This study was the first to determine the concentrations of free SO and SA from day 3 to day 42 of lactation in the milk of healthy mothers and mothers with T1D. ■

References

1. Olsen ASB, Færgeman NJ. Sphingolipids: membrane microdomains in brain development, function and neurological diseases. Open Biol. 2017 May;7(5):170069. doi:10.1098/rsob.170069
2. Wang Y, Niu Y, Zhang Z, Gable K, Gupta SD, Somashekarappa N, et al. Structural insights into the regulation of human serine palmitoyltransferase complexes. Nat Struct Mol Biol. 2021 Mar;28(3):240-8. doi:10.1038/s41594-020-00551-9
3. Merrill AH Jr. Sphingolipid and glycosphingolipid metabolic pathways in the era of sphingolipidomics. Chem Rev. 2011 Oct;111(10):6387-422. doi:10.1021/cr2002917
4. Hannun YA, Obeid LM. Principles of bioactive lipid signalling: lessons from sphingolipids. Nat Rev Mol Cell Biol. 2008 Feb;9(2):139-50. doi:10.1038/nrm2329
5. Maceyka M, Milstien S, Spiegel S. Sphingosine-1-phosphate: the Swiss army knife of sphingolipid signaling. J Lipid Res. 2009 Apr;50 Suppl:S272-6. doi:10.1194/jlr.R800065-JLR200
6. Matanes F, Twal WO, Hammad SM. Sphingolipids as biomarkers of disease. Adv Exp Med Biol. 2019;1159:109-38. doi:10.1007/978-3-030-21162-2_7
7. Harden OC, Hammad SM. Sphingolipids and Diagnosis, Prognosis, and Organ Damage in Systemic Lupus Erythematosus. Front Immunol. 2020 Sep 25;11:586737. doi:10.3389/fimmu.2020.586737
8. Tonks KT, Coster AC, Christopher MJ, Chaudhuri R, Xu A, Gagnon-Bartsch J, et al. Skeletal muscle and plasma lipidomic signatures of insulin resistance and overweight/obesity in humans. Obesity (Silver Spring). 2016 Apr;24(4):908-16. doi:10.1002/oby.21448
9. Hannun YA, Obeid LM. Sphingolipids and their metabolism in physiology and disease. Nat Rev Mol Cell Biol. 2018 Mar;19(3):175-91. doi:10.1038/nrm.2017.107
10. Kitatani K, Idkowiak-Baldys J, Hannun YA. The sphingolipid salvage pathway in ceramide metabolism and signaling. Cell Signal. 2008 Jun;20(6):1010-8. doi:10.1016/j.cellsig.2007.12.006
11. Merrill AH Jr, Nimkar S, Menaldino D, Hannun YA, Loomis C, Bell RM, et al. Structural requirements for long-chain (sphingoid) base inhibition of protein kinase C in vitro and for the cellular effects of these compounds. Biochemistry. 1989 Apr 18;28(8):3138-45. doi:10.1021/bi00434a004
12. Höglinger D, Nadler A, Haberkant P, Kirkpatrick J, Schifferer M, Stein F, et al. Trifunctional lipid probes for comprehensive studies of single lipid species in living cells. Proc Natl Acad Sci U S A. 2017 Feb 14;114(7):1566-71. doi:10.1073/pnas.1611096114
13. Fischer CL, Drake DR, Dawson DV, Blanchette DR, Brogden KA, Wertz PW. Antibacterial activity of sphingoid bases and fatty acids against Gram-positive and Gram-negative bacteria. Antimicrob Agents Chemother. 2012 Mar;56(3):1157-61. doi:10.1128/AAC.05151-11
14. Holm LJ, Krogvold L, Hasselby JP, Kaur S, Claessens LA, Russell MA, et al. Abnormal islet sphingolipid metabolism in type 1 diabetes. Diabetologia. 2018 Jul;61(7):1650-61. doi:10.1007/s00125-018-4614-2
15. Sen P, Dickens AM, López-Bascón MA, Lindeman T, Kemppainen E, Lamichhane S, et al. Metabolic alterations in immune cells associate with progression to type 1 diabetes. Diabetologia. 2020 May;63(5):1017-31. doi:10.1007/s00125-020-05107-6
16. Sui J, He M, Wang Y, Zhao X, He Y, Shi B. Sphingolipid metabolism in type 2 diabetes and associated cardiovascular complications. Exp Ther Med. 2019 Nov;18(5):3603-14. doi:10.3892/etm.2019.7981
17. Eizirik DL, Pasquali L, Cnop M. Pancreatic β-cells in type 1 and type 2 diabetes mellitus: different pathways to failure. Nat Rev Endocrinol. 2020 Jul;16(7):349-62. doi:10.1038/s41574-020-0355-7
18. Véret J, Bellini L, Giussani P, Ng C, Magnan C, Le Stunff H. Roles of Sphingolipid Metabolism in Pancreatic β Cell Dysfunction Induced by Lipotoxicity. J Clin Med. 2014 Jun 20;3(2):646-62. doi:10.3390/jcm3020646
19. Galadari S, Rahman A, Pallichankandy S, Galadari A, Thayyullathil F. Role of ceramide in diabetes mellitus: evidence and mechanisms. Lipids Health Dis. 2013 Jul 8;12:98. doi:10.1186/1476-511X-12-98
20. Hahn C, Tyka K, Saba JD, Lenzen S, Gurgul-Convey E. Overexpression of sphingosine-1-phosphate lyase protects insulin-secreting cells against cytokine toxicity. J Biol Chem. 2017

Dec 8;292(49):20292-304. doi:10.1074/jbc.M117.814491
21. Oliveira AM, Cunha CC, Penha-Silva N, Abdallah VO, Jorge PT. Interference of the blood glucose control in the transition between phases I and II of lactogenesis in patients with type 1 diabetes mellitus. Arq Bras Endocrinol Metabol. 2008 Apr;52(3):473-81. Portuguese. doi:10.1590/s0004-27302008000300007
22. Morceli G, França EL, Magalhães VB, Damasceno DC, Calderon IM, Honorio-França AC. Diabetes induced immunological and biochemical changes in human colostrum. Acta Paediatr. 2011 Apr;100(4):550-6. doi:10.1111/j.1651-2227.2010.02070.x
23. Riley RT, Wang E, Merrill AH. Liquid Chromatographic Determination of Sphinganine and Sphingosine: Use of the Free Sphinganine-to-Sphingosine Ratio as a Biomarker for Consumption of Fumonisins. J AOAC Int. 1994 Mar;77(2):533–40. doi:10.1093/jaoac/77.2.533
24. Ribar S, Feher-Turković L, Karmelić I, Mesarić M. Sphingoid bases in infant formulas. Food Chem. 2007;103(1):173-80. doi:10.1016/j.foodchem.2006.07.069
25. Camacho-Morales A, Caba M, García-Juárez M, Caba-Flores MD, Viveros-Contreras R, Martínez-Valenzuela C. Breastfeeding Contributes to Physiological Immune Programming in the Newborn. Front Pediatr. 2021 Oct;9:744104. doi:10.3389/fped.2021.744104
26. Plagemann A. A matter of insulin: developmental programming of body weight regulation. J Matern Fetal Neonatal Med. 2008 Mar;21(3):143-8. doi:10.1080/14767050801929869
27. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Does breastfeeding influence risk of type 2 diabetes in later life? A quantitative analysis of published evidence. Am J Clin Nutr. 2006 Nov;84(5):1043-54. doi:10.1093/ajcn/84.5.1043
28. Ballard O, Morrow AL. Human milk composition: nutrients and bioactive factors. Pediatr Clin North Am. 2013 Feb;60(1):49-74. doi:10.1016/j.pcl.2012.10.002
29. Cantrell Stanford J, Morris AJ, Sunkara M, Popa GJ, Larson KL, Özcan S. Sphingosine 1-phosphate (S1P) regulates glucose-stimulated insulin secretion in pancreatic β cells. J Biol Chem. 2012 Apr 13;287(16):13457-64. doi:10.1074/jbc.M111.268185
30. Katsarou A, Gudbjörnsdottir S, Rawshani A, Dabelea D, Bonifacio E, Anderson BJ, et al. Type 1 diabetes mellitus. Nat Rev Dis Primers. 2017 Mar 30;3:17016. doi:10.1038/nrdp.2017.16
31. Chaurasia B, Kaddai VA, Lancaster GI, Henstridge DC, Sriram S, Galam DL, et al. Adipocyte Ceramides Regulate Subcutaneous Adipose Browning, Inflammation, and Metabolism. Cell Metab. 2016 Dec 13;24(6):820-34. doi:10.1016/j.cmet.2016.10.002
32 Dritsakou K, Liosis G, Valsami G, Polychronopoulos E, Skouroliakou M. The impact of maternal- and neonatal-associated factors on human milk's macronutrients and energy. J Matern Fetal Neonatal Med. 2017 Jun;30(11):1302-8. doi:10.1080/14767058.2016.1212329
33. Jackson MB, Lammi-Keefe CJ, Jensen RG, Couch SC, Ferris AM. Total lipid and fatty acid composition of milk from women with and without insulin-dependent diabetes mellitus. Am J Clin Nutr. 1994 Sep;60(3):353-61. doi:10.1093/ajcn/60.3.353
34. Fujimori M, França EL, Fiorin V, Morais TC, Honorio-França AC, de Abreu LC. Changes in the biochemical and immunological components of serum and colostrum of overweight and obese mothers. BMC Pregnancy Childbirth. 2015 Aug;12;15:166. doi:10.1186/s12884-015-0574-4
35. Wei N, Pan J, Pop-Busui R, Othman A, Alecu I, Hornemann T, et al. Altered sphingoid base profiles in type 1 compared to type 2 diabetes. Lipids Health Dis. 2014 Oct 11;13:161. doi:10.1186/1476-511X-13-161
36. Górska M, Dobrzyń A, Baranowski M. Concentrations of sphingosine and sphinganine in plasma of patients with type 2 diabetes. Med Sci Monit. 2005 Jan;11(1):CR35-CR38

SAŽETAK

Koncentracije slobodnog sfingozina i sfinganina u majčinom mlijeku zdravih žena i žena s dijabetesom tipa 1

Slavica Potočki, Ana Mesić, Zrinka Šakić, Armin Atić, Ana Kulić i Nikolina Bašić Jukić

Sfingoidne baze čine okosnicu sfingolipida. Postoje indikacije da se metabolizam sfingolipida mijenja u bolestima. Svrha ovog istraživanja bila je određivanje koncentracija slobodnog sfingozina (SO) i sfinganina (SA) u majčinom mlijeku zdravih žena i žena s dijabetesom tipa 1 (T1D) tijekom dojenja. Nakon ekstrakcije sfingolipida, provedena je bazna hidroliza kako bi se dobili slobodni SO i SA, koji su potom analizirani tekućinskom kromatografijom visoke djelotvornosti.

U mlijeku zdravih žena koncentracije SO i SA smanjuju se tijekom laktacije. Koncentracije SO i SA u mlijeku žena s T1D smanjuju se do 7. dana te potom rastu počevši od 14. dana laktacije. Kod zdravih žena i žena s T1D pokazale su se značajne razlike u koncentracijama SO i SA po danima laktacije. Usporedbom koncentracija slobodnog SO u mlijeku zdravih žena i žena s T1D uočena je statistički značajna razlika 5. i 14. dana laktacije. Statistički značajna razlika uočena je usporedbom koncentracije slobodnog SA u mlijeku zdravih žena i žena s T1D 14. i 42. dana.

Naše istraživanje po prvi put daje uvid u koncentraciju sfingoidnih baza u majčinom mlijeku.

KLJUČNE RIJEČI

Sfingozin; *Sfinganin*; *Majčino mlijeko*; *Dijabetes tip 1*