

BÖLÜM 36

YENİDOĞAN ENSEFALOPATİLERİ

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GLİKOZ METABOLİZMASI

GİRİŞ

Umbikal kordon klemplendiğinde ve maternal glikoz desteği sona erdiğinde yenidoğan glikoz regülasyonuna başlar. Bu regülasyon kompleks metabolik ve hormonal süreçlerle sağlanır. Bu süreçlerin yetersiz matürasyonu sebebi ile regülasyon doğum sonrası kısa sürede sağlanamayabilir ve plazma glukoz düzeyi normal aralıktaki tutulamayabilir. Yenidoğanın plazma glikoz konsantrasyonuna dair net bir normal aralık tanımlanamadığı için glikoz homeostazının kontrolü ayrıca zordur.¹

Fetal plazma glikoz konsantrasyonu maternal konsantrasyonun %80 kadarıdır.² Doğumdan sonra maternal glikoz desteği sona erdiğinde glikoz ve diğer substratların üretim ve kullanımı için glikojenoliz, glikoneogenez, glikojenez, lipoliz, ketogenez devreye girer.

HİPERGLİSEMI

Genellikle plazma glukoz konsantrasyonunun 150 mg/dl üzerinde olması hiperglisemi olarak tanımlanır.³ Azalmış insülin yanıtına bağlı olarak düşük doğum ağırlıklı yenidoğanlar ve

pretermler hiperglisemi için en yüksek riskli gruptur. Ayrıca cerrahi prosedürler veya sepse bağılı neonatal stres, parenteral beslenme gibi durumlar da hiperglisemi riskini artırır. Düşük doğum ağırlıklı hastalarda hiperglisemi ilişkili evre 3-4 intraventriküler kanama, hastane yataş süresinde uzama ve hatta mortalite bildirilmiştir.^{3,4,5}

Neonatal diabetes mellitus hayatın genellikle ilk altı ayında ortaya çıkan nadir (1/90000) bir monogenik diyabet kliniğiidir. KCNJ11, ABCC8 ve INS mutasyonları en sık neden olan mutasyonlardır.

Neonatal diabetes mellitus saptanan hastaların yarısı geçici ya da kalıcı infüzyon replasmanlarına ihtiyaç duyar. 6q24 mutasyonu olan hastalarda oral sülfonilüreye geçiş de mümkün olabilmektedir.^{6,7}

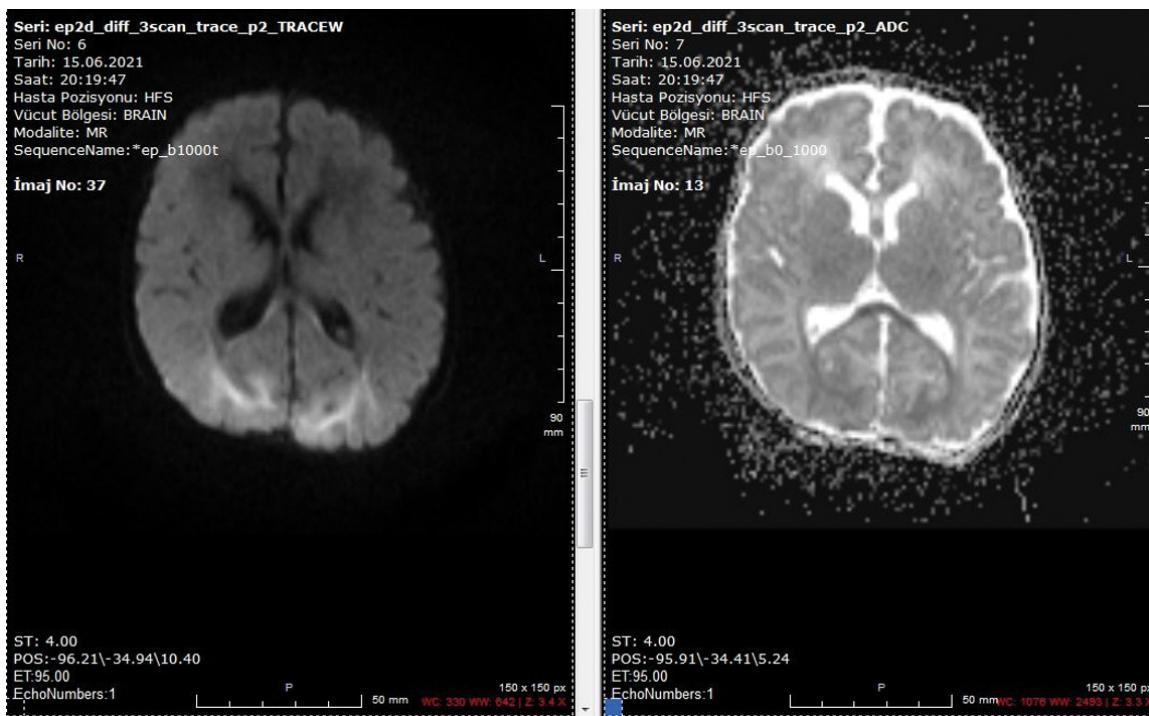
Hiperglisemi genellikle asemptomatiktir ancak osmotik diütereze bağlı dehidratasyon, kilo kaybı, büyümeye geriliği, ateş, glikozüri, ketoza ve metabolik asidoz görülebilir.

Kısa süreli ve ılımlı hiperglisemi, glukoz perfüzyon hızı düşürülecek düzeltilebilir. Özellikle plazma glukoz konsantrasyonu 200-250 mg/dl üzerinde seyretmeye devam ederse

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Şekil 1. Hipoglisemi öyküsü olan sekiz günlük kız olgunun manyetik rezonans görüntülemesi. Özellikle beynin posterior kesimlerini tutan beyaz cevher tutulumu gözlenmektedir.

KAYNAKLAR

- Cornblath M, Hawdon JM, Williams AF et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. *Pediatrics*. 2000;105(5):1141-5. doi: 10.1542/peds.105.5.1141. PMID: 10790476.
- Garg M, Devaskar SU. Glucose metabolism in the late preterm infant. *Clin Perinatol*. 2006;33(4):853-70; abstract ix-x. doi: 10.1016/j.clp.2006.10.001. PMID: 17148009.
- Hays SP, Smith EO, Sunehag AL. Hyperglycemia is a risk factor for early death and morbidity in extremely low birth-weight infants. *Pediatrics*. 2006;118(5):1811-8. doi: 10.1542/peds.2006-0628. PMID: 17079549.
- Jagla M, Szymońska I, Starzec K, Kwinta P. Impact of early glycemic variability on mortality and neurologic outcome of very low birth weight infants: Data from a continuous glucose monitoring system. *Dev Period Med*. 2019;23(1):7-14. PMID: 30954975.
- Auerbach A, Eventov-Friedman S, Arad I, Peleg O, Bdolah-Abram T, Bar-Oz B, Zangen DH. Long duration of hyperglycemia in the first 96 hours of life is associated with severe intraventricular hemorrhage in preterm infants. *J Pediatr*. 2013;163(2):388-93. doi: 10.1016/j.jpeds.2013.01.051. Epub 2013 Mar 6. PMID: 23472766.
- Beltrand J, Busiah K, Vaivre-Douret L, Fauret AL, Berdugo M, Cavé H, Polak M. Neonatal Diabetes Mellitus. *Front Pediatr*. 2020;30:8.540718. doi: 10.3389/fped.2020.540718. PMID: 33102403; PMCID: PMC7554616.
- Gurgel LC, Moisés RS. Diabetes melito neonatal [Neonatal diabetes mellitus]. *Arq Bras Endocrinol Metabol*. 2008;152(2):181-7. Portuguese. doi: 10.1590/s0004-27302008000200005. PMID: 18438528.
- Stanley, C. A., & Pallotto, E. K. (2005). Disorders of carbohydrate metabolism. In H. W. Taeusch, R. A. Ballard, & C. A. Gleason (Eds.), *Avery's diseases of the newborn* (8th ed., pp. 1410–1422). Philadelphia: Elsevier Saunders.
- Gökşen Şimşek D, Ecevit A, Hatipoğlu N, et al. Neonatal Hyperglycemia, which threshold value, diagnostic approach and treatment?: Turkish Neonatal and Pediatric Endocrinology and Diabetes Societies consensus report. *Turk Pediatri Ars* 2018; 53(Suppl 1): S234-S238.
- Whipple AO, Frantz VK. Adenoma of islet cells with hyperinsulinism: a review. *Ann Surg*. 1935;101(6):1299-1335. doi:10.1097/00000658-193506000-00001

11. Hawdon JM. Identification and Management of Neonatal Hypoglycemia in the Full-Term Infant. British Association of Perinatal Medicine Framework for Practice, 2017. *J Hum Lact.* 2019;35(3):521-523. doi: 10.1177/0890334419846128. Epub 2019 May 3. PMID: 31051094.
12. Thompson-Branch A, Havranek T. Neonatal Hypoglycemia. *Pediatr Rev.* 2017;38(4):147-157. doi: 10.1542/pir.2016-0063. PMID: 28364046.
13. Hay WW Jr, Raju TN, Higgins RD, Kalhan SC, Devaskar SU. Knowledge gaps and research needs for understanding and treating neonatal hypoglycemia: workshop report from Eunice Kennedy Shriver National Institute of Child Health and Human Development. *J Pediatr.* 2009;155(5):612-617. doi: 10.1016/j.jpeds.2009.06.044
14. McGowan JE, Price-Douglas W, Hay WW. Glucose homeostasis. In: Merenstein GB, Gardner SL, eds. *Handbook of neonatal intensive care.* 6th ed. St Louis: Mosby Elsevier; 2006. p. 368-90.
15. Mitchell NA, Grimbley C, Rosolowsky ET et al. Incidence and Risk Factors for Hypoglycemia During Fetal-to-Neonatal Transition in Premature Infants. *Front Pediatr.* 2020;11:8:34. doi: 10.3389/fped.2020.00034. PMID: 32117839; PMCID: PMC7026247.
16. Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. *J Pediatr.* 2012 Nov;161(5):787-91. doi: 10.1016/j.jpeds.2012.05.022. Epub 2012 23. PMID: 22727868.
17. Duvanel CB, Fawer CL, Cotting J, Hohlfeld P, Matthieu JM. Long-term effects of neonatal hypoglycemia on brain growth and psychomotor development in small-for-gestational-age preterm infants. *J Pediatr.* 1999;134(4):492-8. doi: 10.1016/s0022-3476(99)70209-x. PMID: 10190926.
18. Adamkin DH. Neonatal hypoglycemia. *Curr Opin Pediatr.* 2016;28(2):150-5. doi: 10.1097/MOP.0000000000000319. PMID: 26780301.
19. Stanley CA, Rozance PJ, Thornton PS, De Leon DD, Harris D, Haymond MW, Hussain K, Levitsky LL, Murad MH, Simmons RA, Sperling MA, Weinstein DA, White NH, Wolfsdorf JI. Re-evaluating "transitional neonatal hypoglycemia": mechanism and implications for management. *J Pediatr.* 2015 Jun;166(6):1520-5.e1. doi: 10.1016/j.jpeds.2015.02.045. Epub 2015;25. PMID: 25819173; PMCID: PMC4659381.
20. Richard M. Cowett, Robert E. Rapoza, Nancy L. Gelardi, Insulin counterregulatory hormones are ineffective in neonatal hyperinsulinemic hypoglycemia, Metabolism, Volume 48, Issue 5, 1999, Pages 568-574, ISSN 0026-0495, [https://doi.org/10.1016/S0026-0495\(99\)90052-5](https://doi.org/10.1016/S0026-0495(99)90052-5).
21. Aral YZ, Güçüyener K, Atalay Y, Hasanoğlu A, Türk-yılmaz C, Sayal A, et al. Role of excitatory amino-acids in neonatal hypoglycemia. *Acta Paediatr Jpn* (1998) 40:303-6. doi: 10.1111/j.1442-200X.1998.tb01936.x
22. Sensi SL, Paoletti P, Koh JY, Aizenman E, Bush AI, Hershfinkel M. The neurophysiology and pathology of brain zinc. *J Neurosci.* 2011;31(45):16076-85. doi: 10.1523/JNEUROSCI.3454-11.2011. PMID: 22072659; PMCID: PMC3223736.
23. De Angelis LC, Brigati G, Polleri G, Malova M, Parodi A, Minghetti D, Rossi A, Massirio P, Tragliai C, Maghnie M, Ramenghi LA. Neonatal Hypoglycemia and Brain Vulnerability. *Front Endocrinol (Lausanne).* 2021;16:12:634305. doi: 10.3389/fendo.2021.634305. PMID: 33796072; PMCID: PMC8008815.
24. Alkalay AL, Sarnat HB, Flores-Sarnat L, Simmons CF. Neurologic aspects of neonatal hypoglycemia. *Isr Med Assoc J.* 2005;7(3):188-92. Erratum in: *Isr Med Assoc J.* 2005 Apr;7(4):267. PMID: 15792267.
25. Rozance PJ. Update on neonatal hypoglycemia. *Curr Opin Endocrinol Diabetes Obes.* 2014;21(1):45-50. doi: 10.1097/MED.0000000000000027. PMID: 24275620; PMCID: PMC4012366.
26. Tam EW, Widjaja E, Blaser SI, Macgregor DL, Sato-dia P, Moore AM. Occipital lobe injury and cortical visual outcomes after neonatal hypoglycemia. *Pediatrics.* 2008;122(3):507-12. doi: 10.1542/peds.2007-2002. PMID: 18762519.
27. Barkovich AJ, Ali FA, Rowley HA, Bass N. Imaging patterns of neonatal hypoglycemia. *AJNR Am J Neuroradiol.* 1998;19(3):523-8. PMID: 9541312.
28. Tam EW, Haeusslein LA, Bonifacio SL, et al. Hypoglycemia is associated with increased risk for brain injury and adverse neurodevelopmental outcome in neonates at risk for encephalopathy. *J Pediatr.* 2012;161:88-93.
29. Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics.* 2008;122(1):65-74. doi: 10.1542/peds.2007-2822. PMID: 18595988.
30. Goode RH, Rettiganti M, Li J, Lyle RE, Whiteside-Mansell L, Barrett KW, Casey PH. Developmental Outcomes of Preterm Infants With Neonatal Hypoglycemia. *Pediatrics.* 2016;138(6):e20161424. doi: 10.1542/peds.2016-1424. Epub 2016 4. PMID: 27940690; PMCID: PMC5127066.
31. McKinlay CJD, Alsweiler JM, Anstice NS, Burakovich N, Chakraborty A, Chase JG, Gamble GD, Harris DL, Jacobs RJ, Jiang Y, Paudel N, San Diego RJ, Thompson B, Woulde TA, Harding JE; Children With Hypoglycemia and Their Later Development (CHYLD) Study Team. Association of Neonatal Glycemia With Neurodevelopmental Outcomes at 4.5 Years. *JAMA Pediatr.* 2017;171(10):972-983. doi: 10.1001/jamapediatrics.2017.1579. PMID: 28783802; PMCID: PMC5710616.
32. Shah R, Harding J, Brown J, McKinlay C. Neonatal Glycaemia and Neurodevelopmental Outcomes: A Systematic Review and Meta-Analysis. *Neonatology.*

- 2019;115(2):116-126. doi: 10.1159/000492859. Epub 2018;8. PMID: 30408811.
33. Fong CY, Harvey AS. Variable outcome for epilepsy after neonatal hypoglycaemia. *Dev Med Child Neurol.* 2014;56(11):1093-9. doi: 10.1111/dmcn.12496. Epub 2014 May 26. PMID: 24861161.
34. Narvey MR, Marks SD. The screening and management of newborns at risk for low blood glucose. *Paediatr Child Health.* 2019 ;24(8):536-554. doi: 10.1093/pch/pxz134. Epub 2019 9. PMID: 31844395; PMCID: PMC6901164.
35. Adamkin DH. Neonatal hypoglycemia. *Semin Fetal Neonatal Med.* 2017;22(1):36-41. doi: 10.1016/j.siny.2016.08.007. Epub 2016 Sep 4. PMID: 27605513.
36. Lilien LD, Pildes RS, Srinivasan G, Voora S, Yeh TF. Treatment of neonatal hypoglycemia with minibolus and intravenous glucose infusion. *J Pediatr.* 1980;97(2):295-8. doi: 10.1016/s0022-3476(80)80499-9. PMID: 7400902.
37. Weston PJ, Harris DL, Battin M, Brown J, Hegarty JE, Harding JE. Oral dextrose gel for the treatment of hypoglycaemia in newborn infants. *Cochrane Database Syst Rev.* 2016;4;(5):CD011027. doi: 10.1002/14651858.CD011027.pub2. PMID: 27142842.
38. Plecko B, Stoeckler-Ipsiroglu S, Schober E, Harrer G, Mlynarik V, Gruber S, Moser E, Moeslinger D, Silgoner H, Ipsiroglu O. Oral beta-hydroxybutyrate supplementation in two patients with hyperinsulinemic hypoglycemia: monitoring of beta-hydroxybutyrate levels in blood and cerebrospinal fluid, and in the brain by in vivo magnetic resonance spectroscopy. *Pediatr Res.* 2002 ;52(2):301-6. doi: 10.1203/00006450-200208000-00025. PMID: 12149510.
39. Milcic T. L. (2008). Neonatal glucose homeostasis. *Neonatal network : NN,* 27(3), 203–207. <https://doi.org/10.1891/0730-0832.27.3.203>