

Kedves Kollégák!

Gyakran szembesül a klinikus azzal a problémával, hogy a hipervolémiás, ödémás betegnél nem kellően hatékonyak a diuretikumok.

Mellékelek egy rövid áttekintést a diuretikum rezisztencia okairól és a lehetséges kezelésről.

Remélem használható a beteggy melllett.

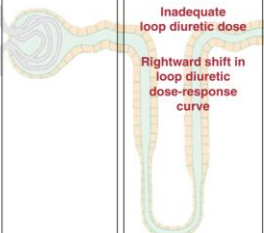
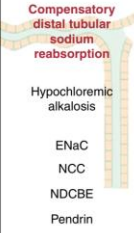
Dr. Ferdinandy Csilla

A diuretikum rezisztencia

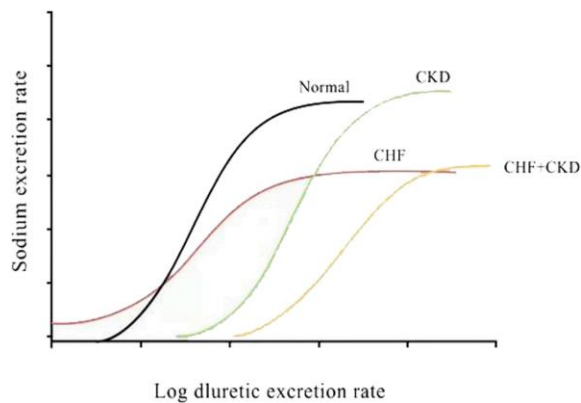
Gyakori probléma az intenzív terápiában a pozitív folyadék egyensúly és az annak kezelését gátló diuretikum rezisztencia (Coté JM et al: Diuretic strategies in patients with resistance to loop-diuretics in the intensive care unit: A retrospective study from the MIMIC-III database. *Journal of Critical Care* 65 (2021) 282–291).

Több **definíciója** is van (Luxuan Guo et al: Diuretic resistance in patients with kidney disease: Challenges and opportunities. *Biomedicine & Pharmacotherapy* 157 (2023) 114058), az egyik lehetséges: **kacs-diuretikum adása után a vizelet Na < 50 mmol/l** (Doering et al. Markers of diuretic resistance in emergency department patients with acute heart failure. *International Journal of Emergency Medicine* (2017) 10:17. Gupta R et al: Diuretic Resistance in Heart Failure. *Curr Heart Fail Rep.* 2019 April ; 16(2): 57–66).

A diuretikum rezisztencia osztályozása (Cox ZL et al: Classic and Novel Mechanisms of Diuretic Resistance in Cardiorenal Syndrome. *KIDNEY360* 3: 954–967, 2022.)

Importance of specific cause/mechanism on diuretic resistance	Diuretic Resistance Categorization			
	Extra-Tubular	Tubular		
		Pre-Loop of Henle	Loop of Henle	Post-Loop of Henle
Significant Unknown but hypothesized to be significant	Venous congestion Increased intra-abdominal pressure Kidney vasoconstriction and hypoperfusion			

Diuretikum rezisztencia **vesebetegségekben** (Luxuan Guo et al: Diuretic resistance in patients with kidney disease: Challenges and opportunities. *Biomedicine & Pharmacotherapy* 157 (2023) 114058)



A diuretikum rezisztencia okai, kórtana (Luxuan Guo et als: Diuretic resistance in patients with kidney disease: Challenges and opportunities. *Biomedicine & Pharmacotherapy* 157 (2023) 114058. Novak JE et als: Diuretics in States of Volume Overload: Core Curriculum 2022. *Am J Kidney Dis.* XX(XX):1- 13.):

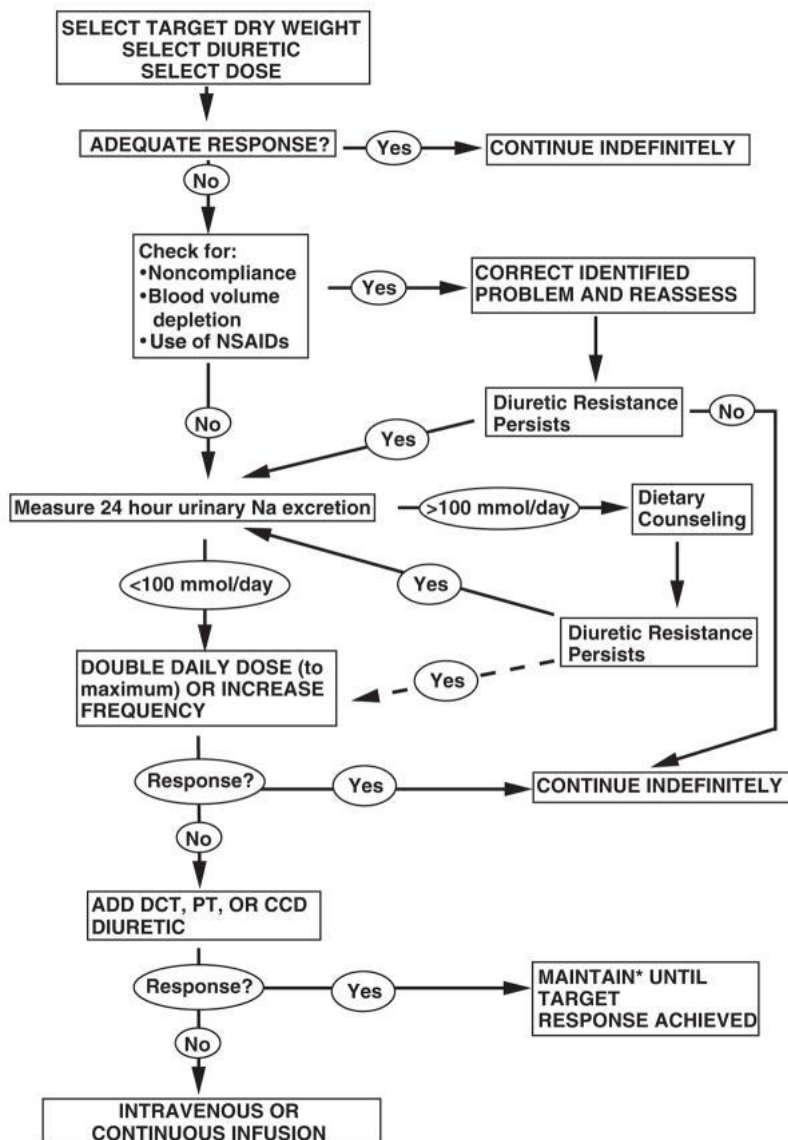
- elégtelen a diuretikum adag
- nem jut el a diuretikum a veséhez
- hypalbuminaemia
- hypovolaemia
- elégtelen RBF
- elégtelen vesetömeg (krónikus veseelégtelenség)
- elégtelen GFR
- a disztális tubulus funkció károsodása (ter Maaten JR et als: Renal tubular resistance is the primary driver for loop diuretic resistance in acute heart failure. *European Journal of Heart Failure* (2017) 19, 1014–1022)
- hyponatraemia
- hypochloraemia
- hypokalaemia
- metabolikus alkalosis
- magas karbamid szint
- vesekárosító gyógyszerek (NSAID szerek, trimethoprim, stb.)
- súlyos májelégtelenség (Runyon BA: Ascites in adults with cirrhosis: Diuretic-resistant ascites *UpToDate*, 2023, július. <https://www.medilib.ir/uptodate/show/1258>. Betrosian AP et als: Acute renal dysfunction in liver diseases. *World J Gastroenterol* 2007 November 14; 13(42): 5552-5559)
- nagy hasúri nyomás (Copur S et als: Abdominal compartment syndrome: an often overlooked cause of acute kidney injury. *Journal of Nephrology* (2022) 35:1595–1603. Sun Jing et als: Intra-abdominal hypertension and increased acute kidney injury risk: a systematic review and meta-analysis. *Journal of International Medical Research*, 2021, 49(5) 1–10. Jacobs R et als: Fluid Management, Intra-Abdominal Hypertension and the Abdominal Compartment Syndrome: A Narrative Review. *Fluid Management, Intra-Abdominal Hypertension and the Abdominal Compartment Syndrome: A Narrative Review. Life*, 2022, 12, 1390. Rajasuriya V et als: Abdominal compartment syndrome: Often overlooked conditions in medical intensive care units. *World J Gastroenterol* 2020 January 21; 26(3): 266-278)
- szívelégtelenség, nagyvénás pangás (Wilcox CR et als: Pathophysiology of Diuretic Resistance and Its Implications for the Management of Chronic Heart Failure. *Hypertension*. 2020; 76:1045-1054. Cox ZL et als: Classic and Novel Mechanisms of Diuretic Resistance in Cardiorenal Syndrome. *KIDNEY* 3: 954–967, 2022. Shams E et als: January 18, 2022 Diuretic Resistance Associated With Heart Failure. *Cureus* 14(1): e21369. Kim JA et als: Recent Developments in the Evaluation and Management of Cardiorenal Syndrome: A Comprehensive Review. *Curr Probl Cardiol* 2023; 48:101509. Kristjánsdóttir I et als: Congestion and Diuretic Resistance in Acute or Worsening Heart Failure. : *Cardiac Failure Review* 2020;6:e25)
- RAA rendszer hiperaktivitása
- endokrin betegség (pl. hypadrenia)
- kacs-diuretikum tolerancia hosszas alkalmazás után (braking effektus, plafon-effektus)

Az adott betegnél az **ok tisztázásában** és a **kezelésben** segíthet a **mesterséges intelligencia = AI**

(Gelman R et al: A second-generation artificial intelligence-based therapeutic regimen improves diuretic resistance in heart failure: Results of a feasibility open-labeled clinical trial. *Biomedicine & Pharmacotherapy* 161 (2023) 114334). Mercier JA et al: A Machine Learning Model to Predict Diuretic Resistance. *KIDNEY360* 4: 15–22, 2023.)

A diuretikum rezisztencia lehetséges kezelései

ábra (Hoorn EJ et al: Diuretic Resistance. *Am J Kidney Dis.* 2017 January ; 69(1): 136–142)



Elsődlegesen az **okot kell kezelni, korrigálni** (Luxuan Guo et al: Diuretic resistance in patients with kidney disease: Challenges and opportunities. *Biomedicine & Pharmacotherapy* 157 (2023) 114058)

Vese **perfúziós nyomás** javítása: pl. vazopresszorral. A **noradrenalin** csak a súlyos septicus betegnél javítja a vesefunkciót, de nem septicus betegnél nem (Albanese J et al: Renal Effects of Norepinephrine in Septic and Nonseptic Patients. *Chest*, 2004; 126:534–539. Herget-Rosenthal S et al: Approach to Hemodynamic Shock and Vasopressors. *Clin J Am Soc Nephrol* 3: 546-553, 2008. UpToDate: Use of vasopressors and inotropes. 2023 július. Guzman JA et al: Vasopressin vs. norepinephrine in endotoxic shock: systemic, renal, and splanchnic hemodynamic and oxygen transport effects. *J Appl Physiol* 95: 803–809, 2003. Post and

Vincent: Renal autoregulation and blood pressure management in circulatory shock. *Critical Care* (2018) 22:81). Nem indokolt magas MAP alkalmazása, elegendő a **normotenzió** (Tran et al. Higher blood pressure versus normotension targets to prevent acute kidney injury: a systematic review and meta-regression of randomized controlled trials *Critical Care* (2022) 26:364). A **vazopresszin** és analógjai inkább javítják a GFR-t, mint a noradrenalin, mert az efferens arteriolákon erősebb a hatásuk (Busse LW et al: Vasopressor Therapy and Blood Pressure Management in the Setting of Acute Kidney Injury. *Semin Nephrol* 2019, 39:462-472. Bellomo R et al: Vasoactive drugs and acute kidney injury. *Crit Care Med* 2008; 36[Suppl.]:S179–S186).

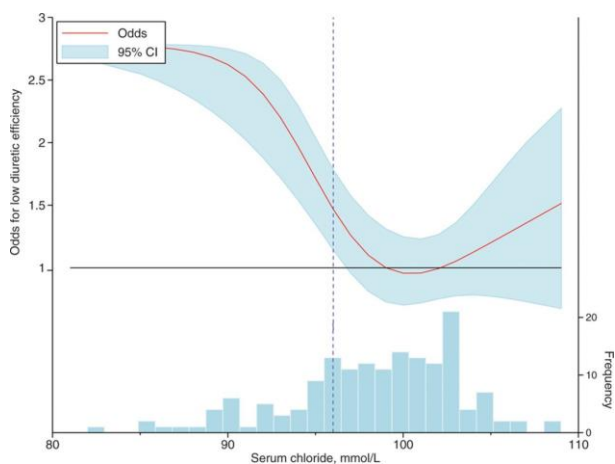
A vénás pangás csökkentése – ennek leghatékonyabb módja a korai **ultrafiltráció** (Eder M et al: Venous Congestion, Not Cardiac Index is Associated with Diuretic Resistance, *S30 Journal of Cardiac Failure* Vol. 26 No. 10S October 2020. Cox ZL et al: Classic and Novel Mechanisms of Diuretic Resistance in Cardiorenal Syndrome. *KIDNEY* 3: 954–967, 2022)

A hasúri nyomás csökkentése (Copur S et al: Abdominal compartment syndrome: an often overlooked cause of acute kidney injury. *Journal of Nephrology* (2022) 35:1595–1603.).

Nátrium pótlás (Acar S et al: Pharmacologic and interventional paradigms of diuretic resistance in congestive heart failure: a narrative review. *International Urology and Nephrology* (2021) 53:1839–1849. Masella C et al: Diuretic Resistance in Cardio-Nephrology: Role of Pharmacokinetics, Hypochloremia, and Kidney Remodeling. *Kidney Blood Press Res* 2019;44:915–927).

Klór pótlás (Hanberg JS et al: Hypochloremia and Diuretic Resistance in Heart Failure. *Mechanistic Insights. Circ Heart Fail.* 2016;9:e003180. Masella C et al: Diuretic Resistance in Cardio-Nephrology: Role of Pharmacokinetics, Hypochloremia, and Kidney Remodeling. *Kidney Blood Press Res* 2019;44:915–927).

ábra: (Hanberg JS et al: Hypochloremia and Diuretic Resistance in Heart Failure. *Mechanistic Insights. Circ Heart Fail.* 2016;9:e003180)



Kálium-pótlás (Kristjánsdóttir I et al: Congestion and Diuretic Resistance in Acute or Worsening Heart Failure. *Cardiac Failure Review* 2020;6:e25)

A diuretikum **adagjának emelése, folyamatos adása** (Coté JM et al: Diuretic strategies in patients with resistance to loop-diuretics in the intensive care unit: A retrospective study from the MIMIC-III database. *Journal of Critical Care* 65 (2021) 282–291). A **furosemid** infúziós adagja 50-100 mg / óra, maximális adagja felnőtteknek 1500 mg / nap (ogyei.gov.hu).

Kombinált diuretikum terápia: thiazid diuretikum, karboanhidráz-bénítő, szulfonamid diuretikum, aldosteron antagonist (HCT, acetazolamid, indapamid, klopamid, eplerenon, amilorid, spironolakton, tolvaptán, klórtalidon) hozzáadása (3T trial. *Diuretic Strategies for Loop Diuretic Resistance in Acute Heart Failure. J Am Coll Cardiol HF* 2020; 8:157–68. Malik BA et al: Effect of Acetazolamide as Add-On Diuretic Therapy in Patients With Heart Failure: A MetaAnalysis. *Cureus*, 2023, 15(4): e37792. Cox ZL et al: Multinephron Segment Diuretic Therapy to Overcome Diuretic Resistance in Acute Heart Failure: A Single-Center Experience. *J Cardiac Fail* 2022; 28:21–31. The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology. *European Journal of Heart Failure* (2019) 21, 137–155)

Albumin segíthet: minél alacsonyabb a szérumszintje és minél nagyobb az alkalmazott adagja, annál

inkább (Kitsios GD et als: Co-administration of furosemide with albumin for overcoming diuretic resistance in patients with hypoalbuminemia. *Journal of Critical Care* 29 (2014) 253–259. Fernandes J et als: Co-Administration of Albumin and Furosemide in Acute Heart Failure with Diuretic Resistance. *Acta Med Port* 2023 Mar;36(3):193-201. Phakdeekitcharoen B et als: The added-up albumin enhances the diuretic effect of furosemide in patients with hypoalbuminemic chronic kidney disease: a randomized controlled study. *BMC Nephrology* 2012, 13:92. Tao Han Lee et als: Diuretic effect of co-administration of furosemide and albumin in comparison to furosemide therapy alone: An updated systematic review and meta-analysis. *PLoS ONE* 2021, 16(12): e0260312)

Teofillin származékok javítják a diuresist (Van Siang Lian Mang P et als: The diuretic effect of adding aminophylline or theophylline to furosemide in pediatric populations: a systematic review. *European Journal of Pediatrics* (2023) 182:1–8).

SGLT2-gátlók – ezek natriuretikus hatásúak is (Acar S et als: Pharmacologic and interventional paradigms of diuretic resistance in congestive heart failure: a narrative review. *International Urology and Nephrology* (2021) 53:1839–1849. Lameire, N. Renal Mechanisms of Diuretic Resistance in Congestive Heart Failure. *Kidney Dial.* 2023, 3, 56–72. Verma A et als: SGLT2 Inhibitor: Not a Traditional Diuretic for Heart Failure. *Cell Metabolism* 32: 13-14.2020. Wojcik C et als: Mechanisms and Evidence for Heart Failure Benefits from SGLT2 Inhibitors. *Current Cardiology Reports* (2019) 21:130. Vallon V et als: Effects of SGLT2 Inhibitors on Kidney and Cardiovascular Function. *Annu. Rev. Physiol.* 2021. 83:503–28)

Alsó végtagikompressziós kezelés (fásli, rugalmas harisnya) (Gong S et als: Elastic Bandage vs Hypertonic Albumin for Diuretic-Resistant Volume-Overloaded Patients in Intensive Care Unit: A Propensity Match Study. *Mayo Clin Proc.* August 2020;95(8):1660-1670)

Ultrafiltráció, peritoneális dialízis: amennyiben ezek a szerek és terápiák hatástalanok maradnak

(Regolisti G et als: Management of congestion and diuretic resistance in heart failure. *Nephrology @ Point of Care* 2016; 2(1): e73-e87. Pethő ÁG et als: The Importance of the Nephrologist in the Treatment of the Diuretic-Resistant Heart Failure. *Life* 2023, 13, 1328. Wankowicz Z et als: Extracorporeal versus peritoneal ultrafiltration in diuretic-resistant congestive heart failure – a review. *Med Sci Monit*, 2011; 17(12): RA271-281. da Silva FG et als: Diuretic-resistant heart failure and the role of ultrafiltration: A proposed protocol. *Revista Portuguesa de Cardiologia xxx (xxxx) xxx---xxx article in press*)

A javasolt UF tempó: <10 ml/kg/óra (Chou JA et als: Volume Balance and Intradialytic Ultrafiltration Rate in the Hemodialysis Patient. *Curr Heart Fail Rep.* 2017 October ; 14(5): 421–427. Assimon MM et als: Ultrafiltration Rate and Mortality in Maintenance Hemodialysis Patients. *Am J Kidney Dis.* 2016 December ; 68(6): 911–922)