GLP-1 receptor agonists may enhance the effects of desmopressin in individuals with AVP deficiency: a case series and proposed mechanism



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Human GLP1



Nature Reviews | Nephrology

Muskiet MHA et al. GLP-1 and the kidney: from physiology to pharmacology and outcomes in diabetes. Nat Rev Nephrol. 2017







Native GLP-1 Compared to Approved GLP-1 Receptor Agonists



Half life = 1-2 minutes

Half life = 13 hours

Andersen, A., Lund, A., Knop, F.K. et al. Glucagon-like peptide 1 in health and disease. Nat Rev Endocrinol 14, 390–403 (2018).



קווים משיקים ברפואת הילדים 7.3.2024, מרכז רפואי שמיר

Half life = 165 hours





Muskiet MHA et al. GLP-1 and the kidney: from physiology to pharmacology and outcomes in diabetes. Nat Rev Nephrol. 2017 Nature Reviews | Nephrology



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GLP1-RA and Renal Autoregulation





Mima A et al. Protective effects of GLP-1 on glomerular endothelium and its inhibition by PKCB activation in diabetes. Diabetes. 2012



Zhuo JL et al. New Insights into the Critical Importance of Intratubular Na⁺/H⁺ Exchanger 3 and Its Potential Therapeutic Implications in Hypertension. Curr Hypertens Rep. 2021



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Impact of GLP-1 RA on Desmopressin in AVP-D

Impact of GLP-1 RA on Desmopressin in AVP-D •Case Overview:

- **Subject:** Three patients with AVP-D
- **Treatment:** Stable desmopressin regimen
- Intervention:
 - Introduction of GLP-1 RA for type 2 diabetes or obesity
- •Findings:
 - Weight Loss: 6–7% reduction in body weight
 - **Desmopressin Reduction:** 40–50% decrease in dosage
 - Thirst and Urine Output: Remained normal
 - **Medications/Diet:** No diuretics, lithium, low-sodium diet involved







- Hypothesized Effect: GLP-1 RAs may enhance desmopressin's antidiuretic effect.
- **Discussion Focus:** Interaction mechanisms and potential therapeutic implications.





Proposed mechanism of GLP-1 RA impact on sodium and water homeostasis in the kidney



Nakhleh A, Shehadeh N, Mansour B. GLP-1 receptor agonists may enhance the effects of desmopressin in individuals with AVP deficiency: a case series and proposed mechanism. Pituitary. 2024



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7.3.2024, מרכז רפואי שמיר

VASOPRESSIN SIGNAL TRANSDUCTION





ACE maintains a balance between the vasodilatory and natriuretic actions of bradykinin and the vasoconstrictive and saltretentive effects of angiotensin II. By disrupting this balance, ACE inhibitors promote natriuresis. This could theoretically weaken the natriuretic effect of GLP-1 RAs in patients taking ACE inhibitors

valsartan, an angiotensin II type 1 receptor AT1R antagonists inhibit sodium reabsorption in the proximal tubule leading to natriuresis via activation of unblocked angiotensin II type 2 receptors by angiotensin III. This could theoretically attenuate the natriuretic effect of GLP-1 RAs



Category	Patient 1	Patient 2	Patient 3
Profile	67-year-old woman	49-year-old woman	70-year-o
Medical History	AVP-D post resection of pituitary stalk tumor (14 years ago)	AVP-D post resection of non- secreting pituitary macroadenoma (4 years ago)	AVP-D po third vent (24 years
Initial Desmopressi n Dose	200 mcg/day	250 mcg/day	400 mcg/
Background Diseases	- Obesity - Hypertension - Hyperlipidemia - T2DM	- Secondary hypothyroidism - Depression - Psoriatic arthritis - Obesity	- Obesity - Hyperter - Hyperlip - Depress - T2DM - Hypoadu - Seconda hypothyro
GLP-1 RA	Semaglutide; 1 mg weekly	Liraglutide; 3 mg/day	Semagluti
Treatments	- Desmopressin - Prednisolone - Levothyroxine - Valsartan - Amlodipine - Atorvastatin	- Desmopressin - Levothyroxine - Venlafaxine - Methotrexate - Liraglutide	Desmop - Enalapri - Lercanid - Atorvast - Escitalop
Outcomes After 3-4 Months	- Weight loss: 87 kg to 82 kg	- Weight loss: 99 kg to 92 kg	- Weight I kg
Thirst	- Decreased, then normal	- Modest decrease, then normal	- Reduced
24-h Urine Volume	- 2100 ml	- 2300 ml	- 2400 ml
Desmopressi n Dose Reduction	- Reduced to 100 mcg/day	- Reduced to 150 mcg/day	- Reduced

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Hypothyroidism, if chronically uncontrolled, it may be associated with a decreased capacity for free water excretion and hyponatremia. This is due to elevated AVP levels, mainly attributed to the hypothyroidism-induced decrease in cardiac output

Glucocorticoid deficiency can lead to impaired renal free water clearance, causing water retention and dilutional hyponatremia. Additionally, cortisol deficiency stimulates the hypothalamus to increase production of CRH



CONCLUSION

Nonetheless, existing evidence supports our hypothesis and provides a plausible explanation for the observed decrease in desmopressin requirements in patients with AVP-D treated with GLP-1 RAs. However, further research is needed to confirm this hypothesis and elucidate the underlying mechanisms.





THANK YOU



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