Role of vasopressin V2 receptor in preeclampsia and therapeutic potential of its antagonist MQ232

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Preeclampsia is a common and serious complication of pregnancy. Its pathophysiology is not clearly understood, and this lack of understanding leads to a lack of therapeutics. Recent studies have suggested the involvement of vasopressin and its receptors, especially the V2 receptor (V2R). The team of Dr. KECK has developed a new model of preeclampsia using desmopressin (a specific V2R agonist) infusion in rats. In parallel, the laboratory has developed a highly specific V2R antagonist derived from the venom of the green mamba snake, named MQ232, which shows promising results for the treatment of preeclampsia.

V2R expression was quantified by Western blot in the placenta of preeclamptic and non-preeclamptic women. Pregnant rats were infused with desmopressin, with or without MQ232, and proteinuria and blood pressure were measured. The expression of sFLT1 and PlGF were measured in the rat placenta, using qPCR method.

The V2R is expressed in the human placenta, with higher levels in preeclamptic women. Pregnant rats infused with desmopressin developed symptoms of preeclampsia, like proteinuria and hypertension. Animals treated with MQ232 didn’t developped this symptoms. The sFLT1/PlGF ratio was significantly elevated in the placenta of preeclamptic rats, and returned to normal stage with MQ232.

This is the first report of V2R expression in the placenta. Its higher expression in preeclamptic women suggests its involvement. Desmopressin infusion induces symptoms of preeclampsia, while the addition of the V2R antagonist MQ232 blocks the development of these symptoms. These results suggest the potential use of MQ232 as a treatment for preeclampsia.
Topic/s: Endocrinologie

What is the impact of one-hour of supine rest on phospho-calcic metabolism ?

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Introduction: The calcium loading test, first described by Pak et al., is used to distinguish forms of hypercalciuria, although protocols vary widely. Our protocol includes a one-hour supine rest before calcium administration. While prolonged bed rest affects calcium metabolism, the impac of short-term rest remains unclear. We aimed to assess whether one hour of supine rest induces measurable changes in phosphocalcic homeostasis.

Methods: We conducted a retrospective single-centre study in Lyon including patients undergoing a calcium loading test with one hour of supine rest. Indications were hypercalciuria and elevated PTH with normocalcaemia, with or without nephrolithiasis. After a three-day low-calcium diet and a 12-hour fast, blood and urine samples were collected at baseline and after one hour, then 2 and 4 hours after oral calcium (1 g). Primary comparisons included ionised calcium, phosphate, PTH, and urinary calcium-to-creatinine ratio. Additional parameters were assessed in a subset.

Results: Among 343 patients (62% women; median age 51 years), one hour of supine rest was associated with increased ionised calcium and urinary calcium excretion, and decreased PTH and phosphate (all $p < 0.001$). Women showed a greater increase in calciuria, whereas men had a larger decrease in phosphate. No significant changes were observed in c-terminal and intact FGF23, 1,25dihydroxyvitamin, or bone markers. Renin and aldosterone decreased, with increased urinary sodium excretion, while blood pH remained unchanged.

Conclusion: One hour of supine rest induces rapid changes in phosphocalcic homeostasis and may influence calcium loading test interpretation, supporting the need for protocol standardisation.

Topic/s: Endocrinologie

EVALUATION OF CONTROLATERAL SUPPRESSION IN ADRENAL VEIN SAMPLING FOR PREDICTION OF LATERALIZATION AND POSTOPERATIVE OUTCOME IN PRIMARY ALDOSTERONISM

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Introduction

Lateralized primary aldosteronism is diagnosed by adrenal vein sampling (AVS). However, up to 70% of procedures are not bilaterally selective (hence non interpretable) and approximately 10% of patients with a lateralization index (LI) above the threshold indicating adrenalectomy ar not cured after surgery, suggesting cases of asymmetric bilateral secretion. We evaluated the performance of the Relative Aldosterone Secretion Index (RASI), defined as the ratio of adrenal to peripheral aldosterone-to-cortisol ratio, in the non-dominant adrenal ($RASI_{min}$), to predict lateralization and outcome after surgery.

Methods

We retrospectively analyzed patients who underwent AVS for primary aldosteronism at Bichat Hypertension Center (Paris, France) between 2012 and 2024. Patients with LI>4 were referred for surgery. Biochemical remission status at one year was assessed using the PASO criteria.

Results

A total of 142 selective AVS were analyzed (51% men, 45±10 years). Among them, 73 were non lateralized (51%) and 69 were lateralized (49%). The ROC-curve AUC of the $RASI_{min}$ for predicting AVS lateralization was 0.89. Twenty-eight patients (20% of the cohort) had a $RASI_{min}$ <0.44 and all were lateralized, yielding 100% specificity and positive predictive value, with 41% sensitivity. A $RASI_{min}$ cutoff value of 1 had a sensitivity of 72% and a specificity of 92%; above this threshold, only 22% of patients were lateralized.

Among patients who underwent surgery and had follow-up data available (N=51), complete biochemical success was achieved in 45 patients (88%). The ROC-curve AUC of $RASI_{min}$ for predicting biochemical cure was 0.82. Twenty-one patients (41%) had a $RASI_{min}$ below 0.44, an they all achieve complete biochemical cure, corresponding to a specificity and positive predictive value of 100%, with a sensitivity of 47%. Thirty patients (59%) had a RASI >0.44,

among whom 6 (20%) did not achieve biochemical cure. However, a high $RASI_{min}$ had limited ability to predict the absence of biochemical cure.

Conclusion

These results suggest that RASI may provide a valuable contribution to AVS interpretation. A non-dominant RASI < 0.44 may predict both AVS lateralization (with potential interest in cases of unilaterally selective AVS) and biochemical cure of primary aldosteronism (of help to safely recommend surgery). Although a high non-dominant RASI does not exclude biochemical cure, patients with lateralized AVS and a RASI >0.44 have a 20% risk of not achieving biochemical success, so that surgical decision should be cautious in these patients.

Topic/s: Endocrinologie