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Evaluation of relationship between androgen levels and cerebrospinal fluid opening pressure in women diagnosed with idiopathic intracranial hypertension

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Abstract

Objective: In this study, we evaluated the relationship of plasma and cerebrospinal fluid (CSF) testosterone and dehydroepiandrosterone sulfate (DHEA-S) levels with CSF opening pressure in women diagnosed with idiopathic intracranial hypertension (IIH). *Method:* We prospectively evaluated 52 female patients (aged 15-45 years) diagnosed with IIH according to modified Dandy criteria. In the plasma and CSF samples collected simultaneously, testosterone and DHEA-S levels were measured using chemiluminescence microparticle immunoassay (CMIA). The patients were assigned into two groups based on CSF opening pressure. The hormone levels were compared and correlation and ROC analyses were performed. *Results:* In the group with high CSF pressure ($\geq$ 40 cmH_2O), the plasma testosterone, plasma DHEA-S and CSF testosterone levels were found to be significantly higher ($p<0.05$). In addition, strong positive correlations were observed with CSF opening pressure and plasma testosterone ($r=0.856$), CSF testosterone ($r=0.870$) and plasma DHEA-S ($r=0.915$) levels. In the ROC analysis, the cut-off value was determined as $\geq$ 3.45 nmol/L for plasma testosterone, $\geq$ 295 µg/dL for plasma DHEA-S and $\geq$ 0.08 nmol/L for CSF testosterone.
Conclusion: Plasma testosterone and DHEA-S levels showed a significant relationship with CSF opening pressure. These findings suggest that plasma androgen levels can be used as a potential biomarker to predict intracranial pressure in a non-invasive manner.

Keywords: Idiopathic intracranial hypertension, androgens, testosterone, dehydroepiandrosterone sulfate, cerebrospinal fluid, biomarkers

INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a clinical syndrome characterized by elevated intracranial pressure without apparent cause, which often involves obese women at reproductive age.[1] Major risk factors include obesity and weight gain.[2] The markedly higher incidence among women indicates the possible role of hormonal factors in the pathogenesis.[3]

In recent studies, it has been suggested that IIH can be related with endocrine disorders. It has been proposed that excess androgens and imbalances in sex hormones, in particular, may contribute the disease pathophysiology by affecting CSF secretion.[4]

Current studies revealed that IIH is not only a neurological disorder but a complex disease involving endocrine and metabolic components; and that sex hormones and adipokines may influence on CSF dynamics.[5,6]

Therefore, it is thought that androgen levels measured in plasma and CSF can be potential, non-invasive biomarkers which can be used to predict intracranial pressure.

In this study, we investigated possible role of hormonal markers in the physiology of intracranial pressure by assessing the relationship between CSF opening pressure and serum and CSF testosterone and dehydroepiandrosterone sulfate (DHEA-S) levels in women diagnosed with IIH.

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METHOD

Study design and subjects

This prospective, observational study was conducted in Neurology Clinic of Van Yuzuncu Yil University, Dursun Odabaş Health Center between January 2024 and July 2024. The study included 52 women (aged 15 - 45 years) diagnosed with idiopathic intracranial hypertension (IIH) according to Modified Dandy criteria. Eligible patients were assessed consecutively throughout the study period, without any additional selection. All female patients who met the inclusion and exclusion criteria were invited to participate and were prospectively enrolled.

The exclusion criteria were male gender, presence of systemic disease, history of endocrine disease, age <15 years or >45 years (as the postmenopausal hormonal alterations may affect CSF and plasma androgen levels).

The study was approved by Ethics Committee on Clinical Research of Van Yüzüncü Yıl University, Medicine School (Approval date: 06.12.2023, Approval#: 10). All subjects gave written informed consent before participation.

Sampling and hormone measurements

The CSF and peripheral venous blood samples were drawn simultaneously with lumbar puncture. The blood samples were centrifuged at 4000 rpm for 5 minutes. The CSF and plasma samples obtained were store at -40°C until assays. The samples were thawed at room temperature. All samples were analyzed simultaneously.

In both plasma and CSF samples, the testosterone and DHEA-S levels were measured using chemiluminescence micro-particle immunoassay (CMIA) (Architect i2000SR, Abbott Diagnostics, USA).

For women, the laboratory reference intervals are 0.38–1.97 nmol/L for plasma total testosterone and 74.8–410.2 µg/dL for DHEA-S. No laboratory reference intervals are available for CSF testosterone or CSF DHEA-S.

Statistical analysis

Descriptive statistics including mean, standard deviation, median and minimum-maximum were used. Normality of data distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests.

Quantitative data were assessed using independent sample t test and Mann Whitney U test while qualitative data were assessed using Chi-square test. The correlation analyses were performed using Spearman's correlation test. Cut-off values and their discriminative power were calculates using ROC analysis.

All statistical analyses were performed using SPSS version 27.0. A p value < 0.05 were considered as statistically significant.

RESULTS

The study included 52 female patients diagnosed with IIH. The mean age was 32.6 ± 7.2 years while mean body mass index (BMI) was 31.2 ± 4.5 kg/m². The mean CSF opening pressure was measured as 43.1 ± 16.2 cmH_2O (Table 1). According to the laboratory reference intervals, plasma total testosterone was above the upper reference limit in 39/52 patients (75.0%), whereas plasma DHEA-S was above the upper reference limit in 2/52 patients (3.8%).

In the study, the subjects were assigned into two groups based on threshold CSF opening pressure (40 cmH_2O) corresponding to median CSF opening pressure calculated: Group 1 (≥ 40 cmH_2O, n=27) and Group 2 (< 40 cmH_2O, n=25). It was found that the plasma testosterone, plasma DHEA-S and CSF testosterone levels were found to be significantly higher in Group 1 when compared to Group 2 ($p < 0.05$ for all variables). CSF DHEA-S level was lower in Group 1 than in Group 2; however, the difference did not reach statistical significance ($p = 0.182$) (Table 2).

Based on correlation analysis, a strong, positive correlation was observed with CSF opening pressure and plasma testosterone level ($r=0.856$; $p<0.001$). Similarly, strong, positive correlations were detected between opening pressure and CSF testosterone level ($r = 0.870$; $p < 0.001$) and plasma DHEA-S level ($r=0.915$) levels. On the other hand, no significant correlation was detected between CSF opening pressure and CSF DHEA-S level ($r = -0.033$, $p = 0.815$)

In the ROC analysis, the plasma DHEA-S, plasma testosterone and CSF testosterone levels showed high discriminative power for predicting Group 1 patients. The cut-off value for plasma DHEA-S was ≥ 295 µg/dL (Area Under Curve [AUC]: 0.934) with a sensitivity of 92.6% and specificity of 92.0. The cut-off value for plasma testosterone was ≥ 3.45 nmol/L (AUC: 0.966) with a sensitivity of 81.5% and specificity of 96.0. The cut-off value for CSF testosterone was ≥ 0.08 nmol/L (AUC: 0.952) with a sensitivity of 96.3% and specificity of 96.3 (Figure 1).

Table 1: Demographic and hormonal characteristics of subjects

Characteristic	Mean ± SD / n (%)
Age (years)	32.6 ± 7.2
Body mass index (kg/m²)	31.2 ± 4.5
CSF opening pressure (cmH_2O)	43.1 ± 16.2
Plasma DHEA-S (µg/dL)	236.2 ± 135.3
CSF DHEA-S (µg/dL)	0.1 ± 0.2
Plasma testosterone (nmol/L)	3.0 ± 1.5
CSF testosterone (nmol/L)	0.1 ± 0.1

DHEA-S: Dehydroepiandrosterone sulfate

DISCUSSION

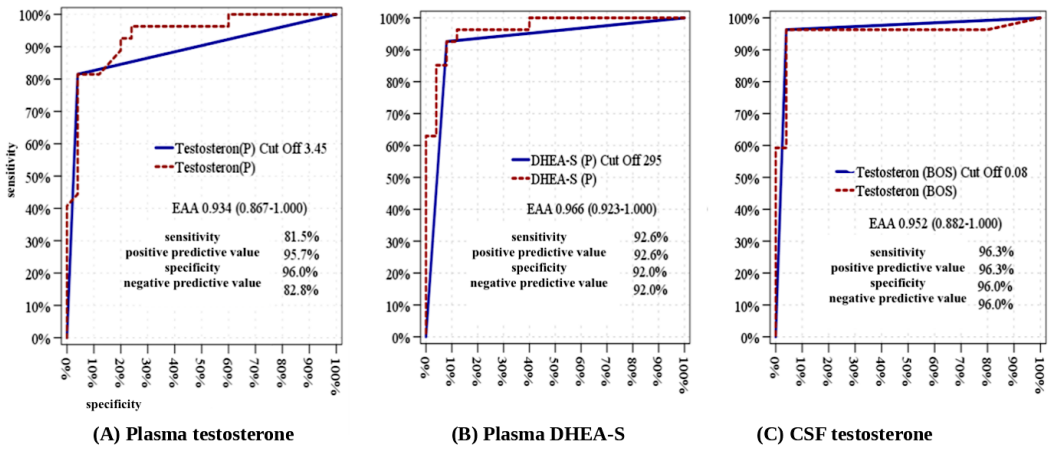
Recent studies have suggested that androgen metabolism may play a potential role in the pathophysiology of IIH. It was shown that the choroid plexus is a structure sensitive to sex hormones and that it can affect cerebrospinal fluid (CSF) composition and secretion mechanisms via androgen receptors.[7] In animal studies, it was suggested that androgens such as testosterone and DHEA-S may increase CSF secretion at the level of the choroid plexus through Na^+/K^+ ATPase and NKCC1 pump activity.[8,9] The fact that androgen receptors were demonstrated to be present in the human choroid plexus also supports the possibility that this mechanism may also be true for human physiology.[10,11] Furthermore, the case reports of IIH development in transgender individuals undergoing testosterone therapy indicate that androgen levels may have not only theoretical but also clinically significant effects.[12,13] The above-mentioned evidence suggest that the relationship between androgen levels and CSF pressure is not merely a statistical correlation but may also reflect a significant interaction in physiological and clinical manner.

Our findings are supportive above-mentioned hypotheses. In our study, it was found that plasma testosterone and DHEA-S levels as well as CSF testosterone levels showed significant positive correlation with CSF opening pressure. In the literature, there are studies on the relationship between androgen levels and CSF pressure, reporting similar findings; however, different conclusions were shown in other studies. For instance, O'Reilly *et al*. failed to show a significant relationship between plasma and CSF androgen levels and CSF opening pressure in individuals with IIH.[8] In contrast, in an experimental study using rat model, Wardman *et al*. reported a significant correlation between both plasma and CSF androgen levels and intracranial pressure.[14] Our study makes an important contribution to the literature by demonstrating a significant relationship between both plasma and CSF hormone levels and CSF opening pressure in a human sample. The diagnostic and clinical implications of such relationship are also noteworthy.

The potential effects of androgens on CSF dynamics emphasize the importance of novel diagnostic approaches for evaluating intracranial pressure. Although CSF opening pressure measurement is still considered the gold standard for assessing intracranial pressure, there is a need for the development of non-invasive alternative methods due to its invasive nature and associated risk of complications. In a review published in 2022, Dong *et al.* suggested that

Table 2: Comparison of plasma and CSF testosterone and DHEA-S levels between group 1 and 2

Androgen Level	Group 1	Group 2	p value
Plasma DHEA-S (µg/dL)	340.1 ± 57.8	123.9 ± 99.8	<0.05
Plasma testosterone (nmol/L)	4.03 ± 0.95	1.93 ± 1.08	<0.05
CSF testosterone (nmol/L)	0.22 ± 0.11	0.03 ± 0.04	<0.05
CSF DHEA-S (µg/dL)	0.04 ± 0.13	0.12 ± 0.25	0.182



(A) Plasma testosterone **(B) Plasma DHEA-S** **(C) CSF testosterone**

Figure 1. ROC curves for plasma and CSF androgen levels

various non-invasive techniques including optic nerve sheath diameter measurement, transcranial Doppler ultrasonography, tympanometry, near-infrared spectroscopy, electroencephalography, retinal vascular analysis, and optical coherence tomography have potential for use in the evaluation of intracranial pressure.[15] In this context, the use of readily available non-invasive biomarkers such as plasma hormone levels have gained increasing attention in this field. The significant correlations of plasma testosterone and DHEA-S levels with CSF pressure, in particular, allow that these parameters could be considered as practical diagnostic tools in clinical practice.

In this study, we not only described the relationship between plasma and CSF hormone levels and CSF opening pressure, but also explored ROC-derived cut-off values for plasma testosterone, plasma DHEA-S and CSF testosterone within the IIH cohort. In our sample, these cut-off values showed relatively high sensitivity and specificity for distinguishing patients with CSF opening pressure ≥40 cmH_2O from those with lower pressures. These findings suggest a possible role for these hormones as non-invasive markers of intracranial pressure severity in women with IIH. However, because the study did not include a healthy control group and was conducted in a single center, these cut-off values should be regarded as preliminary and hypothesis-generating rather than definitive diagnostic thresholds for IIH. They should not be used as stand-alone tools for clinical decision-making and should be confirmed in independent cohorts, preferably multicenter and including appropriate control groups.

From a clinical perspective, it seems that the diagnostic value of CSF testosterone levels is limited. Since CSF samples are obtained during procedures that already directly measure intracranial pressure, using hormone levels from the same sample for predictive purposes does not offer an additional practical advantage. Therefore, plasma testosterone and DHEA-S levels appear to be more relevant in clinical practice due to their accessibility and ease of measurement.

On the other hand, this study has some limitations. First, it was a single-center study, which may limit the generalizability of our findings. Second, the cut-off values calculated to predict cases with a CSF opening pressure ≥40 cmH_2O may not sufficiently identify IIH patients with CSF pressure ranging from 25 to 40 cmH_2O. In order to obtain a more reliable evaluation in this group, plasma testosterone and DHEA-S levels should be compared with those of healthy controls with normal CSF pressure. Our study focused on investigating the relationship between CSF and plasma androgen levels and CSF opening pressure. However, it was not possible to make a direct comparison with a control group, as the ethical approval did not allow lumbar punctures to be performed in healthy individuals. Future comparative studies based solely on plasma samples may help to clarify this relationship.

In conclusion, this study showed that plasma testosterone and DHEA-S levels are significantly

associated with CSF opening pressure in female patients with IIH. Our findings suggest that plasma androgen levels may have potential as non-invasive biomarkers of intracranial pressure severity; however, this requires further validation.

In addition, the cut-off values defined for plasma and CSF hormone levels provide preliminary information that may guide future work on non-invasive diagnostic approaches in this field. Overall, the findings support the role of hormonal mechanisms in the pathophysiology of IIH and provide a basis for future research on non-invasive diagnostic strategies.

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DISCLOSURE

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Conflict of interest: None

REFERENCES

1. Raoof N, Hoffmann J. Diagnosis and treatment of idiopathic intracranial hypertension. *Cephalalgia* 2021;41(4):472-8. doi:10.1177/0333102421997093.
2. Daniels AB, Liu GT, Volpe NJ, *et al*. Profiles of obesity, weight gain, and quality of life in idiopathic intracranial hypertension (pseudotumor cerebri). *Am J Ophthalmol* 2007;143:635-41. doi:10.1016/j.ajo.2006.12.040.
3. Toshniwal SS, Kinkar J, Chadha Y, *et al.* Navigating the enigma: A comprehensive review of idiopathic intracranial hypertension. *Cureus* 2024;16:e56256. doi:10.7759/cureus.56256.
4. Grech O, Mollan SP, Wakerley BR, Alimajstorovic Z, Lavery GG, Sinclair AJ. Emerging themes in idiopathic intracranial hypertension. *J Neurol* 2020;267:3776-84. doi:10.1007/s00415-020-10090-4.
5. Markey KA, Mollan SP, Jensen RH, Sinclair AJ. Understanding idiopathic intracranial hypertension: mechanisms, management, and future directions. *Lancet Neurol* 2016;15:78-91. doi:10.1016/S1474-4422(15)00298-7.
6. Abdelghaffar M, Hussein M, Abdelkareem SA, Elshebawy H. Sex hormones, CSF and serum leptin in patients with idiopathic intracranial hypertension. *Egypt J Neurol Psychiatry Neurosurg* 2022;58:39. doi:10.1186/s41983-022-00473-x.
7. Santos CR, Duarte AC, Quintela T, *et al*. The choroid plexus as a sex hormone target: Functional implications. *Front Neuroendocrinol* 2017;44:103-21. doi:10.1016/j.yfrne.2016.12.002.
8. O'Reilly MW, Westgate CS, Hornby C, *et al*. A unique androgen excess signature in idiopathic intracranial hypertension is linked to cerebrospinal fluid dynamics. *JCI Insight* 2019;4:e125348. doi:10.1172/jci.insight.125348.
9. Lowe M, Berman G, Sumithran P, Mollan SP. Current understanding of the pathophysiology of idiopathic intracranial hypertension. *Curr Neurol Neurosci Rep* 2025;25:31. doi:10.1007/s11910-025-01420-y.
10. Potter O, Menon V, Mollan SP. Risk factors and disease associations in people living with idiopathic intracranial hypertension. *Expert Rev Neurother* 2024;24:681-9. doi:10.1080/14737175.2024.2359420.
11. Li H, Liu L, Zhou Y, *et al.* Metabolic dysfunction in idiopathic intracranial hypertension: current theories and updates. *Aging Dis* 2024;16(6):3311-34. doi:10.14336/AD.2024.1147.
12. Hornby C, Mollan SP, Mitchell J, *et al.* What do transgender patients teach us about idiopathic intracranial hypertension? *Neuroophthalmology* 2017;41:326-9. doi:10.1080/01658107.2017.1316744.
13. Sigireddi RR, Lyons LJ, Lee AG. Idiopathic intracranial hypertension in a transgender female. *Can J Ophthalmol* 2019;54:e35-8. doi:10.1016/j.jcjo.2018.04.021.
14. Wardman JH, Jensen MN, Andreassen SN, *et al*. Modelling idiopathic intracranial hypertension in rats: contributions of high fat diet and testosterone to intracranial pressure and cerebrospinal fluid production. *Fluids Barriers CNS* 2023;20:44. doi:10.1186/s12987-023-00436-1.
15. Dong J, Li Q, Wang X, Fan Y. A review of the methods of non-invasive assessment of intracranial pressure through ocular measurement. *Bioengineering* (Basel) 2022;9:304. doi:10.3390/bioengineering9070304.