## **Cyproterone acetate**

Cyproterone acetate (CPA), sold alone under the brand name Androcur or with ethinylestradiol under the brand names Diane or Diane-35 among others, is an antiandrogen and progestin medication used in the treatment of androgen-dependent conditions such as acne, excessive hair growth, early puberty, and prostate cancer, as a component of feminizing hormone therapy for transgender women, and in birth control pills.

It is formulated and used both alone and in combination with estrogen, and is available for use by mouth. CPA is taken by mouth one to three times per day.

## Systematic review and meta-analysis

A systematic review and meta-analysis attempted to assess real-world evidence of the association between CPA and the occurrence of intracranial meningiomas. Systematic searches of Ovid MEDLINE, Embase and Cochrane Controlled Register of Controlled Trials, were performed from database inception to 18th December 2021. Four retrospective observational studies reporting 8,132,348 patients were included in the meta-analysis. There was a total of 165,988 subjects with usage of CPA. The age of patients at meningioma diagnosis was generally above 45 years in all studies. The dosage of CPA taken by the exposed group (n = 165,988) was specified in three of the four included studies. All studies that analyzed high versus low dose CPA found a significant association between high dose CPA usage and increased risk of meningioma. When high and low dose patients were grouped together, there was no statistically significant increase in risk of meningioma associated with use of CPA (RR = 3.78 [95% CI 0.31-46.39], p = 0.190). Usage of CPA is associated with increased risk of meningioma at high doses but not when low doses are also included. Routine screening and meningioma surveillance by brain MRI offered to patients prescribed with CPA is likely a reasonable clinical consideration if given at high doses for long periods of time. Our findings highlight the need for further research on this topic <sup>1)</sup>.

## **Case series**

A study prospectively followed 108 women with 262 intracranial meningiomas and documented progestin cyproterone acetate (PCA) use. A per-meningioma analysis was conducted. Changes in meningioma volumes over time, and meningioma growth velocities, were measured on magnetic resonance imaging (MRI) after stopping PCA treatment.

Mean follow-up time was 30 (standard deviation [SD] 29) mo. Ten (4%) meningiomas were treated surgically at presentation. The other 252 meningiomas were followed after stopping PCA treatment. Overall, followed meningiomas decreased their volumes by 33% on average (SD 28%). A total of 188 (72%) meningiomas decreased, 51 (20%) meningiomas remained stable, and 13 (4%) increased in volume of which 3 (1%) were surgically treated because of radiological progression during follow-up after PCA withdrawal. In total, 239 of 262 (91%) meningiomas regressed or stabilized during follow-up. Subgroup analysis in 7 women with 19 meningiomas with follow-up before and after PCA withdrawal demonstrated that meningioma growth velocity changed statistically significantly (P = .02). Meningiomas grew (average velocity of 0.25 mm3/day) while patients were using PCA and shrank (average velocity of -0.54 mm3/day) after discontinuation of PCA.

Ninety-one percent of intracranial meningiomas in female patients with long-term PCA use decrease or stabilize on MRI after stopping PCA treatment. Meningioma growth kinetics change significantly from growth during PCA usage to shrinkage after PCA withdrawal<sup>2</sup>.

## **Case reports**

a 69-year-old transgender woman who underwent gender-affirming surgery in 1998 and genderaffirming hormone therapy (cyproterone acetate (CPA) and estradiol) since this time. Following an MRI scan to investigate tremor in 2013, an incidental left anterior clinoid and right petrous meningioma were identified. Subtotal surgical resection was achieved for the anterior clinoid meningioma (WHO grade 1, meningothelial subtype). At follow-up in 2016, an olfactory groove meningioma and left greater wing of sphenoid meningioma were identified. By 2017, both tumours, along with the petrous meningioma, demonstrated significant growth. In 2018, clinical decline was evident and MRI demonstrated further tumour growth. Surgery was scheduled and the olfactory groove meningioma was completely resected (WHO grade 2, chordoid subtype). Hormones were stopped, after which regression of the petrous meningioma was observed. This case demonstrates an association between high-dose CPA and estradiol and the development, growth and regression of meningiomas in a transgender woman <sup>3)</sup>.

1)

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