

Nilutamide and chromatopsia

Introduction

Nilutamide is indicated for *the palliative treatment of inoperable prostate carcinoma combined with pharmacological or surgical castration* [1]. The most common adverse drug reactions are impaired adaptation to darkness and nausea [2]. Visual disturbances associated with nilutamide are well known. Nilutamide (Anandron®) has been approved for marketing in the Netherlands in 1996.

The Summary of Product Characteristics mentions a delayed adaptability to darkness in about 50% of the patients [1]. The Netherlands Pharmacovigilance Centre received two reports of patients who experienced chromatopsia associated with the use of nilutamide. Chromatopsia is a condition in which objects appear to be abnormally coloured or tinged with colour.

Reports

Patient A is a 71-year-old male who had been using nilutamide 150 mg tid for prostate carcinoma. Concomitant medication used was cortisone 20 mg three times daily, enalapril 10 mg once daily and clodronate 520 mg twice daily. Within one day after starting nilutamide he experienced a defective colour vision together with problems with adaptation to darkness. The objects he observed had a yellowish colour and white surfaces appeared to be purple. In addition he reported nausea and dizziness which diminished after continuing drug use. However, the disturbance in colour vision persisted.

Patient B is a 66 year-old male who had been using nilutamide 150 mg twice daily for one month, after which the dosage was reduced to 150 mg once daily. Concomitant medication used was magnesiumhydroxide 724 mg tid, esomeprazole 20 mg once daily, cyklokapron 500 mg once daily and solifenacin 10 mg once daily, prednisone 5 mg twice daily and buserelin 9.45 mg injections every three months. Two weeks after starting nilutamide he got a reddish vision especially looking at lamps, together with a delayed adaptability to darkness. The outcome of the complaints is unknown.

Other sources of information

Literature

Delayed adaptability to darkness, characterized as a delay in recovering visual function after bright illumination (sun, bright light), is the most frequent effect, of prostatic carcinoma patients receiving nilutamide alone or combined with orchiectomy or luteinising hormone-releasing hormone (LHRH) agonists. Detailed ophthalmological examination revealed an increase in the photostress recovery time to an average of 9 minutes, while the upper limit of normal is 1 minute and 20 seconds [3]. The photostress recovery time is the time required to read the Snellen test letters on the line above that of best corrected visual acuity.

A randomized double-blind study, comparing orchiectomy combined with nilutamide versus orchiectomy (n=78) combined with placebo (n=72) in patients with prostate cancer mentioned the occurrence of chromatopsia in 2 (3%) patients in the orchiectomy combined with nilutamide arm, whereas this ADR was not found in the placebo-arm [2].

Databases

In the database of the Uppsala Monitoring Centre, chromatopsia has been reported three times. A delayed adaptability to darkness cannot be reported as such, since no code is available in the WHO terminology.

Discussion

Chromatopsia has been associated with the use of various drugs. In the human eye, the cones that are mainly situated in the macula, are maximally receptive to short, medium, and long wavelengths and response to blue, greenish and red light. Colour perception is therefore mainly a function of the macula. The study of Harois *et al.* showed a delayed photostress recovery time, which is also indicative of an impaired function of the macula [3]. Although the mechanism associated with the change in colour perception associated with nilutamide is not known, it is very likely that a differential adaptation to light of the various types of cones of the macula might play a role in the pathogenesis of this phenomenon. This is supported by the fact that both patients reported a change in colour vision together with this delayed adaptability to darkness.

Conclusion

Next to a delayed adaptability to darkness, chromatopsia may occur during the use of nilutamide. Although both adverse reactions may be related, it should be clear for the patients involved that also disturbances of the colour vision may occur.

References

1. Dutch SPC Anandron (version date 21 august 2006). Assessed 2006.
2. Janknegt RA, Abbou CC, Bartoletti R, Bernstein-Hahn L, Bracken B, Brisset JM et al. Orchiectomy and nilutamide or placebo as treatment of metastatic prostatic cancer in a multinational double-blind randomized trial. *J Urol.* 1993;149:77-82.
3. Harois C, Malenfant M, Dupont A, Labrie F. Ocular toxicity of Anandron in patients treated for prostatic cancer. *Br J Ophthalmol.* 1986;70:471-3.