

IBUPROFEN-INDUCED VISION DAMAGE: A CASE REPORT AND LITERATURE REVIEW

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Abstract: Background: Ibuprofen-induced vision damage is a rare but potentially grave complication, and there is lack of special treatment for this adverse drug reaction. After analyzing this case report and the literature, we highlighted the importance of early recognition of drug-induced vision damage and discussed the probable mechanism of ibuprofen-induced vision damage, so that the offending drug can be withdrawn, and recurrences prevented. **Case presentation:** We reported a case of a 65-years old Chinese man with the diagnosis of ibuprofen-induced vision damage. The man was treated with 300 mg ibuprofen capsules orally twice a day for headache, after 3 days, the vision of both eyes was blurred with the sense of vision decreased. After medication, the vision of both eyes returned to 0.6 during the 6-month follow-up period. **Conclusion:** When abnormalities in vision are found after medication of ibuprofen, drug-related vision damage should be considered, and the medication situation should be analyzed and treated symptomatically as soon as possible.

Keywords: Ibuprofen; Vision damage; Case report

Introduction

Ibuprofen is an antipyretic and analgesic, a non-steroidal anti-inflammatory drug (NSAID). This drug can inhibit cyclooxygenase, reduces prostaglandin synthesis, and produces analgesic and anti-inflammatory effects. It also acts as an antipyretic by regulating the center of hypothalamic body temperature[1]. It is widely used in relieving chronic or mild to moderate pain such as headache, joint pain, migraine, toothache, muscle pain, etc. It is also for fever caused by common cold or influenza. Although the main adverse drug reaction (ADR) of ibuprofen is the gastrointestinal adverse reactions, including indigestion, burning sensation, stomach pain, nausea and vomiting, vision damage is rarely observed and reported[2,3]. Since ibuprofen is considered as OTC drugs which can be bought in the public-pharmacy shop, so to know the ADR of ibuprofen is quite important. In this report, we introduced and analyzed a case of visual damage/adverse events caused by ibuprofen oral preparations. The aim is to understand its risk factors and provide considerations for clinical rational drug use.

Case Presentation

In this report, we presented a patient who had an optic nerve disorder during the short-term use of ibuprofen. The patient is a 65-years old man,

complained for continuous headaches from Oct 15th to Oct 22nd 2019, mainly in the forehead and top of the head. He was diagnosed as "angiopathic headache" and treated with 300 mg ibuprofen capsules orally twice a day. After 3 days, the headache was relieved, but he felt nausea, vomiting, and the vision of both eyes was blurred with the sense of vision decreased gradually, no light in the left eye, the right eye only visible low light.

These symptoms were diagnosed as "acute optic neuritis in both eyes" by an ophthalmologist. So, the pharmacist reported this ADR from Adverse Drug Reaction Reporting System in China in 5 days. After discontinuation of the drug and treatment with 10mg intravenously guttae once a day Dexamethasone and 40mg intravenously guttae once a day Ganglioside for 10 days and then changed Dexamethasone into Prednisone 30mg orally once a day, 10mg orally once a day, 5mg orally once a day for 7 month. During the medication therapy course, we tested CYP2C19 genes to find out whether this ADR is caused by the gene type, after this patient discharged from the hospital, we had kept following up for a long time. And the following up results showed that the vision of both eyes returned to 0.6 during the 6-month follow-up period. In order to clarify the whole treatment of this patient, we tried to set up a timeline of medical treatment during his inpatient time (Fig. 1).

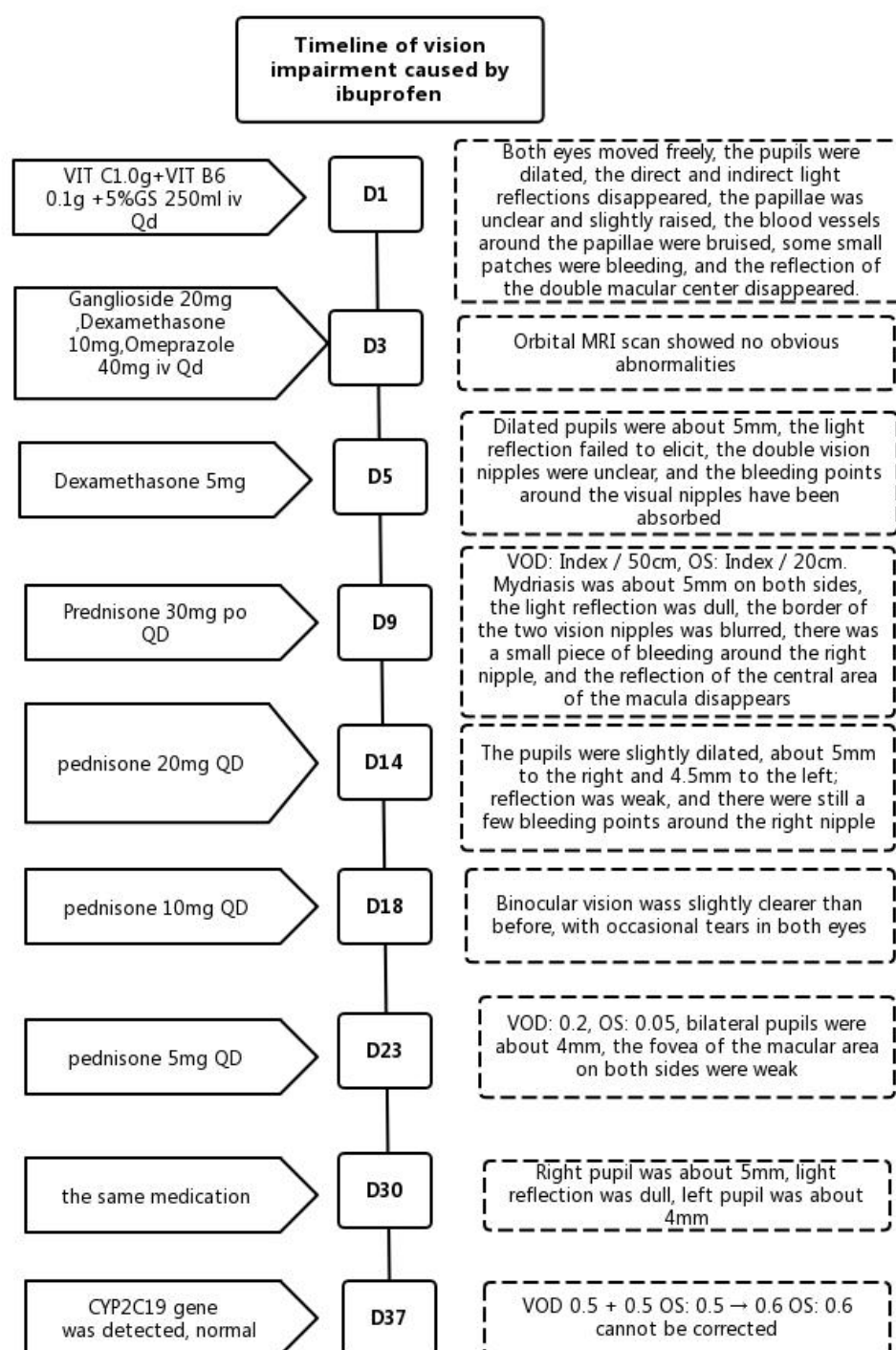


Fig. 1 The timeline of the vision impairment and medical treatment of the patient (VIT: Vitamin; GS: Glucose injection solution; VOD: Visio Oculus Dexter; OS: Oculus Sinister; MRI: Magnetic Resonance Imaging)

Discussion

Overview of ADR/ADE and visual abnormalities of ibuprofen

In order to find out whether there were similar ADR reports published. We searched the literature on these

databases on the website. There are many reports of ADR / ADE in the literature, mainly involving allergic reactions (drug rash, anaphylactic shock, *etc.*), digestive system reactions (gastrointestinal bleeding, drug-induced hepatitis, hypoglycemia, *etc.*),

nervous system reactions (meninges, inflammation, dizziness, etc.), urinary system reactions (acute renal failure, etc.), respiratory system reactions, cardiovascular and hematological reactions. But there was just little literature about vision damage reported[4-6].

The earliest case was reported in February 1970, ibuprofen was thought to be the cause of the reduced visual acuity and visual field defects of a woman aged 71[7].

Compared with other NSAIDs such as celecoxib, rofecoxib, the visual abnormalities caused by ibuprofen are rare (reported the rate is less than 1 %)[8], and its clinical manifestations are mainly blurred vision, blind spots, weak visual, color changes, and visual contrast sensitivity are reduced[9]. Consistent of the data in our case report, the visual abnormalities reported in the literature can be improved and the prognosis is good when the drug is stopped.

From the database, we observed that the vision damage has been rarely associated with ibuprofen intake in normal dose. We reported this case of ocular toxicity resulted in the vision damage following a short-term but regular dose of ibuprofen in-taking. Although idiopathic optic neuritis cannot be completely ruled out, following the evaluation criteria of WHO for ADR and Naranjo's APS scoring we discussed the correlation between ADR and ibuprofen, analyzed the time of medication, absence of other risk factors and additional findings over the improvement after discontinuation of the drug, etc. As a result, Naranjo's APS score was 7, and the correlation between ADR and ibuprofen was considered as possible following the evaluation criteria of WHO.

The mechanism of ibuprofen visual abnormality

Although, visual abnormalities caused by ibuprofen are very rare (reported incidence is less than 1 %) [10], and its clinical manifestations are mainly blurred vision, visual blind spots, amblyopia, color changes, and reduced visual contrast sensitivity [11-13]. Consistent with this case report, the visual abnormalities reported in the literature can be improved after stopping the drug.

However, the mechanism of the vision damage caused by ibuprofen is not clear, we searched the literature and find out some suggestions as follows: The analgesic mechanism of ibuprofen is by blocking cyclooxygenase(COX), thereby preventing arachidonic acid converting into prostaglandin (PG) and thromboxane (TX) to exert analgesia, anti-inflammatory and antipyretic effects, its ADR / ADE may occur with its non-selective inhibition of COX-1 and COX-2. Retinal endothelial cells can release a variety of active substances to regulate retinal blood flow amount of arachidonic acid [such as cycloprostaglandin (PGI2) and prostaglandin F2a (PGF2a)] can swell retinal blood vessels and increase

blood flow; thromboxane A2 (TXA2) reduces blood flow. The effect of COX-2 inhibitors on vision maybe through this mechanism that COX-2 inhibitors can directly inhibit the release of PGI2, there by inhibiting the secretion of vascular endothelial cells. A vasodilator substance NO and affect it to regulate retinal blood flow. A vasodilator substance NO and affect it to regulate retinal blood flow. PGI2 stimulating factor (PSF) stimulates PGI2 synthesis by endothelial cells[8]. Hata Y[14] *et al.* found that PSF is expressed and regulated in rat retinal cells and artificially cultured bovine retinal cells. By immunohistochemical analysis, PSF was mainly expressed in the retinal vessel wall. The researchers further demonstrated that PGI2 can increase blood flow in the retina of normal and diabetic rats, and that changes in retinal blood flow are related to retinal PSF. In addition, according to Weber A[15] *et al.*, COX-2 inhibitors reduce intraocular pressure and cause visual abnormalities. As a non-steroidal anti-inflammatory drug and a COX-2 inhibitor, ibuprofen may reduce the retinal blood flow and reduce the intraocular pressure through the above routes, leading to visual abnormalities.

Ibuprofen is absorbed orally quickly, though the absorption is getting slowly with food, the absorption does not decrease with the ibuprofen plasma protein binding rate was 99 %. The blood drug concentration reached a peak of 1 to 2 hours after taking the drug, $T_{1/2}$ was 1.82 hours after one dose, and the synovial fluid drug concentration was equal to the plasma drug concentration after 5 hours of administration. The synovial drug concentration was higher than the plasma drug concentration within 12 hours^[1].

And as the same as other NSAIDs, such as celecoxib, rofecoxib, ibuprofen is metabolized mainly by cytochrome P450(CYP)2C9: one of the CYP liver microsomal enzyme. In some researches, comparisons were made between matched populations of patients with visual disturbance, comparing CYP2C9 genotypes of patients from the intensive medicines monitoring program (IMMP) treated with celecoxib or rofecoxib with those of patients treated with the COX-2 inhibitors without any adverse effect. In the small study, there were no differences between cases in the frequencies of the variant alleles of CYP2C9 that were likely to lead to a difference in response. We also tested this genotype of this patient, the result is similar as that study, there were no more gene mutation of CYP2C9 of this patient.

Conclusion

Visual abnormalities caused by ibuprofen may not be related to age, gender, and primary disease, and this kind of ADR can occur under normal usage and dosage. Generally, withdrawal or after symptomatic treatment and other measures, most of the symptoms of visual abnormalities can disappear within 1 to 3

days[16]. Although rare reports of ocular toxicity of ibuprofen were reported, it must also be taken seriously attention by doctors. When abnormalities in vision are found after medication of ibuprofen, drug-related vision damage should be considered, to avoid recurrence of severe ADR/ADE.

Competing Interests

The authors declare that they have no competing interests in this section.

Contributions

Qi Chen analyzed and interpreted the patient data and was a major contributor in writing the manuscript. Wen-wu Peng and Hai Zhang participated in the whole clinical treatment of all the patient. All authors read and approved the final manuscript.

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Ethics Approval And Consent To Participate

Written informed consent for publication of this paper was obtained from the patient.

Availability Of Data And Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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