

## Atypical Macular Distortion After Chlorine Dioxide Administration Case Report

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### ABSTRACT

Chlorine dioxide, and its byproducts, chlorite, and chlorate, at daily dose of 5 ppm, administered to normal healthy adult male volunteers for 12 weeks, was accompanied by no clinically important physiological effects. An extensive battery of tests was used to evaluate the physiological impact of the ingested water disinfectants [1].

Chlorination of potable water supplies has been the standard method of disinfection for about 75 years. Recently, concern has been raised about the propensity of chlorination to introduce potentially carcinogenic trihalomethanes (THM) such as chloroform into finished water. An alternative to chlorination which does not generate THM during disinfection is chlorine dioxide, but there are concerns about the acute and chronic toxicity of ClO<sub>2</sub> and its disinfection by-products, chlorite, and chlorate. Deleterious effects of moderately high levels of these oxychlorines have been demonstrated experimentally on red blood cells, thyroid function, and development in laboratory animals [2]. In this paper, we describe the severe involvement of the left macula because of chlorine dioxide self-administered at doses well above 40 ppm for 10 month.

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### Introduction

Disinfection is the last treatment stage of any Drinking Water Treatment Plant (DWTP) and is carried out to maintain a residual concentration of disinfectant in the water distribution system. Chlorine dioxide (ClO<sub>2</sub>) is a widely used chemical employed for this purpose. However, chlorine dioxide leads to the highest production of chlorite and chlorate.

The world-wide deployment of cruise liners and naval units has caused an increased need for the disinfection of drinking water. The main cause for this is the unknown quality of drinking water in foreign harbors--besides the formation of bio-films due to the climatically disadvantageous conditions in the operational area. Water conduits on board are currently disinfected with calcium hypochlorite in case of microbiological contamination [3]. Similar methods are used in airplanes.

Chlorine dioxide has been historically used as a disinfecting agent for drinking water supplies and surfaces. Widespread use as an alternative option for prevention and treatment of COVID-19 has emerged due to a lack of specific treatment [4]. Chlorine

dioxide has come into widespread use as a potential treatment or prevention option despite the absence of evidence regarding safety and efficacy. Thereby, acute kidney injury (AKI), decreased red blood cell counts, oxidation of hemoglobin to methemoglobin, depletion of glutathione concentration, increasing the levels of hydrogen peroxide, lipid peroxidation, intravascular hemolysis, cell injury, myocardial damage, have been reported due to chlorine dioxide ingestion [5-9].

Also, altered mental status, abdominal pain, diarrhea, arterial hypotension, anuria, nausea, vomiting, diarrhea, and mild confusion, cyanotic, lowered consciousness, vomiting and incontinence were published already [10-12].

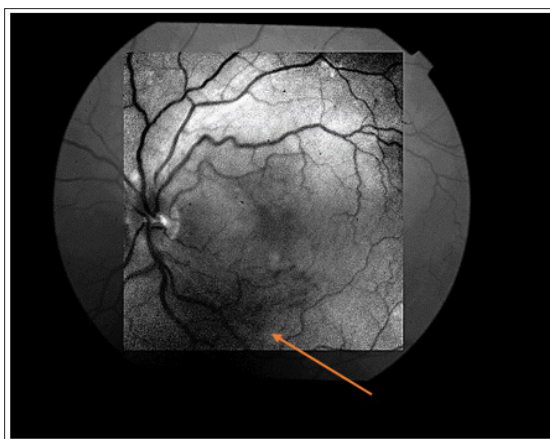
There is scarce information regarding the toxicity of chlorine dioxide, but some important side effects have been reported. We present the case of an 80-year-old female who developed an atypical worsening of macular degeneration.

### Clinical case

Female patient, with date of born 07/04/1946, the patient is being treated since 04/08/2008, in our clinic, for bilateral macular degeneration, with good results [13]. (Figure 1)



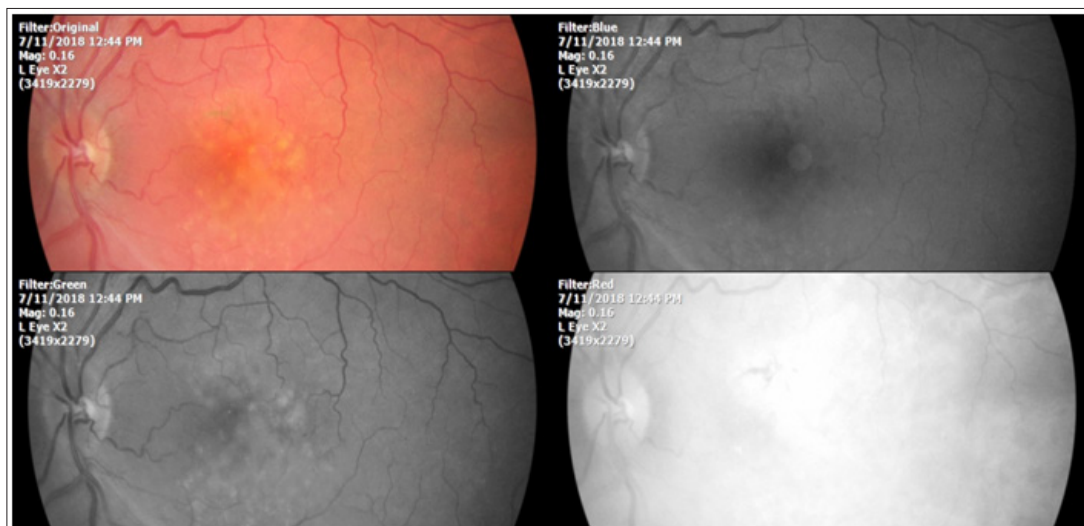
**Figure 1:** Ocular fundus, right eye, this photograph was taken at 04/08/2008, during first consultation. Orange arrow shows an exudate



**Figure 2:** Photograph of the left eye, taken at 04/08/2008, first consultation, shown macular edema, exudates, and hemorrhages in inferior part of macular region (arrow)



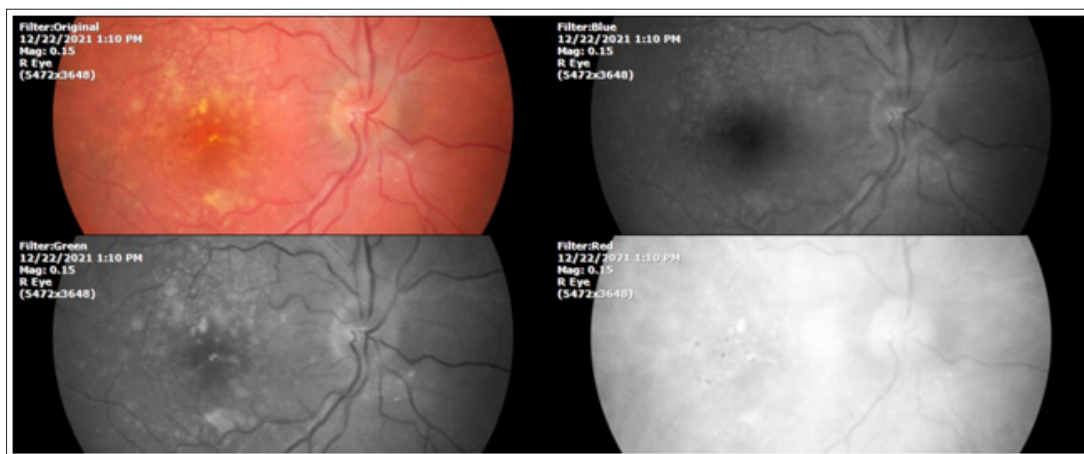
**Figure 3:** Photography of right eye, taken at 07/11/2018. After 10 years of continuously treatment with QIAPI 1®, the appearance of macular area is acceptable, and her vision 20/30. The macular imagen with blue filter (upper right), seems particularly good. The morphologic characteristics of the optic disk are well preserved.



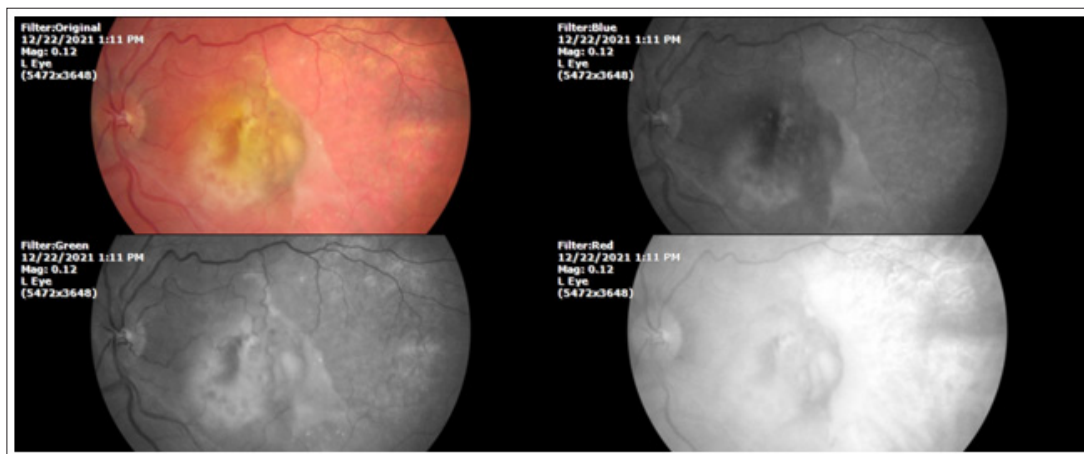
**Figure 4:** Left eye, fundus photography taken at 07/11/2018. Morphologic characteristics of macula are relatively well preserved, the visual acuity was 20/25. Appearance of optic disk is unremarkable

The patient began to take chlorine dioxide, by own decision, without knowing the concentration, and without medical supervision, about ten months before going to the last consultation at 12/22/2021.

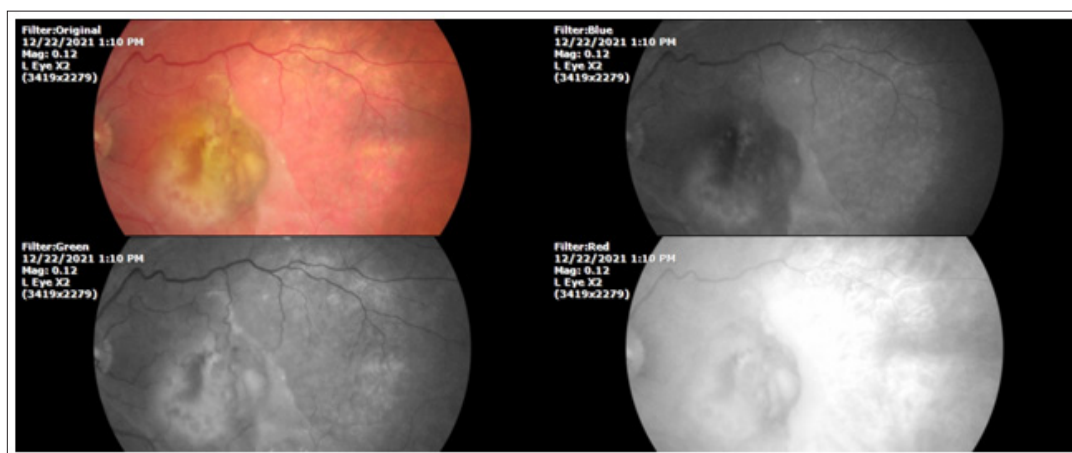
In the consultation of December 22, 2021, the patient reports low vision in the left eye that began gradually has been getting worse, and on examination we found an unusual distortion of the anatomy of the macula of the left eye.



**Figure 5:** There is a relative decrease in soft exudates in the temporal region of the macula of the right eye. In the lower right image (red filter), the presence of dark spots is observed, which partially obstruct the lumen of the choroid vessels.



**Figure 6:** The image of the left macula shows a very marked deterioration, the choroid vessels of the temporal region of the macula are observed bloodless, and the overlying retina shows even reactive gliosis with the formation of an epiretinal membrane in the temporal side of macular region.



**Figure 7:** In this photograph the extent of choroidal involvement is observed

The fragmented-like appearance of choroidal layer, glial activation, and distorted morphology of the left macula, forming a sui generis pattern with significant differences of other frequent maculopathies, suggesting adverse effects of chlorine dioxide in presumable higher doses than 40 ppm.

The lightening property of chlorine dioxide could exploit the deleterious effects on the choroid, by affecting the properties of the pigments in the area, for example melanin, hemoglobin, and cytochrome P450; which would affect the complex and astonishingly exact biochemical logic of the retina, pigmented epithelium, and choroid.

The recommendation about the use of chlorine dioxide as a panacea usually comes from people without adequate medical training, so they are not able to recognize the adverse effects of a compound that is not normally found in nature. The wide availability of chlorine compounds, and the scarce information about their adverse effects, make this compound a dangerous agent for the physical integrity of patients.

### Comment

Chlorine dioxide (CD) is a yellow to reddish-yellow manufactured gas. It does not occur naturally in the environment. When added to water, chlorine dioxide forms chlorite ion, which is also a very reactive chemical. Chlorine dioxide is used as a bleaching agent at paper manufacturing plants, and in public water treatment facilities to make water safe to drink. In 2001, chlorine dioxide and chlorite were used to decontaminate several public buildings following the release of anthrax spores in the United States [14].

The market available water disinfectant solutions have an average concentration of 5 ppm, a way beyond of empirically recommended dose of 7000 ppm, thereby is not rare accidental intoxications and some even with fatal outcome.

CD at concentrations ranging from 1 to 100 ppm produced potent antiviral activity, inactivating  $\geq 99.9\%$  of the viruses with a 15 sec treatment for sensitization [15]. However, the biochemical processes in the different living entities are like each other, so low doses that inactivate viruses or bacteria or fungi, also affect the biochemical processes of eukaryotic cells, and worse, the proper control of a gas such as CD is particularly difficult and prone to accidents.

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