



### **G143 Death Following Retrobulbar Injection of Desmopressin for the Treatment of Non-Arteritic Anterior Ischemic Optic Neuropathy: Which Implications of an Off-Label Use**

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After attending this presentation, attendees will be aware of the possible clinical and legal implications following off-label use of corticosteroids and desmopressin for the treatment of Non-Arteritic Ischemic Optic Neuropathy (NAION).

This presentation will impact the forensic science community by illustrating a case of fatal acute myocardial infarction after retrobulbar injection of synthetic replacement of vasopressin.

Since a standard treatment for NAION with proven efficacy is not available to date, most therapeutic approaches are empirical and include a wide range of agents presumed to act on thrombosis, on the blood vessels, on the disk edema, or presumed to have a neuroprotective effect. Among other proposed treatments retrobulbar injection of corticosteroid and desmopressin represents an invasive approach, with potential local and systemic complications. Which is believed to have never been documented before. The rationale for using desmopressin in the treatment of NAION is uncertain and probably consists in experimental findings demonstrating that desmopressin induces ciliary artery relaxation in dogs via V1-receptors through a mechanism which involves nitric oxide. In turn, this would enhance vascular permeability, thus facilitating the re-absorption of optic edema. A similar vasodilation effect can be attributed to corticosteroids.

A 60-year-old man, apparently healthy with negative history for cardiovascular diseases, was hospitalized because of a unilateral sudden and painless severe visual loss (20/200) on waking in the morning. The optic disc appeared hyperemic and edematous, with a focal severe swelling. Relative inferior altitudinal scotoma was present at visual field examination. The patient presented with erythrocyte sedimentation rate 20mm/h and normal levels of plasma fibrinogen and C-reactive protein. The diagnosis of NAION was made. Two separate and immediately consecutive injections of betamethasone (2mg/0.5ml) and desmopressin (2mcg/0.5ml) were performed in the retrobulbar space. The administration of any preoperative medication or cardiovascular examination is not documented. In the patient medical records, the total volume of the injections and the size of the needle used are not specified. The procedure was technically uncomplicated without any monitoring in progress during injections such as ECG, peripheral oxygen saturation, or blood pressure measurement. Fifteen minutes later, the patient suddenly developed cold sweat, dyspnea, thoracic pain and severe hypotension. ST segment elevation Acute Myocardial Infarction (AMI) was diagnosed by ECG. Intensive care support was initiated. However, despite cardiopulmonary resuscitation, the patient died of irreversible cardio-respiratory arrest. At autopsy, the heart presented with a normal shape and weight (350g); coronary arteries showed significant atherosclerotic luminal narrowing. Histological investigation showed a stenotic atherosclerotic plaque (95%) complicated by culprit thrombosis of the Left Anterior Descending (LAD) artery, 2cm after its origin. Examination of the other organs was unremarkable, except for mild pulmonary edema and polyvisceral stasis. There was no evidence of increased orbital volume or sign of vagal compression secondary to retrobulbar hemorrhage.

Professional autonomy in the health care decision-making process renders the physician free to prescribe a drug for purposes other than that which it has been approved, where it is considered both safe and effective according to his/her professional judgement.

The use of unlicensed and off-label medicines is a widely used medical practice mainly in certain clinical settings.

Physician's autonomy in healthcare decision making represents an instrument to guarantee the progress and evolution of scientific knowledge and to realize in the meantime the most effective safeguard of health protection and promotion.

Though off-label prescription is common and sometimes necessary for providing a pathway to clinical practice innovation, it presents significant risks. This practice may lack rigorous scientific scrutiny and there is little known about the degree of scientific evidence supporting it. According to the literature, a high percentage, around 73%, of off-label use had little or no scientific confirmation.

Unexpected, adverse effects represent a possible risk. Since the off-label practice may expose patients to avoidable risks, it is mandatory for doctors to follow the lawful direction and ethical recommendation.

This case is out of the ordinary for the forensic scientist because of the possible recognition of medical liability for personal injuries and murder when a patient has psycho-physical damage or dies as consequence of the administration of an off-label drug.

#### **Desmopressin, Non-Arteritic Anterior, Off-Label Prescriptions**