

EXPERIMENTAL PROTOCOL OF DENTAL PROCEDURES IN PATIENTS WITH HEREDITARY ANGIOEDEMA: THE ROLE OF ANXIETY AND THE USE OF NITROGEN OXIDE

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SUMMARY

Hereditary angioedema (HAE) is a rare disease, little known to the medical and dental community, but with a growing rate of hospitalization over the years. HAE is due to a deficit/dysfunction of C1 esterase inhibitor which leads to an increase in vascular permeability and the appearance of edemas widespread in all body areas.

The airways are the most affected and laryngeal swelling, which can occur, it is dangerous for the patient's life, is also a sensitive spot in our daily practice, therefore, it is also important to be aware of all the signs of this disease.

Episodes of HAE have no obvious cause, but it can be triggered by anxiety, invasive procedures and trauma. So this disease is a major problem in oral and maxillofacial surgery, ENT, endoscopy, emergency medicine and anesthesia because even simple procedures can cause laryngeal edema.

The recommendations on the management of HAE include long- and short- term prophylaxis and treatment for acute attacks, however, the importance of anxiety control during the operating phases is undervalued. The present work suggests an experimental protocol for the surgery management of HAE patients with the help of nitrous oxide, with a brief review of the literature on this topic.

Key words: hereditary angioedema, dental surgery.



Introduction

The Hereditary Angioedema (HAE) is a rare genetic disease that affects a number of people between 1:10,000 and 1:50,000 (1), presents a chronic course, disabling and like all rare disease is difficult to diagnose if not promptly evaluated in a center that specializes in the diagnosis and care.

In the specific case of hereditary angioedema, the diagnosis can arrive even after 15 years during the onset of symptoms (2). Hereditary angioedema is inherited as an autosomal dominant trait and is caused by a mutation of the gene en-

coding the C1 inhibitor which is located on chromosome 11. The C1 inhibitor is an inhibitory protein of the complement system. The complement is a multienzyme system of the plasma formed from about 30 proteins; the majority of which is synthesized by the liver.

The mutations cause a defect of the inhibitor of C1, which results in a reduced level of serum to decreased synthesis or in a reduced activity of the inhibitor of C1 esterase: in both cases occurs an uncontrolled activation of the complement system which can not be inhibited. This activation, uncontrolled, generates vasoactive mediators that induce edema.

They recognize two types of Hereditary An-

gioedema: type I is the most common form (85% of patients) and is characterized by a quantitative defect; the type II, (15% of patients) is characterized by a protein not working.

Symptoms typically include attacks of edema of the face, extremities, the trunk, the upper airway and the abdominal viscera which apparently occur spontaneously or subsequent to trauma. Edema of the skin is the most common symptom (97%), mainly affects extremities, hands, arms, feet and in 60% of cases the upper limbs.

In 78% of patients with edema of the skin also it shows edema of the face and in most cases this phenomenon can affect the larynx, with change of voice (deep voice, hoarseness, aphonia), associated with wheezing and a feeling of suffocation (3). The aims of treatment are addressed to avoid behavior/therapies that favor the onset of attacks. The treatment is twofold: short-term prophylaxis to be made with Berinert or Cirnyze in the hours prior to any outpatient surgery; long-term treatment with the same drugs to be carried out in patients with high rate of acute attacks. Anxiety is a major cause of perioperative stress that affects the quality of life, increasing the perception of pain and impairing the result (4).

In cases of HAE, careful anxiety management can reasonably expect to be important in preventing the attacks, as well as having an overall positive impact on patient prognosis and overall quality of care. The scarcity in the literature about the management of this rare condition has necessitated the development of an experimental protocol for the drafting of standardized guidelines about dental procedures. This protocol, in addition to ensuring the rapid clinical diagnosis of angioedema and the consequent correct therapeutic approach, has the ultimate goal of sending the patient to the next and appropriate diagnostic procedure.

It is, therefore, extremely important to manage the patient through careful psycho-physical assessment of the subject.

Control of anxiety was associated with dental practices and the use of conscious sedation is the first choice for the prevention of acute events of hereditary angioedema.

Materials and methods

Records of HAE patients, treated at the UOSD of diagnosis, hygiene and oral prevention of the "Tor Vergata" Hospital of Rome from 2013 to 2015, were 6. They were considered for the study, only patients with a confirmed diagnosis of HAE and with appropriate clinical histories, including relevant details on the course of their HAE. All patients were placed in Day Surgery and followed up with a protocol developed by our team. This protocol provides a first part anamnestic, a second clinical-pathological part through the use of a questionnaire designed by our team in order to inquire about the pathology and finally a last part psycho-clinical through the Italian version of the dental Scale of Corah anxiety (CDAS) and the visual analogue scale for anxiety (VAS-A) during the intraoperative assessment (5-8). A CDAS score of 12 and/or a VAS-A score of 50 (out of a 100 mm scale) were considered as the threshold of distinction between the levels of low and high anxiety. Conscious sedation and local anesthesia was used in all patients according to the protocol. Patients had an age between 26 and 54, and their average values of CDAS and VAS-A were 16 ± 1.56 respectively. For the purposes of comparison, the average values of CDA and VAS-A in the Italian general population are 10.29 ± 3.55 and 4.49 ± 2.52 , respectively. The frequency of previous exacerbations of HAE was not known for three cases, while it ranged from 1 to 30 of swelling attacks for year in 2 patients. One patient reported that his father suffered a tracheotomy following an attack of HAE. All patients were subjected to tooth extractions, and dental implants in 2 patients were also inserted. Two patients were on long-term prophylaxis, also short-term prophylaxis with C1 - INH concentrate (Berinert) 20 U/kg/e.v. It was administered to all patients one hour before surgery. The conscious sedation technique is enough to relieve anxiety and wellness in all patients while keeping them conscious and cooperative. Surgical treatment was uneventful in all cases. No patients had acute

events during surgery and in the postoperative period.

Results

Anxiety is a major cause of perioperative stress, which affects the quality of life, increasing the perception of pain, and compromising the result. In cases of HAE, careful anxiety management can reasonably important to be pointed at preventing strokes, as well as having an overall positive impact on patient prognosis and overall quality of care as well as standing up pathogenesis of various acute clinical pictures, including HAE attacks, acute coronary syndromes and inflammatory disorders (9-12).

A feature of HAE that is particularly relevant for dentists, dental hygienists and maxillofacial surgeons is that the most dangerous attacks initially occur in the mouth and then spread to the airway (13-16). The short-prophylaxis with Berinert should be given even before the mini-invasive procedures and whenever there is some uncertainty regarding the potential risk of an acute attack during a treatment (17). Treatment of HAE with C1-INH in conjunction with the use of nitrous oxide has been proven effective in the management of the disease and of the high anxiety. The most common cause of disease-related death in patients with HAE is resulting in asphyxia laryngeal swelling, with a mortality rate ranging from 30 to 50% (13-18). The number of episodes of laryngeal edema in the duration of HAE can range from 1 to 200, with 80% of these laryngeal attacks that occur between 11 and 45 years of age. Although the majority of the laryngeal swelling attacks subside spontaneously, so that they can be managed with patient monitoring, sedation, and oxygen therapy, it is important to be prepared for the risk of severe respiratory complications.

The risk of airway obstruction and suffocation must be thoroughly discussed with patients, their family and the doctors. Patients should be carefully trained to recognize the early symp-

toms of obstruction of the upper airways, seek proper medical and self-administer an effective therapy. In oral surgery, professionals and patients should be aware of the risk of laryngeal edema, even after a latency period without symptoms, until the second day after surgery (13, 14). Its correct diagnosis and its treatment may be delayed for years. Meanwhile, patients can receive ineffective treatments and can be subjected to unnecessary medical procedures, resulting in physical and psychological disabilities that can generate significant levels of anxiety, depression and a general ill health related to quality of life (13). The data on this sample of patients with HAE confirm the high levels of preoperative anxiety. This was particularly evident with the VAS-A, of which the average value was higher than the CDAS score (scale of dental anxiety Corah) suggesting that patients were more concerned about the risk of complications that do not the dental treatment in itself. Patients with severe systemic disease often have higher levels of dental anxiety, relative to their previous experiences of illness and treatment (19, 20). This is one of the reasons why the dental anxiety is not easy to measure in a single test. Our perioperative protocol is based on the following considerations:

- the first essential step for the proper management of the disease is to ensure that patients are well informed and make a psycho;
- physical assessment by clinical - pathological questionnaire (19, 21);
- antibiotics should be administered before surgery in accordance with the Italian guidelines for perioperative antibiotic prophylaxis (22);
- analgesia is guaranteed with:
 1. ketorolac 600 mg orally, 1 hour prior to surgery, followed by 1 g paracetamol to need;
 2. local anesthesia with plexus and infiltrative Articaine (23-25);
- premedication with oral midazolam, followed by inhalation of N₂O always preceded with 100% oxygen and followed by titration of anesthetic in 10% intervals. During analgesia/anxiolysis, the concentration of N₂O must

not exceed 50% of routine (26). It is important that the patient breaths through the nose so that the gas enters directly in the respiratory tree (27-29).

Conclusion

The rarity of the disease prevents any conclusions to be drawn on the incidence of HAE attacks and the role of sedation in their prevention. However, our experience suggests that the use of conscious sedation techniques for dental procedures in these patients is justified for the following reasons:

- patients with HAE are prone to high levels of anxiety;
- the high risk of attacks of hereditary angioedema associated with dental treatments is not completely prevented by a short-term prophylaxis;
- both the physical and psychological stress are known to trigger attacks.

Therefore the first essential step in the correct patient management is conduct a psycho-physical assessment of the subject.

Control of anxiety was associated with dental practices and the use of conscious sedation techniques for dentophobia management is the first choice for the prevention of acute events of hereditary angioedema.

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