ORIGINAL

Management of Dental-Oral Procedures in Patients With Hereditary Angioedema due to C1 Inhibitor Deficiency

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Abstract

Background: Hereditary angioedema due to C1 inhibitor deficiency (HAE-C1-INH) has considerable implications for dental health care providers, since dental procedures may trigger severe and even life-threatening episodes. The aim of the present study was to analyze the efficacy and safety of premedication with attenuated androgens (AAs), plasma-derived human C1 esterase inhibitor concentrate (pdhC1INH), or both to prevent the development of upper airway angioedema after dental-oral procedures in patients with HAE-C1-INH.
Material and Methods: All dental-oral procedures performed on patients with HAE-C1-INH who were followed up at La Paz University Hospital, Madrid, Spain were reviewed. Demographic data, maintenance treatment, preprocedure prophylaxis, disease severity, and occurrence of upper airway angioedema were recorded.
Results: Twenty-four patients (14 male/10 female; mean age, 42.6 years) underwent 66 procedures. Most procedures were performed on patients with severe HAE-C1-INH (20 procedures) or moderate HAE-C1-INH (26 procedures). Only 9 procedures were performed without short-term prophylaxis. Mild upper airway angioedema developed after 3 procedures performed without short-term prophylaxis in patients with minimal or asymptomatic HAE-C1-INH. A statistically significant association was found between development of mild postprocedure upper airway angioedema and lack of maintenance treatment with AA, lack of increased dose of preprocedure AA, and failure to administer preprocedure pdhC1INH (*P*=.002, Fisher exact test).
Conclusions: Increased doses of prophylactic AA, administration of pdhC1INH, or both were good options for ambulatory management of dental-oral procedures in patients with HAE-C1-INH. Prophylaxis with pdC1INH or increased doses of AA is advisable before dental-oral procedures, even in patients with low disease severity.

Key words: Hereditary angioedema. C1 esterase inhibitor. Acute pharyngeal-laryngeal attack. Dental-oral procedures. Dental surgery. Plasma-derived human C1 inhibitor concentrate. Bradykinin. Attenuated androgen.

Resumen

Antecedentes: El angioedema hereditario por déficit de C1 Inhibidor (AEH-C1-INH) tiene unas importantes implicaciones para los profesionales de la salud bucodental ya que una cirugía dental puede desencadenar episodios de angioedema potencialmente mortales. El objetivo del estudio fue analizar la eficacia y seguridad de los andrógenos atenuados (AAs) y/o del concentrado plasmático de C1 Inhibidor derivado de humanos (pdhC1INH) para prevenir el desarrollo de angioedema de vías respiratorias superiores tras procedimientos odontoestomatológicos en pacientes con AEH-C1-INH.
Material y métodos: Se revisaron los procedimientos odontoestomatológicos realizados en el Hospital Universitario La Paz. Se consideraron datos demográficos, tratamiento de mantenimiento, profilaxis pre-procedimiento, grado de severidad de la enfermedad y aparición de angioedema faringolaríngeo.
Resultados: Veinticuatro pacientes (14H/10M) (edad media: 42,6 años) se sometieron a 66 procedimientos. La mayor parte se realizaron en pacientes con estadio grave (20 procedimientos) o moderado (26 procedimientos) de la enfermedad. Sólo nueve procedimientos se realizaron sin profilaxis de corto plazo (PCP). En tres procedimientos realizados sin PCP se desarrolló angioedema faríngeo leve ocurriendo en pacientes en estadio asintomático o mínimo de la enfermedad. Se encontró una asociación estadísticamente significativa entre desarrollo mínimo de angioedema de vías respiratorias superiores y ausencia de tratamiento de mantenimiento con AA, ausencia de incremento de dosis y no-administración de pdhC1INH preprocedimiento (Test exacto de Fisher: P=.002).
Conclusiones: El aumento de dosis preprocedimiento de AA y/o la administración de pdhC1INH son buenas opciones para el manejo ambulatorio

de los procedimientos odontoestomatológicos en pacientes con AEH-C1-INH. El tratamiento profiláctico con pdC1INH o el incremento de dosis de AA es recomendable antes de la manipulación dental, incluso en pacientes con estadio bajo en la escala de gravedad de la enfermedad.

Palabras clave: Angioedema hereditario. Inhibidor de la C1 Esterasa. Ataque agudo faringo-laríngeo. Procedimientos odonto-estomatológicos. Cirugía dental. Concentrado plasmático de C1 inhibidor derivado de humanos. Bradicinina. Andrógeno atenuado.

Introduction

Angioedema due to C1 inhibitor deficiency is characterized by episodes of recurrent, circumscribed, nonpruritic swelling and is classified as hereditary (HAE-C1-INH) or acquired (AAE-C1-INH). HAE-C1-INH is further classified into 2 types [1]: type I HAE-C1-INH (85%), which involves a decrease in C1-INH levels (resulting in reduced functional activity), and type II HAE-C1-INH (15%), which is characterized by normal or increased C1-INH levels with reduced levels of functional C1-INH (the molecule itself being dysfunctional) [2].

Almost any part of the body can be affected, although the subcutaneous and submucosal tissues of the limbs, genitals, face, mouth, and bowels are the usual sites of swelling [3,4].

Angioedema attacks can be precipitated by estrogens, trauma, infections, and stress [5]. Microtrauma can also precipitate the onset of acute attacks; therefore, dental-oral procedures carry a high risk of causing such attacks and increasing the risk of death due to asphyxiation [6], since they are performed close to the airway.

In the past, overall mortality after dental surgery without adequate treatment was around 30%-40% in patients with HAE-C1-INH [7], and a significant number of dental-oral procedures were carried out even before the disease was diagnosed. Standard management of dental procedures in these patients consisted of increasing the dose of attenuated androgens (AAs) [8] or administering intravenous plasma-derived human C1 esterase inhibitor concentrate (pdhC1INH: 500-1000 IU, depending on body weight) [9] 30 to 60 minutes before the procedure [10,11]. Availability of pdhC1INH and a better understanding of preprocedure prophylaxis have reduced the incidence of localized upper airway angioedema associated with dental procedures and subsequent death due to asphyxia [7].

The period between the dental procedure and the development of upper airway angioedema can vary, although it usually lasts a few hours [12]. Nevertheless, progression as quick as 20 minutes has been reported [13]. Since upper airway angioedema can lead to asphyxia and death, airway accessibility should be adequately monitored and appropriate emergency treatment should be available. If the airway is threatened despite treatment, the patient should be intubated immediately or an emergency tracheotomy performed [14,15]. However, dental-oral health care professionals often do not know how to manage C1-INH deficiency, and lack of awareness among physicians can lead to misdiagnosis of HAE-C1-INH.

The aim of this study was to analyze the efficacy and safety of premedication with AA, pdhC1INH, or both in order to prevent the development of upper airway angioedema after dental procedures in patients with HAE-C1-INH.

Material and Methods

We carried out a retrospective review of the clinical histories of patients with HAE-C1-INH after obtaining the approval of the local ethics committee.

Inclusion criteria: Patients were included if they had a confirmed diagnosis of type I or type II HAE-C1-INH, required any dental-oral procedure, were over 14 years of age, and were followed-up at La Paz University Hospital in Madrid, Spain. We reviewed dental-oral procedures carried out between February 1996 and February 2009.

Exclusion criteria: Patients were excluded if they had other types of angioedema (AAE, estrogen-related hereditary angioedema, type III HAE, hereditary angioedema associated with a mutation in *F12*, angiotensin-converting enzyme [ACE] inhibitor–induced angioedema, idiopathic angioedema) or, even if they had HAE-C1-INH and were receiving antifibrinolytic agents or pdhC1INH as maintenance treatment.

Demographic data (gender, age at the time of the procedure), type of HAE-C1-INH, maintenance treatment, short-term prophylaxis (increased dose of AA, administration of pdhC1INH), disease severity, and occurrence of upper airway angioedema in the 24 hours following the procedure were recorded and entered into a custom-designed database.

The results were processed using SPSS 17.0. The Mann-Whitney test was used to compare the means of quantitative variables, while the Fisher exact test was used to compare the means of qualitative variables.

Patients were followed up in the allergology department, and, if a dental-oral problem was reported or detected, the oral and maxillofacial surgery department or the patient's current dentist was contacted, and a decision was made regarding the necessary procedures.

Patients were prescribed short-term prophylaxis as follows: danazol (Sanofi-Aventis: 200 mg every 8 hours), stanozolol (Desma Laboratorio Farmacéutico S.L.: 2 mg every 8 hours, from 5 days before to 3 days after the procedure), or pdhC1INH (CSL-Behring GmbH: 500-1000 IU intravenously 1 hour before the procedure and readministered in the case of complications). pdhC1INH was made available for emergency treatment.

Data on prophylaxis were collected from the clinical history (actual dose taken and type of drug).

Upper airway angioedema was defined as the presence of dysphonia, dysphagia, or dyspnea in the 48 hours following the dental procedure. Disease severity was calculated for every patient retrospectively using the HAE-C1-INH disease severity score published by Agostoni et al [9].

Patients were followed up at our outpatient office every 4 to 6 months or at 12 months, according to their

Table 1. Treatment Options

Group	Number of Patients	Preprocedure Dental-Oral Treatment Options		
		Long-term Prophylaxis With AA	Increased Doses of Preprocedure AA	Preprocedure pdhC1INH
1	9	No	No	No
2	11	No	No	Yes
3	0	No	Yes	No
4	1	No	Yes	Yes
5	13	Yes	No	No
6	11	Yes	No	Yes
7	3	Yes	Yes	No
8	18	Yes	Yes	Yes

Abbreviations: AA, attenuated androgens; pdhC1INH, plasma-derived human C1 esterase inhibitor concentrate.

Table 2. Patients With Hereditary Angioedema who Underwent Dental-Oral Procedures

No. of patients	14
No. (%) of dental-oral procedures (total)	66 (100)
No. (%) of procedures carried out by dentists in private clinics	25 (37.87)
– Extraction (with locoregional anesthesia)	13
– Dental cleaning (without anesthesia)	11
– Orthodontia (without anesthesia)	1
No. (%) of procedures carried out in the oral and maxillofacial surgery department (with locoregional anesthesia)	41 (62.12)
– Extraction	37
– Mucocele excision	2
– Postextraction dental abscess drainage	1
– Cystectomy for mandibular cyst (dental)	1
No. (%) of sessions with tooth extractions	37 (100)
– Impacted or semi-impacted teeth (third molar) (mean number of teeth, sessions)	15 (1-3 teeth extractions) (28, 1.88)
– No impacted teeth; tooth or root extraction (mean number of teeth, sessions)	22 (1-3 teeth extractions) (98, 4.45)

HAE-C1-INH severity score. A complete blood count, blood biochemistry, and serology testing for parvovirus B19, human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV) were performed at regular intervals.

Based on the 3 main treatment options (preprocedure increased doses of AAs, preprocedure administration of pdhC1INH, and long-term prophylaxis with AAs), 8 treatment combinations were possible (Table 1).

Results

Twenty-four patients (14 female and 10 male) underwent 66 procedures (mean age, 42.6 [15.31] years; median [IQR] age, 44.12 [29.5-55.9] years]), 64 as outpatients and 2 with a 24-hour hospital stay. All patients weighed between 50 and 100 kg. Only 1 of the 24 patients presented type II HAE-C1-INH.

Basic data from the dental-oral procedures are shown in Table 2. Two procedures were performed in the operating room and the other in a dental chair, as is usual with individuals who have this disease. The 2 patients who underwent procedures in the operating room (a mandibular cyst and a postextraction abscess) required a 24-hour hospital stay before discharge; the remainder did not require hospital admission.

Most procedures were performed in patients who had severe HAE-C1-INH (20 procedures, 30.3%) and moderate HAE-C1-INH (26 procedures, 39.4%), while 12 procedures (18.2%) were performed in patients with asymptomatic HAE-C1-INH, 6 procedures (9.1%) in patients with minimal HAE-C1-INH, and 2 procedures (3.0%) in patients with mild HAE-C1-INH.

pdhC1INH was administered in 42 procedures (53.6%), and only 9 procedures (13.6%) were performed without prophylaxis.

Three patients (with asymptomatic or minimal HAE-C1-INH) experienced mild upper airway angioedema after their procedures (2 extractions and 1 bridge), although this resolved spontaneously. None of the 3 patients were receiving maintenance treatment with AAs, and no preprocedure prophylaxis was administered.

A statistically significant association was found between the development of mild postprocedure upper airway angioedema and lack of maintenance treatment with AAs (P=.034, Fisher exact test) and lack of preprocedure pdhC1INH (P=.019, Fisher exact test).

A statistically significant association was found between the development of mild postprocedure upper airway angioedema and lack of maintenance treatment with AAs, increased preprocedure dose or introduction of AAs, and preprocedure administration of pdhC1INH (P=.002, Fisher exact test).

It is worth noting that 1 of the patients who tolerated placement of braces after receiving 500 IU of pdhC1INH developed mild edema of the palate in the following months. According to the severity scale, this patient had minimal HAE-C1-INH.

A significant association was found between the development of upper airway angioedema and mild HAE-C1-INH in the year before the procedure (P=.02217, Mann-Whitney test).

In order to clarify whether treatment with AAs (a variable that significantly affects final HAE-C1-INH severity scores) was a confounding factor, we reanalyzed the possible association between the HAE-C1-INH score and development of angioedema by subtracting the points attributable to AA maintenance treatment from the final score [9]. We found that the significant association between mild HAE-C1-INH

and development of angioedema disappeared (*P*=.1833, Mann-Whitney test), confirming that treatment with AAs was a confounding factor in HAE-C1-INH severity scores.

No patient seroconverted to parvovirus B19, HIV, HBV, or HCV, and none reported any adverse event during or after infusion of pdhC1INH, such as allergic reactions, headache, or increases/decreases in body temperature. No acute adverse events related to AA for short-term prophylaxis prior to dental procedures were recorded.

Discussion

Upper airway angioedema after dental procedures has traditionally been prevented using short-term prophylaxis with AAs [16-19], tranexamic acid [20,21], and pdhC1INH [22,23]. In countries where pdhC1INH is not available, fresh frozen plasma can be administered 24 hours or immediately before the surgical procedure [24,25], although some patients developed mild edema [12,20,25]. Several series and case reports address management of dental procedures in patients with HAE-C1-INH [7,16,22].

In our series, a significant association was found between the use of AAs or pdhC1INH and the absence of upper airway angioedema after dental procedures. The largest published series on management of dental procedures in patients with HAE-C1-INH is that of Bork et al [26], although, as with our series, the study was observational and not a randomized controlled trial.

The 3 patients who experienced mild upper airway angioedema were not on maintenance treatment with AA or pdhC1INH. No short-term prophylaxis was administered, since their HAE-C1-INH was mild and the patients themselves did not consider pretreatment necessary, although they had been advised by the doctor to take it. Bork et al [26] reported facial swelling, potentially life-threatening laryngeal edema, or both, in 124/577 extractions (21.5%) without prophylaxis (pdhC1INH). Similar symptoms were recorded in a lower proportion of patients undergoing tooth extractions (16/128, 12.5%) after short-term prophylaxis with pdhC1INH. However, although the authors did not provide data on long-term prophylaxis, these patients were probably not being treated concomitantly with AAs or the pdhC1INH dose was not adequate.

The prevalence of upper airway angioedema after dental procedures in our series is very low (approximately 4.5%), and much lower than that reported by Bork et al [25] (21%), perhaps because we included all types of dental-oral procedures, not just extractions. However, none of our patients developed angioedema after extraction, despite having up to 6 teeth removed in a single procedure; in addition, 44/66 procedures were performed while the patients were taking AA as long-term prophylaxis.

One of the patients who had braces fitted after receiving 500 IU of pdhC1INH developed mild edema of the palate in the following months, possibly because of sustained microtrauma, once the half-life of pdhC1INH was complete (31.75 to 46.5 hours) [27,28]. This patient was not receiving maintenance treatment with AA, tranexamic acid, or pdhC1INH.

Most patients in our series had severe HAE-C1-INH (20 procedures, 30.3%) and moderate HAE-C1-INH (26 procedures, 39.4%) [10]. However, all patients who experienced upper airway angioedema during the 24 hours following the procedure had mild HAE-C1-INH. These patients were not taking AAs, antifibrinolytic agents, or pdhC1INH as long-term prophylaxis, nor had they taken short-term prophylaxis, although they had been advised to do so. Thus, it is important to emphasize the need for prophylaxis prior to dental procedures in patients with HAE-C1-INH, regardless of their severity score. Both pdhC1INH and AAs are good options for preventing the development of life-threatening upper airway angioedema. It is worth noting that the disease severity score does not take into account the dose of AAs used for maintenance treatment (long-term prophylaxis) [9] and assigns the same score to patients with different doses (eg, stanozolol 2 mg twice a week vs stanozolol 2 mg every 8 hours). The HAE-C1-INH disease severity score published in 2003 has not been validated. Therefore, the disease severity score appears to be more related to maintenance treatment or prophylaxis than to disease severity itself. Our group decided to use the score of Agostoni et al [9] to classify the severity of HAE-C1-INH, because it was the only HAE-C1-INH score published, although its significance has yet to be established.

Preprocedure administration of nanofiltered C1 inhibitor (C1-INH-nf) was recently described as an effective treatment in preventing edema attacks during or following 98% of medical or surgical procedures, including dental-oral procedures [29]. In addition, Clemens [30] provided the first report of effective short-term prophylaxis with icatibant acetate before 2 operations on the head and neck in a patient with type II HAE-C1-INH. The risk of developing angioedema as a result of dental-oral procedures cannot be completely avoided with preoperative prophylaxis [31]; therefore, acute treatment (pdhC1INH, icatibant acetate, rhC1-INH, or ecallantide) should always be available, and patients should be informed of the possible development of upper airway angioedema and instructed what to do if they experience an episode. In our series, which is one of the largest published to date, no upper airway angioedema was seen in HAE-C1-INH patients who received short-term prophylaxis with AA, pdhC1INH, or both. It is important to note that concomitant medications such as long-term treatment with AAs should be taken into account when evaluating the effectiveness of preprocedure prophylaxis in HAE-C1-INH.

In the future, new drugs such as recombinant human C1 esterase inhibitor (rhC1INH: Pharming Technologies BV), C1-INH-nf (Viropharma Inc), ecallantide (Dyax Corp), and icatibant acetate (Jerini AG) [31], all of which recently came onto the market or are under development for the treatment of acute HAE-C1-INH attacks, should be considered. The European Medicines Agency has recently approved C1-INH-nf in adults and adolescents with hereditary angioedema for routine prevention, preprocedure prevention, and acute treatment of attacks. Theoretically, drugs that decrease formation of bradykinin (pdhC1INH, rhC1INH, AAs, and ecallantide) could be more efficacious as short-term prophylaxis than those that merely block bradykinin receptors. Trauma triggers acute edema attacks in HAE-C1-INH patients through activation of

F-XII, conversion of prekallikrein into kallikrein, and formation of bradykinin from high-molecular-weight kininogen. Although Cicardi et al [32] reported data on administration of ecallantide and fresh frozen plasma as short-term prophylaxis, more studies are necessary before final conclusions can be drawn.

Conclusions

Dental procedures carry a high risk of edema, even in patients with mild HAE-C1-INH. In our study, premedication with AA (increased doses or introduction thereof), administration of pdhC1INH, or both were good options for outpatient management of dental-oral procedures in patients with HAE-C1-INH.

Short-term prophylaxis should be administered to all patients with HAE-C1-INH prior to dental-oral procedures, regardless of their HAE-C1-INH severity score. Acute treatment should be available in dental offices for immediate acute treatment if laryngeal edema develops.

Conflict of Interest

Dr Jesús Jurado-Palomo has taken part in clinical trials sponsored by CSL-Behring and Pharming NV.

Dr Jesús Manuel Muñoz-Caro declares that he has no conflicts of interest.

Dr María Concepción López-Serrano has received sponsorship for educational purposes, has been paid for providing consultancy services, and has taken part in clinical trials sponsored by Jerini AG/Shire, CSL-Behring, Dyax Corp, and Pharming NV.

Dr Nieves Prior has received sponsorship for educational purposes and has taken part in clinical trials sponsored by Jerini AG/Shire, CSL-Behring, Dyax Corp, and Pharming NV.

Dr Rosario Cabañas has received sponsorship for educational purposes and has taken part in clinical trials sponsored by CSL-Behring, Dyax Corp, and Pharming NV.

Dr María Pedrosa has received sponsorship for educational purposes and has taken part in clinical trials sponsored by Jerini AG/Shire, CSL-Behring, and Pharming NV.

Dr Miguel Burgueño declares that he has no conflicts of interest.

Dr Teresa Caballero has received sponsorship for educational purposes, has been paid for providing consultancy services, and has taken part in clinical trials sponsored by Jerini AG/Shire, CSL-Behring, Dyax Corp, Pharming NV, and Viropharma Pharmaceutical.

References

1. Rosen FS, Charche P, Pensky J, Donaldson V. Hereditary angioneurotic edema. Two genetic variants. Science. 1965;148:957-8.
2. Caballero T, Baeza ML, Cabañas R, Campos A, Cimbollek S, Gómez-Traseira C, González-Quevedo T, Guilarte M, Jurado-Palomo J, Larco JI, López-Serrano MC, López-Trascasa M, Marcos C, Muñoz-Caro JM, Pedrosa M, Prior N, Rubio M, Sala-Cunill A. Consensus statement on the diagnosis, management and treatment of angioedema mediated by bradykinin. Part I. Classification, epidemiology, pathophysiology, genetics, clinical symptoms, and diagnosis. J Investig Allergol Clin Immunol. 2011;21:333-47.
3. Agostoni A, Cicardi M. Hereditary and acquired C1-inhibitor deficiency: biological and clinical characteristics in 235 patients. Medicine (Baltimore). 1992;71:206-15.
4. Frank MM, Gelfand JA, Atkinson JP. Hereditary angioedema: the clinical syndrome and its management. Ann Intern Med. 1976;84:580-93.
5. Fay A, Abinun M. Current management of hereditary angioedema (C1 esterase inhibitor deficiency). J Clin Pathol. 2002;55:266-70.
6. Atkinson JC, Frank MM. Oral manifestations and dental management of patients with hereditary angioedema. J Oral Pathol Med. 1991;20:139-42.
7. Bork K, Barnstedt SE. Laryngeal edema and death from asphyxiation after tooth extraction in four patients with hereditary angioedema. J Am Dent Assoc. 2003;134:1088-94.
8. Sturdy KA, Beastall RH, Grisius RJ, Oatis GW Jr. Hereditary angioedema controlled with danazol. Report of a case. Oral Surg Oral Med Oral Pathol. 1979;48:418-20.
9. Agostoni A, Aygören-Pürsün E, Binkley KE, Blanch A, Bork K, Bouillet L, Bucher C, Castaldo AJ, Cicardi M, Davis AE, De Carolis C, Drouet C, Duponchel C, Farkas H, Fáy K, Fekete B, Fischer B, Fontana L, Füst G, Giacomelli R, Gröner A, Hack CE, Harmat G, Jakenfelds J, Juers M, Kalmár L, Kaposi PN, Karádi I, Kitzinger A, Kollár T, Kreuz W, Lakatos P, Longhurst HJ, Lopez-Trascasa M, Martinez-Saguer I, Monnier N, Nagy I, Németh E, Nielsen EW, Nuijens JH, O'grady C, Pappalardo E, Penna V, Perricone C, Perricone R, Rauch U, Roche O, Rusicke E, Späth PJ, Szendei G, Takács E, Tordai A, Truedsson L, Varga L, Visy B, Williams K, Zanichelli A, Zingale L. Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. J Allergy Clin Immunol. 2004;114(3 Suppl):S51-131.
10. Bowen T, Cicardi M, Farkas H, Bork K, Kreuz W, Zingale L, Varga L, Martinez-Saguer I, Aygören-Pürsün E, Binkley K, Zuraw B, Davis A 3rd, Hebert J, Ritchie B, Burnham J, Castaldo A, Menendez A, Nagy I, Harmat G, Bucher C, Lacuesta G, Issekutz A, Warrington R, Yang W, Dean J, Kanani A, Stark D, McCusker C, Wagner E, Rivard GE, Leith E, Tsai E, MacSween M, Lyanga J, Serushago B, Leznoff A, Waserman S, de Serres J. Canadian 2003 International Consensus Algorithm For the Diagnosis, Therapy, and Management of Hereditary Angioedema. J Allergy Clin Immunol. 2004;114:629-37.
11. Gompels MM, Lock RJ, Abinun M, Bethune CA, Davies G, Grattan C, Fay AC, Longhurst HJ, Morrison L, Price A, Price M, Watters D. C1 inhibitor deficiency: consensus document. Clin Exp Immunol. 2005;139:379-94.
12. Bork K, Hardt J, Schicketanz KH, Ressel N. Clinical studies of sudden upper airway obstruction in patients with hereditary angioedema due to C1 esterase inhibitor deficiency. Arch Intern Med. 2003;163:1229-35.
13. Bork K, Siedlecki K, Bosch S, Schopf RE, Kreuz W. Asphyxiation by laryngeal edema in patients with hereditary angioedema. Mayo Clin Proc. 2000;75:349-54.
14. Wall RT, Frank M, Hahn M. A review of 25 patients with

hereditary angioedema requiring surgery. Anesthesiology. 1989;71:309-11.
15. Caballero T, Baeza ML, Cabañas R, Campos A, Cimbollek S, Gómez-Traseira C, González-Quevedo T, Guilarte M, Jurado-Palomo J, Larco JI, López-Serrano MC, López-Trascasa M, Marcos C, Muñoz-Caro JM, Pedrosa M, Prior N, Rubio M, Sala-Cunill A. Consensus statement on the diagnosis, management, and treatment of angioedema mediated by bradykinin. Part II. Treatment, follow-up, and special situations. J Investig Allergol Clin Immunol. 2011;21:422-41.
16. Farkas H, Gyeney L, Gidófalvy E, Füst G, Varga L. The efficacy of short-term danazol prophylaxis in hereditary angioedema patients undergoing maxillofacial and dental procedures. J Oral Maxillofac Surg. 1999;57:404-8.
17. Sheffer AL, Fearon DT, Austen KF, Rosen FS. Tranexamic acid: preoperative prophylactic therapy for patients with hereditary angioneurotic edema. J Allergy Clin Immunol. 1977;60:38-40.
18. Crosher R. Intravenous tranexamic acid in the management of hereditary angioedema. Br J Oral Maxillofac Surg. 1987;25:500-6.
19. Leimgruber A, Jacques WA, Spaeth PJ. Hereditary angioedema: uncomplicated maxillofacial surgery using short-term C1 inhibitor replacement therapy. Int Arch Allergy Immunol. 1993;101:107-12.
20. Langton D, Weiner J, Fary W. C1-esterase inhibitor concentrate prevents upper airway obstruction in hereditary angioedema. Med J Aust. 1994;160:383-4.
21. Zuraw BL. Current and future therapy for hereditary angioedema. Clin Immunol. 2005;114:10-6.
22. Pence HL, Evans R, Guernsey LH, Gerhard RC. Prophylactic use of epsilon aminocaproic acids for oral surgery in a patient with hereditary angioneurotic edema. J Allergy Clin Immunol. 1974;53:298-302.
23. Atkinson JC, Frank MM. Oral manifestations and dental management of patients with hereditary angioedema. J Oral Pathol Med. 1991;20:139-42.
24. Hardie J, Ringland T, Yang WH, Wagner V. Potentially fatal hereditary angioedema: a review and case report. J Can Dent Assoc. 1990;56:1096-9.
25. De Serres J, Groner A, Lindner J. Safety and efficacy of pasteurized C1 inhibitor concentrate (Berinert P) in hereditary angioedema: A review. Transfus Apher Sci. 2003;29:247-54.
26. Bork K, Hardt J, Staubach-Renz P, Witzke G. Risk of laryngeal edema and facial swellings after tooth extraction in patients with hereditary angioedema with and without prophylaxis with C1 inhibitor concentrate: a retrospective study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011;112:58-64.
27. Cicardi M, Zingale L. How do we treat patients with hereditary angioedema. Transfus Apher Sci. 2003;29:221-7.
28. Martinez-Saguer I, Rusicke E, Aygören-Pürsün E, von Hentig N, Klingebiel T, Kreuz W. Pharmacokinetic analysis of human plasma-derived pasteurized C1-inhibitor concentrate in adults and children with hereditary angioedema: a prospective study. Transfusion. 2010;50:354-60.
29. Lumry W, Busse P, Baker J, Davis-Lorton M, Hurewitz D, Grant A, White M, Mariano D, Kalfus I, Sampson M. Pre-procedure administration of C1 esterase inhibitor (human) for the prevention of hereditary angioedema attacks after medical, dental, or surgical procedures. Poster Nr1085. Allergy. 2011;66 Suppl 94:417-8.
30. Clemens P. Short-term prophylactic treatment of hereditary angioedema type II with icatibant. Allergy 2011;66 Suppl 94;429.
31. Maves KK, Weiler JM. Tonsillectomy in a patient with hereditary angioedema after prophylaxis with C1 inhibitor concentrate. Ann Allergy. 1994;73:435-8.
32. Cicardi M, González-Quevedo T, Caballero T, Börk K, Williams A. DX-88 a recombinant inhibitor of human plasma kallikrein. Efficacy and safety in hereditary and acquired angioedema. Mol Immunol 2003;40:197-8.

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