

Efficacy of tranexamic acid in sporadic idiopathic bradykinin angioedema

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Key words: angioedema; bradykinin; tranexamic acid.

Angioedema (AO) without urticaria is uncommon but may be life threatening. When AO is not controlled by H1-anti-histamines or corticoids or adrenalin, and there is no medication with non steroid anti-inflammatory drugs or aspirin, bradykinin AO (BAO) should be considered. Most of the BAO are caused by a hereditary or acquired deficient C1inhibitor, diagnosed by weight and function measurements. This deficiency leads to an accumulation of bradykinin, a vasoactive peptide responsible for the occurrence of edema (1).

Sporadic idiopathic bradykinin angioedema (SIBAO) represent a rare entity sharing clinical similarities with hereditary angioedemas. Therefore, patients who fulfilled criterias of SIBAO were prescribed with tranexamic acid, first during an episode, then daily. All the patients with the 3 grams daily regimen had a satisfying response on the duration, the intensity and the frequency of the episodes. There were no secondary effects for a mean follow-up of 20 months.

Possible treatments are the C1inhibitor concentrate, danazol which up regulates the C1inhibitor gene transcription and tranexamic acid (TA) which prevents the plasmin-dependent formation of bradykinin (2).

In some rare cases, BAO have no deficient C1inhibitor. The accumulation

of bradykinin can then be caused by stimulation of the kininogenases or by deficient kininases (3). Thus, three causes should be considered as follows: angiotensin convertase enzyme (ACE) inhibitors because ACE is a kininase and AO occur up to 1%; a type III hereditary AO in which gain-of-function mutations of the coagulation factor XII can be involved; and idiopathic bradykinin AO that can be either familial or sporadic. In contrast with the well-known hereditary AO, this subset seems to be less severe. It was specifically studied in only two major series but with sporadic and familial cases, which can represent at least two different entities (4, 5). A series of seven French sporadic cases was described by Bouillet et al. (6). By analogy with hereditary AO, daily TA was given to these patients with a good response up to 100%.

In our retrospective study, we were interested in sporadic idiopathic BAO. Thirty-five patients between 2003 and

2007 were studied (Fig. 1). There were 14 women and 21 men (*sex ratio*, 0.66). The mean age at onset was 42 years (range, 3 months to 78 years). The mean age at diagnosis was 45.8 years; the mean diagnostic delay was 3.8 years (range, 0–15 years). The mean duration of the episode was 36.34 h (range, 1 h to 4 days). The rhythm varied from daily episodes to <1 episode a year. The topography was also varied, even for a single person, but head and neck were never spared. Eight patients (23%) had had digestive manifestations. Nine patients (26%) had had dyspnea, cough, dysphonia, and/or undiagnosed chest pain. They all had headaches before and during episodes. Nine patients were once hospitalized but without invasive treatment. Twenty-five patients received TA 1 g during an episode. It was well tolerated and efficient on the intensity and the duration of the episode in 23 patients, who were then prescribed with TA 3 g daily. The remaining two

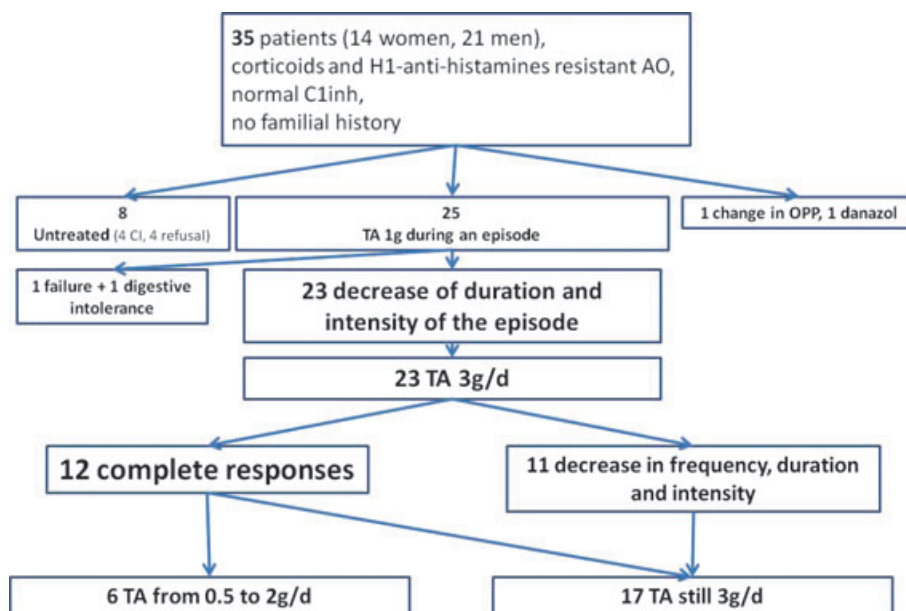


Figure 1. Outline of this series. AO angioedema, C1inh C1 inhibitor, CI contraindication, TA tranexamic acid, OPP estroprogestative pill.

patients gave up because of failure and digestive intolerance, respectively. Twelve patients had a complete remission of the episodes and six of them could have lower dosage of TA. The other eleven noticed an important decrease in the frequency, the duration and the intensity of the episodes. Ten patients did not receive this treatment: four had thromboembolic contraindications, one had danazol, another changed her contraceptive pill first, one refused, and three found the episodes too infrequent to be treated over the long term. The daily treatment was well-tolerated for the 23 patients (mean follow-up, 20 months). In this rare subset of BAO, this study aimed to confirm the efficacy and the good tolerance of daily TA, which tolerance is better than danazol.

When a physician is confronted with corticoids or H1-anti-histamines resistant AO, TA should be used as a therapeutic test if there is no contra-

indication. Contraceptive pill should be changed for pure progestative. If efficient, TA should be prescribed 3 g daily with ophthalmological and liver enzymes follow-up.

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Accepted for publication 18 September 2009
Allergy 2009
© 2009 John Wiley & Sons A/S
DOI: 10.1111/j.1398-9995.2009.02234.x

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