Case Report

Doxazosin Induced Angioedema: A Case Report

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Abstract:

Angioedema, a potentially life-threatening occurrence, is an predominant adverse effect of antihypertensive especially angiotensin converting enzyme inhibitors. However, angioedema due to doxazocin, alfa-1 adrenergic receptor antagonist, was rarely reported in the previous medical literatures. Thus, the aim of this report was to evaluate and report a case of angioedema in a patient taking doxazosin. Healthcare providers should be aware when prescribing doxazosin because there was report of angioedema among patients receiving such agent.

Keywords: ● *Doxazosin* ● *Angioedema* ● *Antihypertensive*

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รายงานผู้ป่วย

กรณีศึกษาการเกิดแอ็งจิโอเอดีมาจากยาดอกซาโซซิน

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บทคัดย่อ

แอ็งจิโอเอดีมาเป็นผลกระทบอันไม่พึงประสงค์ที่อาจเป็นอันตรายถึงชีวิตจากยาลดความดันโลหิตสูงโดยเฉพาะยากลุ่มยับยั้งเอนไซม์ angiotensin converting enzyme อย่างไรก็ตาม การเกิดแอ็งจิโอเอดีมา จากยาดอกซาโซซิน ซึ่งเป็นยากลุ่มยับยั้งตัวรับ alfa-1 adrenergic ก็มีรายงานการเกิดเช่นเดียวกัน แต่ยังมีรายงานการเกิดน้อย ดังนั้นรายงานฉบับนี้ จึงมีวัตถุประสงค์เพื่อประเมินและรายงานกรณีศึกษาการเกิดแอ็งจิโอเอดีมาในผู้ป่วยที่ได้รับยาดอกซาโซซิน เพื่อให้บุคลากรทางการแพทย์เฝ้าระวังการเกิดแอนจิโอเอดีมาในผู้ป่วยที่ได้รับยาดอกซาโซซิน

คำสำคัญ: ● *ดอกซาโซซิน* ● *แอ็งจิโอเอดีมา* ● *ยาลดความดันโลหิต*

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Introduction

Angioedema is submucosal tissue swelling that involves of the skin, mucous membranes, or both including the upper respiratory and intestinal epithelial linings.[1] The pathophysiological of angioedema process is associated various inflammatory mediators eg. Histamine and bradykinins.[1,2] The release of inflammatory mediators are responsible for arteriolar dilatation and increased vascular permeability and tissue swelling. Angioedema is an adverse reaction that is serious and life-threatening. Common causes of angioedema are foods (eg. peanuts, shellfish, milk, eggs), medications, especially penicillin or sulfa antibiotics and their derivatives.[3] However other medications can also cause angioedema such as non-steroidal anti-inflammatory drugs (NSAIDs) and antihypertensive agents that especially angiotensin converting enzyme inhibitors (ACEIs). The incidence of ACEIs induced angioedema was reported about 0.1% to 0.2%.[4,5] Doxazosin, alfa-1 adrenergic receptor antagonist, is an antihypertensive agent and commonly prescribed The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) reported nine percent of related angioedema but this number was overall rate from any medications.[6] However, doxazosin induced angioedema has lacked of substantial report. Therefore, the purpose of this report was to describe about the pattern of angioedema related to doxazosin.

Case Presentation

A 69-year-old Thai man had a medical history of hypertension, type 2 diabetes mellitus, dyslipidemia and end-stage renal disease on peritoneal dialysis. He has been taking his regular medication for more than ten years including hydralazine, spironolactone, furosemide, amlodipine, enalapril, glipizide and simvastatin. He denied history of food or drug allergy. This patient presented to the emergency department with hypertensive emergency. Physical examination was remarkable as follows: alteration of consciousness, mild pale conjunctiva, crepitation both lung and pitting edema at both legs. Serum biochemistry e.g. AST, ALT and neutrophils were normal. He was diagnosed as hypertensive emergency. On the first day of admission, he was referred to the coronary care unit where he received nitroglycerine intravenous infusion then changed to nicardipine infusion. The other medications were the same as his medication prior to admission. One day later, doxazosin was started and the dose of nicardipine was reduced. The patient developed swallen tongue and lips without urticaria or maculopapular rash after two doses of doxazosin that his vital signs were normal. He received intravenous chlorpheniramine administration with immediately nicardipine and doxazosin discontinued. Then the symptoms of angioedema were greatly improved. Finally, doxazocin was not re-administered in this case. The Naranjo adverse drug reaction probability scale rating criteria was evaluated by the pharmacist. The result was shown that the patient had a probability scale as “probable”. (Table 1)

Discussion

Angioedema is a rare adverse drug reaction but potentially life-threatening. The principle cause is thought to be related to inflammatory mediators (histamine or bradykinin).[7] The pathophysiology of angioedema could be classified into two pathway: allergic or histamine-mediated angioedema and bradykinin-mediated angioedema. Typically, histamine-mediated angioedema is the most common and always occurs with urticaria (or rash). The clinical manifestations can occur within several minutes, or up to 2 hours after approaching suspected antigen. With histamine-mediated type, these conditions are remedied by antihistamines, epinephrine, or glucocorticoids. Contrastingly, bradykinin-mediated

Table 1 Naranjo scoring for probability of angioedema by doxazocin

Naranjo questionnaire	Yes	No	Do not know	Case score
1. Are there previous conclusive reports on this reaction?	1	0	NA	1
2. Did the adverse event appear after suspected drug was administered?	2	-1	NA	2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	1	0	NA	1
4. Did the adverse reaction reappear when the drug was re-administered	2	-1	NA	NA
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	2	NA	-1
6. Did the reaction reappear when a placebo was given?	-1	1	NA	NA
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	1	0	NA	NA
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	1	0	NA	NA
9. Did the patient have a similar reaction to the same or similar drug in any previous exposure?	1	0	NA	NA
10. Was the adverse event confirmed by any objective evidence?	1	0	NA	1
Total score				4

angioedema, this type is mostly found in patient taking ACEI. ACEI is inhibit the enzyme of degradation resulting in accumulation of bradykinin. ACEI-angioedema has been documented to occur in a long period use up a year after starting an ACEI. Antihistamines and glucocorticoids are often ineffective due to its different pathway of angioedema.[8]

In the present case, he developed swallen tongue and lips without any skin rash and his symptoms were improved when doxazosin was discontinued and intravenous antihistamine was administrated. Even the pathophysiology of angioedema due to doxazocin is undocumented. Based on the rapid onset and relieved by antihistamine, it might be histamine-mediated angioedema. However, the exact mechanism of angioedema associated with doxazocin has to be further studied.

The onset of angioedema occurs within hours to a week and late onset angioedema may occur after the initiation of the medication and can be recovery within three to four days. However, some cases develop angioedema within month to year after the medication use.[7] The present case with angioedema occurred in 2 days after initiation of doxazosin. Nowadays, there is only ALLHAT study revealing the incidence of doxazocin induced angioedema. Patients receiving doxazocin had angioedema in 5 out of 9061 cases (0.06%). Two of five participants develop angioedema within the first week after randomization in ALLHAT study. The remaining three cases occur within 2 years after doxazocin initiation.[9]

Conclusion

Doxazosin induced angioedema has lacked of substantial report. Until more data is available, this case report emphasized the necessity of monitoring when doxazosin is started especially in patients who receive doxazosin for the first time.

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