

ANAPHYLACTIC REACTION TO CINOXACIN : REPORT OF ONE CASE ASSOCIATED WITH INFERIOR ACUTE MYOCARDIAL INFARCTION

**O. Quercia (MD) ⁽¹⁾, S. Rafanelli (MD) ⁽¹⁾,
F. Emiliani (MD) ⁽¹⁾, G. Francesco Stefanini (MD) ⁽¹⁾**

Summary

Cinoxacin is an oral synthetic antibacterial agent, of the second generation quinolones group, with excellent efficacy in respiratory, intra-abdominal, pelvic, and skin and soft tissue infections. Overall, quinolones are well tolerated drugs, although phototoxicity and photoallergenicity is well demonstrated experimentally.

In this report we show you a case of a man who presented a anaphylactic reaction associated with myocardial infarction, after taking a capsule of cinoxacin.

We suppose that there is a direct participation of the heart in anaphylactic reactions, because activated mast-cells mediators can determine cardiovascular effects.

Then performed double-blind placebo controlled challenge test with an alternative drug. We did not observe any adverse immediate or late adverse reaction to this drug.

Key-words : Cinoxacin - Anaphylactic reaction - Acute myocardial infarction, mast cells - Double blind placebo-controlled challenge test.

INTRODUCTION

A 58 year-old man developed an anaphylactic reaction associated with acute myocardial infarction, after taking a capsule of cinoxacin.

CASE REPORT

The patient, an asthmatic smoker, with a diet controlled type II diabetes, but no previous history of cardiac disease, underwent cystectomy six years ago with bilateral ureterocutaneostomy for bladder cancer.

In the last six years, due to recurrent urinary infections, the patient received several therapeutical courses of treatment with antibacterial drugs (pipemidic acid, betalactamases, sulphonamides, nalidixic acid, cinoxacin, ciprofloxacin) without any adverse reaction.

One month before the severe anaphylactic reaction, while starting a therapeutic course of cinoxacin, he experienced tongue paresthesia and diffuse cutaneous itching after the first 500 mg capsule.

He simply stopped cinoxacin and started a different antibacterial drug.

One month later, forgetting the previous reaction, again taking a 500 mg cinoxacin capsule, the patient experienced a more severe reaction : within a few

⁽¹⁾ Ambulatorio Allergologico, Unità Operativa di Medicina Interna
Ospedale di Faenza (Ravenna) - Italy.

minutes after ingestion he exhibited generalised urticaria, paresthesias, abdominal pain, severe hypotension, sphincter incontinence and loss of consciousness.

At the Emergency Room, the prompt administration of epinephrine subcutaneously, antihistamines and hydrocortisone intravenously, normalised the serious hypotension.

While recovering consciousness, the patient referred a short-lasting jugular pain.

At the same time electrocardiogram (ECG) recorded ST elevation and transitory II grade atrioventricular block, suggesting an ischemic event.

A myocardial infarction was confirmed by the increase in myocardial muscle enzymes (CKMB : 94 mg/dl) and ECG evidence of Q wave and negative T waves.

Considering the need for the patient to be treated for urinary tract infections, and the reported cross-reactivity between different generation quinolones, we performed a double-blind placebo controlled challenge test with an alternative drug according to the SIAIC allergy/intolerance drug reactions Position Paper (1).

DISCUSSION

Cinoxacin is an oral synthetic antibacterial agent, of the second generation quinolones group (2). The quinolones possess excellent efficacy in respiratory, intra-abdominal, pelvic, and skin and soft tissue infections (3); moreover they have a wide spectrum of activity against most uropathogens and achieve high urinary concentrations for extended time periods (4). Overall, quinolones are well tolerated drugs (5), although phototoxicity and photoallergenicity is well demonstrated experimentally (6).

The mechanism of action of cinoxacin, similar in structure to nalidixic acid, of which it is a cinnolinic derivative, involves interactions with both DNA girase, the originally recognised drug target, and topoisomerase IV, a related type II topoisomerase (7).

Cinoxacin owns a broad antibacterial spectrum because of its effective blockade of DNA replication, it is thought to be well-tolerated and it is useful for treatment of initial or recurrent uncomplicated urinary tract infections because of its rapid excretion by kidney and its high urinary concentration (8).

Although an anaphylactoid and/or anaphylactic reactions to fluoroquinolones are estimated to occur in 0.46-

1.2/100.000 patients, a literature review showed many adverse, even severe, allergic or not, drug reactions to quinolones. Principally these reactions are due to fluoroquinolones: a lot of cases of anaphylaxis/anaphylactoid in patients with AIDS (9) and in non AIDS patients (10, 11) to ciprofloxacin, recently a case to levofloxacin (12).

Stricker in 1988 reviewed three cases of acute hypersensitivity reactions to cinoxacin referred to the Netherlands Centre for Monitoring of Adverse Reactions to Drugs and 17 cases notified to the World Health Organisation Collaborating Centre for International Drug Monitoring (13). In all patients there was a clear temporal relation between the intake of cinoxacin and the onset of adverse events; all patients but one had taken cinoxacin before, without ill effect and probably it was then that they were sensitised.

In our case, the short time elapsed between drug assumption and the anaphylactic reaction, makes the allergic origin of the reaction likely. Negative personal and familiar history of atopy does not formally exclude the possibility of anaphylactic reaction. However we cannot rely on skin tests or specific IgE due to their false negative and false positive results.

Our case offers further evidence that there is a direct participation of the heart in anaphylactic reactions (14), because activated mast cells in myocardial tissue, perivascular and among myocytes, release preformed mediators (histamine, carboxypeptidase, tryptase, chymase, adenosin) (15) and de novo induced mediators such as from arachidonic acid (peptido leukotrienes, PGD₂, TXA₂) (16) or PAF.

These mediators can determine cardiovascular effects acting on H₁, H₂, and H₃ receptors both on coronary vessels and on myocytes.

CONCLUSION

In literature we find numerous studies that reveal the existence of cross-reactivity among the different quinolones generation. Due to recent reported cases of anaphylactic reaction with the new molecule belonging to this class of pharmaceuticals, we consider it advisable to avoid administering all quinolones to patients who have suffered an allergic reaction to any one quinolone.

Furthermore, even for an ethical aspect already remarked by the SIAIC Position Paper (1), we don't consider the execution of challenge test with molecules belonging to the same family justified. So we performed

double-blind placebo controlled challenge test with an alternative drug.

We administered to the patient increasing doses of oral nitrofurantoin, belonging to the synthetic antibacterial drug family from the furano nucleus, as urinary antiseptic. We did not observe any adverse immediate or late adverse reaction to this drug

In conclusion, a double blind placebo-controlled challenge test, using a different drug from quinolones, is free of danger and useful for patients with a known allergy to a quinolone.

REFERENCES

1. Commissione per le reazioni avverse ai farmaci della SIAIC. Memorandum SIAIC sulla diagnosi di allergia/intolleranza a farmaci. Giorn Ital Allerg Immunol Clin 1998;8(4):568-595.
2. D. Bassetti. I chinoloni. - In : *Chemioterapici antinfettivi e loro impiego razionale*. Lombardo Editore, Roma 1986:189-197.
3. V.-T. Andriole. - The future of the quinolones. *Drugs* 1999;58 (2):1-5.
4. S. Krcmery *et al.* - Newer quinolones in the long term prophylaxis of recurrent urinary tract infections. *Drugs* 1999;58 (2):99-102.

5. R. Stahlmann, H. Lode. - Toxicity of quinolones. *Drugs* 1999;58(2):37-42.
6. T. Horio *et al.* - Phototoxicity and photoallergenicity of quinolones in guinea pigs. *J Dermatol Sci* 1994;7(2):130-5.
7. R. Stahlmann, H. Lode. - Mode of action of fluoroquinolones. *Drugs* 1999;58(2):6-10.
8. D. Vervollet *et al.* - Quinolones. In : *Drug Allergy*. Pharmacia & Upjohn Sweden 1999:85-86.
9. R.-M. Soetikno *et al.* - Ciprofloxacin-induced anaphylactoid reaction in a patient with AIDS. *Ann Pharmacother* 1993;27(11):1404.
10. G. Erdem *et al.* - Anaphylactic reaction to ciprofloxacin in a toddler: successful desensitization. *Pediatr Infect Dis J* 1999;18(6):563-4.
11. M. Corcoy *et al.* - Intraoperative anaphylactic reaction after ciprofloxacin administration. *Rev Esp Anesthesiol Reanim* 1999;46(9):419-20.
12. M.-A. Smythe *et al.* - Anaphylactoid reaction to levofloxacin. *Pharmacotherapy* 2000;20(12):1520-3.
13. B.-H. Ch Stricker *et al.* - Anaphylactic reactions to cinoxacin. *BMJ* 1988; 297: 1434-1435.
14. A. Genovese *et al.* - Effetti cardiovascolari dei mediatori chimici dell'anafilassi. In : *Reazioni anafilattiche ed anafilattoidi*, G. Marone, Ed. Springer-Verlag, Milano 1997:39-56.
15. G. Marone *et al.* - Human heart mast cells in anaphylaxis and cardiovascular disease. *Int Arch Allergy Immunol* 1995;107 (1-3):72-75.
16. V. Patella *et al.* - Human heart mast cells. Isolation, purification, ultrastructure, and immunologic characterization. *J Immunol* 1995;154(6):2855-65.

- ☐ **OUI, je désire m'abonner à ALLERGIE & IMMUNOLOGIE pour 1 an (10 numéros).**
☐ **Please register my subscription to ALLERGIE & IMMUNOLOGIE (1 year - 10 issues)**

- ☐ France 90 €
☐ Etudiants France* / France - Students rate* 63 €
☐ Etranger/DOM-TOM / France (overseas territories) and foreign rates 119 €
 * joindre un justificatif / *Students are required to provide evidence of matriculation

- ☐ **OUI, je commande la reliure ALLERGIE & IMMUNOLOGIE pratique et solide, elle me permet d'archiver mes revues et de protéger ma collection.**
☐ **Please register my order for ALLERGIE & IMMUNOLOGIE bindings.**

...Reliure(s) à 11,50 € TTC l'unité + Frais de port / ... Bindings x 11.50 euros each (taxes included)

(france Métropolitaine Franco de port) / Postage & Packing :

- ☐ 3,81 € (DOM et Europe) / France (Overseas territories) and Europe
☐ 5,34 € (TOM et autres) / Foreign

Pour un total de € / Total Euros

Nom Name Prénom / Surname

Adresse Address Profession / Occupation

Code Postal Post Code Ville / City E-mail

- ☐ Je choisis le règlement "simplifié", je paie la totalité par prélèvement, je remplis l'autorisation ci-contre. Je n'oublie pas d'y joindre un RIB ou un RIP.
 (*offre réservée à la France)

- ☐ 'Simplified' subscription * or installments with duly signed reference. authorization and bank / PO (* France only)

- ☐ chèque bancaire ou postal / Bank or PO check expire fin :
☐ carte bleue ou visa n° : / Debit card (Visa etc.) No: Expiry date:

Signature obligatoire :

Conformément à la Loi informatique et libertés n°27 du 6/01/78, vous disposez d'un droit d'accès et de rectification aux données vous concernant.