

Gabapentin induces edema, hyperesthesia and scaling in a depressed patient; a diagnostic challenge

Reza Bidaki, Zahra Sadeghi¹, Safiye Shafizadegan¹, Ali Sadeghi¹, Behrang Khalili¹, Alireza Haghshenas¹, Seyyed Mohammad Mahdy Mirhosseini¹

Department of Psychiatry, Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical Sciences, Yazd,
¹Department of Neurosurgery, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Gabapentin is a common drug used as analgesic and anticonvulsant and also is prescribed for insomnia, depression, obsessive – compulsive disorder and panic attack. We report a case of a 48-year-old man who is prescribed gabapentin because of insomnia, headache, and depressed mood. In the first period of using the drug no complication has been seen. However in the next period, side-effects such as hyperesthesia, scaling and severe localized edema has been observed. After several laboratory tests and imaging, no reason was found for his edema. And after discontinuing gabapentin the pain and edema was quite relieved. We found out the brand of the drug has been switched in the second stage. The point which makes our study special is the incidence of side-effects such as severe edema, scaling and hyperesthesia for the first time because of using gabapentin and changing the drug combination.

Key Words: Edema, gabapentin, hyperesthesia, scaling, side-effect

Address for correspondence:

Dr. Seyyed Mohammad Mahdy Mirhosseini, Department of Neurosurgery, Isfahan University of Medical Sciences, Isfahan, Iran.

E-mail: Mahdy_mir2005@yahoo.com

Received: 19.02.2013, Accepted: 18.03.2015

INTRODUCTION

Gabapentin is a common drug which was indicated for treatment of epilepsy^[1] and these years it is also used as an analgesic compound.^[2,3] This drug is a structural analogue of gamma-aminobutyric acid (GABA),^[4] but the mechanism of action of this drug is still unknown.^[2] It seems to have an inhibitory effect on $\alpha 2\delta$ subunit of Ca^{2+} channels in the brain, and it might increase GABA concentration.^[2,5] It decrease the sensitivity of dorsal horn spinal cord neurons and in this way exert its analgesic effect.^[5]

This drug is widely used as analgesic, antiepileptic, postoperative pain reducer, treatment of insomnia,

migraine, neuralgia, brachioradial pruritus, post hepatic neuralgia, acquired nystagmus, bipolar disorder, MS and hepatic and renal disorders in elderly and children.^[2,4,6-11]

The European Federation of Neurological Societies has been approved rules about drug consumption dosage, which is 300 mg/day as initial dosage. Lower dosage is prescribed for the elderly.^[8]

Side-effects such as dizziness, insomnia, somnolence, dose-dependent localized edema, weight gain, ataxia, nystagmus, asthenia, skin rash, nausea, vomiting, and visual disturbance has been reported.^[3,4,12]

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Bidaki R, Sadeghi Z, Shafizadegan S, Sadeghi A, Khalili B, Haghshenas A, *et al.* Gabapentin induces edema, hyperesthesia and scaling in a depressed patient; a diagnostic challenge. *Adv Biomed Res* 2016;5:1.

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.174955

Despite of these side-effects, gabapentin is used as the first option for analgesic usage due to its relative reliability, easy use, high endurance and lack of negative interaction with other drugs.^[3]

In this article, we present a case that has been referred to us because of multiple somatic complaints, insomnia and depressed mood. Hence, we prescribed him gabapentin, but after that, unusual side-effects that have not been seen yet such as scaling, hyperesthesia, and severe localized edema have been observed.

CASE REPORT

A 48-year-old married man with low education and socio-economic level, which is having depressed mood, hopelessness, low self-esteem, anxiety and several somatic complaints has presented to us. He suffered from insomnia and somatic pain and headache also complained from nausea and vomiting and choking. He had experience of chest trauma and genitalia. He had a surgery after the trauma, and as a result he was suffering from physical weakness. There was no history of substance abuse. He has multiple somatic complaints that are not faking insubordinate and attention seeking. The psychiatric diagnosis for the patient was somatization disorder with serious depressive disorder. However before referring the patient to us the prior diagnosis was migraine headache. He has no complain of edema and scaling and hyperesthesia in his lower extremities in the first admission.

Drugs prescribed for the first admission, which was last 45 days, of the patient was: Tablet olanzapine 5 mg Hs, capsule gabapentin 300 mg Hs, tablet valproic acid BID, tablet nortriptylin 10 mg Hs. At the end of the first period patient symptoms was improving partially and no side-effects were been observed.

Drugs were prescribed for the second admission was: Tablet citalopram 20 mg Hs, tablet alprazolam 0.5 mg TDS, tablet maprotiline 15 mg Hs, capsule omeprazole daily, capsule gabapentin 300 mg Hs. Seven days after the administration of the gabapentin, the patient complained from pain and edema and scaling and hyperesthesia in his lower extremities and pitting edema, pain and tenderness. The range of motion of the extremities was been increased. According to the patient statement the gabapentin brand has been changed.

To find out the clear cause of these effects, we suggested different tests and requested him consultation to several specialists. As a result there was no problem in internal and orthopedics consult, femoral pulse

was normal, and dorsalis pedis pulse has not been detected. The extremities were not warm, and it was a little pale. X-ray of foot, chest X-ray and sonography were normal. The pain didn't response to nonsteroidal anti-inflammatory drugs. Wide splitting S2 was reported in cardiology consult.

According to results of tests there was no organic cause for these effects, so we decided to discontinue the consumption of drugs. After 4 days, the pain and edema in extremities was thoroughly relieved.

DISCUSSION

Gabapentin is used as analgesic and antiepileptic among neurologists, although psychologists prescribe it for treatment of insomnia and depression.^[1,2,7] It has an inhibitory effect on $\alpha\delta$ subunit of Ca^{2+} channels in central nervous system and in this way plays its role as an analgesic.^[2,5] As usual side-effects we can mention dizziness, weight gain, asthenia, nausea, and vomiting.^[3,12]

In our case, neuralgia and hyperesthesia has been observed as new side effects. As a noticeable point, gabapentin consumption is for treatment of neuralgia, but here neuralgia is one of the gabapentin side-effects. Furthermore, localized edema is a rare side effect that we faced with severe state of it.^[3] Leg edema might be occurred in systemic and local types. Systemic edema could be caused by congestive cardiac failure, renal failure, hypoalbuminemia, protein losing neuropathy. For localized edema we can note following reasons such as primary and secondary lymphedema, lipedema, deep vein thrombosis and chronic venous disease.^[13,14]

There are many factors could cause above-mentioned side-effects. The first reason we supposed is the incidence of edema due to organic disorders. With the result that we suggested some tests and imaging also referred him to some specialists as we mentioned in case presentation. The negative results of tests and result less referrals convinced us that organic disorders were not responsible for the patient side-effects. Drugs causing edema such as methadone, morphine, manidipine,^[15] bosentan,^[16] felodipine,^[15] alendronate,^[17] insulin^[18] could be our next possibility for the patient edema, but actually the patient did not take these drugs.

As gabapentin was the main drug, has been used in both periods, and these side effects have been only observed during the second period so gabapentin could not be the main cause by itself, but the disappearance of side-effects after discontinuing gabapentin intake shows another factor that somehow related to

gabapentin has caused the side-effects. And regarding to the incidence of side effects despite the reduction of gabapentin dosage in the second admission (reduced from 300 to 150 mg/day) we conclude the most possible reason is switching gabapentin brand. Franek *et al.* have reported switching Alendronate brand could have adverse side-effects.^[19] This study helps us to admit the point that switching brand of gabapentin could cause new side-effects.

It is necessary that the physicians know the side-effects of drugs such as gabapentin and notice that an anti-analgesic drug can cause pain too. Distinguish of drug side-effects can prevent of lab tests of unnecessary.

Acknowledgments

We thank from the patient because of his cooperation in the preparation of this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Cavanna AE, Ali F, Rickards HE, McCorry D. Behavioral and cognitive effects of anti-epileptic drugs. *Discov Med* 2010;9:138-44.
2. Mathew NT, Rapoport A, Saper J, Magnus L, Klapper J, Ramadan N, *et al.* Efficacy of gabapentin in migraine prophylaxis. *Headache* 2001;41:119-28.
3. Erdogan G, Ceyhan D, Güleç S. Possible heart failure associated with pregabalin use: Case report. *Agri* 2011;23:80-3.
4. Bassilios N, Launay-Vacher V, Khoury N, Rondeau E, Deray G, Sraer JD. Gabapentin neurotoxicity in a chronic haemodialysis patient. *Nephrol Dial Transplant* 2001;16:2112-3.
5. Kutschenko A, Liebetanz D. Meningioma causing gabapentin-responsive secondary SUNCT syndrome. *J Headache Pain* 2010;11:359-61.
6. Vedula SS, Bero L, Scherer RW, Dickersin K. Outcome reporting in industry-sponsored trials of gabapentin for off-label use. *N Engl J Med* 2009;361:1963-71.
7. Karam-Hage M, Brower KJ. Open pilot study of gabapentin versus trazodone to treat insomnia in alcoholic outpatients. *Psychiatry Clin Neurosci* 2003;57:542-4.
8. Galluzzi KE. Managing neuropathic pain. *J Am Osteopath Assoc* 2007;107:ES39-48.
9. Clivatti J, Sakata RK, Issy AM. Review of the use of gabapentin in the control of postoperative pain. *Rev Bras Anesthesiol* 2009;59:87-98.
10. Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the treatment of postherpetic neuralgia: A randomized controlled trial. *JAMA* 1998;280:1837-42.
11. Bandini F, Castello E, Mazzella L, Mancardi GL, Solaro C. Gabapentin but not vigabatrin is effective in the treatment of acquired nystagmus in multiple sclerosis: How valid is the GABAergic hypothesis? *J Neurol Neurosurg Psychiatry* 2001;71:107-10.
12. Türe H, Sayin M, Karlikaya G, Bingol CA, Aykac B, Türe U. The analgesic effect of gabapentin as a prophylactic anticonvulsant drug on postcraniotomy pain: A prospective randomized study. *Anesth Analg* 2009;109:1625-31.
13. Tiwari A, Cheng KS, Button M, Myint F, Hamilton G. Differential diagnosis, investigation, and current treatment of lower limb lymphedema. *Arch Surg* 2003;138:152-61.
14. Ruan X, Tadia R, Couch JP, Ruan J, Chiravuri S. Severe peripheral edema during an outpatient continuous epidural morphine infusion trial in a patient with failed back surgery syndrome. *Pain Physician* 2008;11:363-7.
15. Richey FF, Laurent S. Efficacy and safety profiles of manidipine compared with amlodipine: A meta-analysis of head-to-head trials. *Blood Press* 2011;20:54-9.
16. Matucci-Cerinic M, Denton CP, Furst DE, Mayes MD, Hsu VM, Carpentier P, *et al.* Bosentan treatment of digital ulcers related to systemic sclerosis: Results from the RAPIDS-2 randomised, double-blind, placebo-controlled trial. *Ann Rheum Dis* 2011;70:32-8.
17. Manicourt DH, Brasseur JP, Boutsen Y, Depreux G, Devogelaer JP. Role of alendronate in therapy for posttraumatic complex regional pain syndrome type I of the lower extremity. *Arthritis Rheum* 2004;50:3690-7.
18. Bas VN, Çetinkaya S, Agladioglu SY, Kendirici HN, Bilgili H, Yildirim N, *et al.* Insulin oedema in newly diagnosed type 1 diabetes mellitus. *J Clin Res Pediatr Endocrinol* 2010;2:46-8.
19. Franek E, Talalaj M, Wichrowska H, Czerwieńska B, Filip R, Safranow K, *et al.* Switching from one generic alendronate to another – A common procedure in Poland in the years 2001-2005. *Endokrynol Pol* 2011;62:14-7.