

Pregabalin Induced Confusional State with Paranoid Delusions

Leroy Lindsay* and Allison Averill

Rutgers New Jersey Medical School, Newark, New Jersey USA

*Corresponding author: Lindsay L, Rutgers New Jersey Medical School, Physical Medicine and Rehabilitation, 90 Bergen Street, Suite 3200, Newark, New Jersey 07107, USA, Tel: 012403052186; E-mail: leroy.lindsay@gmail.com

Received date: March 04, 2015; Accepted date: June 07, 2015; Published date: June 09, 2015

Copyright: © 2015 Lindsay L, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

CASE DESCRIPTION

A 70-year-old woman presented to an acute inpatient rehabilitation facility on postoperative day three, after undergoing left total knee arthroplasty. Her past medical history included severe osteoarthritis, hypertension, and diabetes mellitus type 2 and was negative for any psychiatric illness. The patient took metformin, celecoxib, and oxycodone/acetaminophen prior to undergoing surgical intervention. After surgery, pregabalin, 50 milligrams twice a day, was added to her previous oral analgesic regimen of celecoxib and oxycodone/acetaminophen. However, on the night of admission postoperative day two (POD #2), she developed mild paranoia. Her husband and nursing staff reassured her the entire night. In the morning, she apologized for acting strangely and participated in all therapy sessions. All medications that could cause psychiatric disturbance or delirium, including oxycodone/acetaminophen and pregabalin, were discontinued. That night, however, her paranoia returned and she remained emotionally labile and delusional despite reassurance and delirium intervention. During the night, she pulled the fire alarm in order to have the police and fire department come to protect her.

The following morning, she was oriented to person, place, time, and situation, but had a fixed delusion and paranoia that she was unsafe. She participated in her therapy sessions, but remained apprehensive and guarded despite her husband's presence and reassurance. Although she had a psychology consultation with more reassurance and relaxation techniques, she remained unsettled. Serial examinations were performed by psychiatry, physical therapy and psychology disciplines, each revealed that the patient was oriented to person, place, time, date, had organized speech, she recognized family members, and could recall all events. The only abnormality was the paranoia, emotionally labile and fixed delusional. While it is difficult to definitively conclude that her mental delusion was induced by pregabalin, similar clinical presentations have been reported throughout the literature.

The patient had her last dose of oxycodone/acetaminophen on POD #3, the documented half-life is 34 hours and we expect to elimination to be completed after 35 half-lives.

That night, she attempted to escape from the hospital and became combative. She was then readmitted to the acute care hospital under the psychiatric service. General blood exams excluded infection or metabolic derangement. While it is unknown if ketamine was used during the perioperative period, it is known that she did not receive an agonist/antagonist during the

perioperative period. However, opioids were used in preop and/or during surgery and in PACU. The patient began exhibiting symptoms prior to the discontinuation of this medication, making opioid withdrawal less likely. During the next two days, she returned to her baseline mental status and was discharged home.

Discussion

As the population ages, there has been greater concern for maintaining and improving quality of life through medical intervention. Many are having elective joint replacements to decrease pain, increase mobility, and improve their quality of life. However, as the number of joint replacements performed increases, the risk of complications has decreased, but not disappeared. One such complication or areas of concern is pain during the perioperative period as it has been established that pain control after surgery is important for quality of life, participation in physical therapy, and other health-related benefits [13]. Given the need for better pain control, novel and multimodal treatment regimens have been developed, utilizing synergistic agents and affecting multiple pain pathways in order to minimize opioid use and limit opioid-related side effects [48]. One agent that has become more popular in multimodal pain regimens and perioperative period is pregabalin [924]. Some literature supports the use of pregabalin in this setting and has shown a reduction in both pain and narcotic consumption [22]. Additionally, the side effect profile has been relatively insignificant making it a good addition to the pain medication regimen [25,26]. However, there must be diligence in further researching the effectiveness of this medication

and its analgesic properties in various clinical scenarios as there are reports of pregabalin causing delirium, psychosis, and other neuropsychiatric sequelae, especially in the context of accelerated dose titration [27, 28]. Even at lower doses we must weigh the risk and benefit to patients.

Structural lesions	CVA, HTN, primary and met tumors, closed trauma
Metabolic cause	hypoxia, hypoglycemia, renal failure, liver failure, vitamin deficiency, acidbase or electrolyte abnormality
Hypoperfusion	shock, CHF, cardiac arrhythmia, anemia
Infectious causes	hyperthermia, meningitis, encephalitis, cerebral infection, PNA, UTI
Drugs	benzodiazepines, barbiturates, etomidate, atropine
Miscellaneous	sleep deprivation, urinary retention, fecal impaction, sensory disturbance

Table 1: Possible causes of postoperative psychiatric disturbance [29]

The documented half-life for pregabalin is 6 hours and we expect to elimination to be completed after 35 half-lives. As pregabalin is renally excreted, elimination is dependent on renal function [22]. While the patient described above had normal BUN/Cr values and assumed normal renal function, there was history of diabetes mellitus, relative dehydration, and post-operative blood loss anemia which all may have

contributed to the altered metabolism of pregabalin as manifested by a prolonged period of psychiatric disturbance.

In this case report we describe delirium and fixed paranoid delusion in an older patient with few medical comorbidities after TKA and while on a low dose of pregabalin. While pregabalin may be effective at treating perioperative neuropathic pain, physicians must be aware that even at low doses patients may experience significant psychiatric disturbance.

Conclusion

In summary, the present report suggests that an acute confusional state and paranoid delusions be considered a possible adverse reaction for pregabalin. Even at low doses in certain clinical scenarios, this medication may have the potential to cause significant distress to patients, their families, as well as health care providers. Discontinuation of the medication at the first sign of an adverse reaction will likely result in symptom resolution.

References

1. National Hospital Discharge Survey: 2010 table, Procedures by selected patient characteristics Number by procedure category and age. http://www.cdc.gov/nchs/data/nhds/4procedures/2010pro4_numberprocedureage.pdf
2. Kurtz SM, Ong KL, Lau E, Bozic KJ (2014) Impact of the economic downturn on total joint replacement demand in the United States: updated projections to 2021. *J Bone Joint Surg Am* 96: 624-630.
3. Singh JA, Vessely MB, Harmsen WS, Schleck CD, Melton LJ 3rd, et al. (2010) A population-based study of trends in the use of total hip and total knee arthroplasty, 1969-2008. *Mayo Clin Proc* 85: 898-904.
4. Lewis C, Gunta K, Mitchell K, Bobay K (2012) Effectiveness of multimodal pain management protocol in total knee arthroplasty patients. *Orthop Nurs* 31: 153-159.
5. Hebl JR, Dilger JA, Byer DE, Kopp SL, Stevens SR, et al. (2008) A pre-emptive multimodal pathway featuring peripheral nerve block improves perioperative outcomes after major orthopedic surgery. *Reg Anesth Pain Med* 33: 510-517.
6. Lee BH, Park JO, Suk KS, Kim TH, Lee HM, et al. (2013) Pre-emptive and multi-modal perioperative pain management may improve quality of life in patients undergoing spinal surgery. *Pain Physician* 16: E217-226.
7. Blanco JS, Perlman SL, Cha HS, Delpizzo K (2013) Multimodal pain management after spinal surgery for adolescent idiopathic scoliosis. *Orthopedics* 36: 33-35.
8. Duellman TJ, Gaffigan C, Milbrandt JC, Allan DG (2009) Multi-modal, pre-emptive analgesia decreases the length of hospital stay following total joint arthroplasty. *Orthopedics* 32: 167.
9. Mathiesen O, Dahl B, Thomsen BA, Kitter B, Sonne N, et al. (2013) A comprehensive multimodal pain treatment reduces opioid consumption after multilevel spine surgery. *Eur Spine J* 22: 2089-2096.
10. Burns LC, Ritvo SE, Ferguson MK, Clarke H, Seltzer Z, et al. (2015) Pain catastrophizing as a risk factor for chronic pain after total knee arthroplasty: a systematic review. *J Pain Res* 8: 21-32.
11. Bremner S, Webster F, Katz J, WattWatson J, McCartney C (2012) Older adults' postoperative pain medication usage after total knee arthroplasty: a qualitative descriptive study. *J Opioid Manag* 8:145-152.
12. Buvanendran A, Kroin JS, Tuman KJ, Lubenow TR, Elmoftoy D, et al. (2003) Effects of perioperative administration of a selective cyclooxygenase 2 inhibitor on pain management and recovery of function after knee replacement: a randomized controlled trial. *JAMA* 290: 2411-2418.
13. Baratta JL, Gandhi K, Viscusi ER (2014) Perioperative pain management for total knee arthroplasty. *J Surg Orthop Adv* 23: 22-36.
14. Arroyo S, Anhut H, Kugler AR, Lee CM, Knapp LE, et al. (2004) Pregabalin add-on treatment: a randomized, double-blind, placebo-controlled, dose-response study in adults with partial seizures. *Epilepsia* 45: 20-27.
15. Lesser H, Sharma U, LaMoreaux L, Poole RM (2004) Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology* 63: 2104-2110.
16. Dworkin RH, Corbin AE, Young JP, Sharma U, LaMoreaux L, et al. (2003) Pregabalin for the treatment of postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology* 60: 1274-1283.
17. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L (1995) The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 38:19-28.
18. Tassone DM, Boyce E, Guyer J, Nuzum D (2007) Pregabalin: a novel gamma-aminobutyric acid analogue in the treatment of neuropathic pain, partial-onset seizures, and anxiety disorders. *Clin Ther* 29: 26-48.
19. Arnold LM, Russell IJ, Diri EW, Duan WR, Young JP, et al. (2008) A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *J Pain* 9: 792-805.
20. Singla NK, Chelly JE, Lionberger DR, Gimbel J, Sanin L, et al. (2014) Pregabalin for the treatment of postoperative pain: results from three controlled trials using different surgical models. *J Pain Res* 8: 9-20.
21. Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, et al. (2015) Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol* 14: 162-173.
22. Mishriky BM, Waldron NH, Habib AS (2015) Impact of pregabalin on acute and persistent postoperative pain: a systematic review and meta-analysis. *Br J Anaesth* 114: 10-31.
23. Martinez V, Cymerman A, Ben Ammar S, Fiaud JF, Rapon C, et al. (2014) The analgesic efficiency of combined pregabalin and ketamine for total hip arthroplasty: a randomised, double-blind, controlled study. *Anaesthesia* 69: 46-52.
24. Solaro C, Tanganelli P (2009) Acute delirium in patients with multiple sclerosis treated with pregabalin. *Clin Neuropharmacol* 32: 236-237.
25. Zaccara G, Gangemi P, Perucca P, Specchio L (2011) The adverse event profile of pregabalin: a systematic review and meta-analysis of randomized controlled trials. *Epilepsia* 52: 826-836.
26. Hickey C, Thomas B (2012) Delirium secondary to pregabalin. *Gen Hosp Psychiatry* 34: 436.
27. Olaizola I, Ellger T, Young P, Bösebeck F, Evers S, et al. (2006) Pregabalin-associated acute psychosis and epileptiform EEG-changes. *Seizure* 15: 208-210.
28. Pedrosa JL, Nakama GY, Carneiro Filho M, Barsottini OG (2012) Delirium, psychosis, and visual hallucinations induced by pregabalin. *Arq Neuropsiquiatr* 70: 960-961.
29. Barbosa FT, da Cunha RM, Pinto AL (2008) Postoperative delirium in the elderly. *Rev Bras Anestesiol* 58: 665-670.