



CASE REPORT

A case report from Nepalese community pharmacy on levofloxacin induced severe abdominal pain



K.C. Bhuvan^{a,*}, Alian A. ALrasheedy^b, Mohamed Izham Mohamed Ibrahim^c

^a *Clinical Pharmacy, Travel Medicine and Socio-Pharmacology Division, Sankalpa Foundation Pvt. Ltd., Pokhara, Nepal*

^b *School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia*

^c *Research and Graduate Studies Affairs, College of Pharmacy, Qatar University, Doha, Qatar*

Received 10 February 2013; accepted 23 April 2013

Available online 10 May 2013

KEYWORDS

Abdominal pain;
Community pharmacist;
Levofloxacin;
Nepal

Abstract A 46-year-old female patient developed severe abdominal pain shortly after taking levofloxacin, 1000 mg for acute bacterial sinusitis. The pain started after taking the first dose of levofloxacin and became worse after the second dose. The patient was unable to do daily physical activities. The pain resolved upon discontinuation of levofloxacin and symptomatic therapy. Other factors that may cause abdominal pain were ruled out. This case is of interest as it documents severe abdominal pain due to levofloxacin requiring discontinuation of therapy and describes its appropriate management. In addition, it highlights the vital role that community pharmacists could play in managing adverse drug reactions (ADRs) and preventing potential Drug Related Problems (DRPs).

© 2013 Production and hosting by Elsevier B.V. on behalf of King Saud University.

1. Introduction

Fluoroquinolone classes are among the best selling drugs in Nepal. Two fluoroquinolone antibiotics are among the 15 top selling drugs in Nepal (Kafle et al., 2007). Levofloxacin is a newer antibiotic from the fluoroquinolone group and is used for the treatment of community-acquired pneumonia, nosocomial pneumonia, chronic bronchitis, acute bacterial sinusitis, urinary tract infection, acute pyelonephritis, and skin or skin

structure infections (Lacy et al., 2010). Common adverse effects of levofloxacin include headache, GI symptoms, insomnia, nausea, diarrhoea and pharyngitis. Although abdominal pain is a reported adverse reaction that may occur due to levofloxacin, in this case a severe abdominal cramp developed during the use of levofloxacin which severely affected patient's physical activity and resulted in discontinuation of therapy.

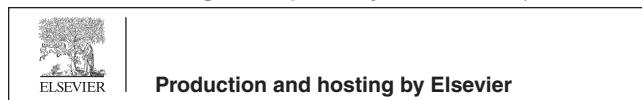
2. Case report

A 46-year-old female with abdominal pain since one day was presented to the community pharmacist. After verifying the location of the pain, severity was assessed using the McCaffery scale (1–10 pain severity assessment scale). The community pharmacist rated her pain to be 7 on a scale of 10 and found that the pain worsened on ambulation (McCaffery and Pasero, 1999). Further assessment by the community pharmacist revealed a severe pain in right upper and left upper quadrant

* Corresponding author. Tel.: +977 9805831957.

E-mail addresses: Kcbhuvan@gmail.com (K.C. Bhuvan), aliana@hotmail.com (A.A. ALrasheedy), mohamedizham@yahoo.com (M.I.M. Ibrahim).

Peer review under responsibility of King Saud University.



and left lower and right lower quadrant leading to abdominal cramp. Further history taking revealed that she was diagnosed with acute bacterial sinusitis recently and was prescribed levofloxacin 1000 mg once daily. The patient was given hyoscine butylbromide 10 mg twice daily PRN (when necessary) to provide symptomatic relief from her abdominal cramp. The pharmacist counselled the patient and asked her to follow up with in case the pain persists. The next day the patient returned to the pharmacy. Her abdominal pain was worse and moreover, she explained that it started after she took levofloxacin. Her pain remained 7 on a scale of 10 and worsened on ambulation.

The community pharmacist suspected the abdominal cramp was due to levofloxacin and performed a complete history taking. Medical history revealed that the patient was diagnosed with hypothyroidism two years ago and was prescribed levothyroxine 100 mcg once daily. As the thyroid level returned normal, the dose was gradually tapered and the patient discontinued levothyroxine supplement since past 6 months on her physicians' advice. The patient was also diagnosed with hypertension three months ago and was on amlodipine 5 mg once daily. The patient was obese and her body mass index (BMI) was 30.6. Four days before, she experienced headache, running nose and flu-like symptoms, and visited hospital nearby. The physician carried out nasal rhinoscopy, blood culture and physical examination of the forehead to check the bones, and diagnosed her with acute bacterial sinusitis. She was prescribed a 5 day course of levofloxacin 1000 mg once daily. After the first day of the regimen, she experienced mild abdominal pain which worsened on the second day of levofloxacin regimen. The patient was unable to continue her daily physical activities and came to the community pharmacy.

On examination, the patient had tender pain and complained of moderate to severe pain in all four abdominal quadrants. She said that the pain increased on ambulation. The pain increase on ambulation and was of the throbbing type affecting her daily life physical activities. The patient reported to experience pain in 2–3 h after taking her daily dose of levofloxacin. Physiologically, the patient was not in her menstrual period. The pharmacist also performed thorough interview to rule out gynaecological issue like menstrual cramp and adverse effect of any oral contraceptive pills (OCP). She was not using OCP such as levonorgestrel which might have an adverse event such as abdominal cramp. The pharmacist asked her to discontinue levofloxacin and to contact her physician immediately. A referral note about her abdominal cramp and its possible relation to levofloxacin dosing was made and attached to her medical report. The physician performed physical examination and confirmed the abdominal cramps. The physician also performed blood test (FBC) to avoid acute pancreatitis and performed endoscopy to rule out peptic ulcer and gastritis. Suspecting the abdominal cramp to be due to levofloxacin, the physician stopped levofloxacin and changed it with co-trimoxazole 960 mg twice daily for 7 days together with ranitidine 150 mg once daily. Her abdominal cramp was significantly improved and the pain was relieved by the second day of discontinuation of levofloxacin. A follow-up by the community pharmacist indicated that, within approximately 1 week of the treatment her sinusitis had improved, and she experienced no sign of abdominal pain during the course of co-trimoxazole treatment. She had no recurrence of pain, and was able to resume walking normally and returns to work.

3. Discussion

We present a case of severe abdominal cramp that developed during the use of levofloxacin by a 46-year-old female. Use of the Naranjo probability scale demonstrated a possible association between levofloxacin and this adverse effect (Naranjo et al., 1981). Although factors that may cause abdominal pain (e.g. irritable bowel syndrome) were ruled out, not all factors that may cause abdominal cramp could be ruled out with certainty. Nevertheless, we believe levofloxacin was the most likely agent, since the patient was pursuing a normal routine lifestyle, she was not on her menstrual period, and she had not experienced any physical strain or injury to her abdominal region. We believe that the abdominal cramp may have been caused by the high dose of levofloxacin.

The fluoroquinolone antibiotic class can cause the gastrointestinal tract problems such as nausea and diarrhoea, and adverse central nervous system (CNS) effects such as headache and dizziness. These adverse events are usually mild and do not require discontinuation of therapy (Mandel and Tillotson, 2002). Although abdominal pain is also listed as an adverse effect of levofloxacin, abdominal cramp due to fluoroquinolone requiring discontinuation of therapy is a rare adverse effect, and makes this case worth sharing. In this patient, abdominal cramp started 2–3 h after taking levofloxacin and was resolved upon discontinuation of levofloxacin.

The fluoroquinolone antibiotic class is generally well tolerated (Mandel and Tillotson, 2002). The incidence of abdominal pain due to levofloxacin is estimated to be 2% (Lacy et al., 2010). Levofloxacin-induced tendinopathy has been well reported, and carriers are required by the United States Food and Drug Administration to display a black box warning describing possible tendinopathy (Ganske and Horning, 2012). To our knowledge, this case is unique, since the case involved severe abdominal cramp believed to be caused by levofloxacin which required stopping levofloxacin and changing to other medication. The exact cause of levofloxacin induced abdominal pain is not known but levofloxacin might have caused inflammation of the parietal peritoneum which caused innervations of somatic nerve. The pain was exacerbated by movement and developed as abdominal rigidity and guarding (Nicki et al., 2010). While systematic studies are lacking, there have been reports of levofloxacin induced abdominal pain by patients in various forms, but most were not as severe as this case. (Treato Pharma, 2012). Another study by eHealthMe (2012) involving 5341 levofloxacin users showed that 155 people (2.90%) reported abdominal pain while taking levofloxacin.

The patient was taking amlodipine 5 mg once daily, and amlodipine is not known to cause severe abdominal pain. The patient was not having a menstrual period which could cause abdominal cramp. Though the patient is obese (BMI 30.6), she was not involved in any strenuous physical activity which could cause or worsen abdominal cramp. The dose of levofloxacin for acute bacterial sinusitis is 500 mg once daily for 10–14 days or 750 mg once daily for 5 days, while this patient received a dose of 1000 mg of levofloxacin once daily. This is higher than the recommended daily dose, and may have caused abdominal cramp, or had a role in worsening abdominal cramp. A multicenter randomized double-blind study conducted in United States comparing the effect of levofloxacin

500 mg once daily for 10 days versus levofloxacin 750 mg once daily for 5 days for acute bacterial sinusitis showed that levofloxacin 750 mg once daily for 5 days was not inferior to the lower dose (Poole et al., 2006). Thus the high dose of levofloxacin was not justified. Though there is not clear evidence for dose-related adverse events with levofloxacin, the higher dose might have caused abdominal cramp or worsened the pain. Treatment for abdominal pain associated with levofloxacin involves discontinuation of therapy, using antispasmodic drugs such as hyoscine butylbromide, proper rest, and avoidance of strenuous physical activity. The symptoms disappear after discontinuation of the drug. Use of subjective assessment tools to determine patients' abdominal pain and careful palpation may be useful in detecting abdominal cramp (McCaffery and Pasero, 1999). Consideration should be given to proper counselling of the patient about the possible adverse effect of medicines. Though Nepal does not provide systematic clinical practice guidelines for the treatment of specific medical conditions, the physician should adhere to the antibiotic dosing recommendations of international professional societies (Rosenfeld et al., 2007). Exceeding the daily recommended dose of antibiotics may lead to an adverse drug reaction, or worsen an existing reaction.

A community pharmacist can play a vital role in counselling the patient during the time of therapy, and provide proper guidance and referral of the patient to a higher care centre after an adverse drug reaction. Furthermore, for a resource-scarce country like Nepal, the community pharmacist can play a great role by promoting the safe use of medicine within the community. Since pharmacists work in close contact with patients and are often the first point of referral for patients at the community level, a community pharmacy run by a pharmacist can act as a bridge between the physician and the patient. A pharmacist can assist the patient with the prescription, and may also intervene at the appropriate time in the case of an adverse drug reaction, such as this case.

4. Conclusion

There is a possible association between the adverse effect (severe abdominal pain) and levofloxacin. The severe pain required immediate intervention and discontinuation of therapy. Thus, community pharmacists, as essential part of primary healthcare system, should play more active roles and counsel and educate patients about the possibility and incidence of adverse drug events.

Conflict of interest

The authors declare that they have no conflicts of interest to disclose.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgements

The authors would like to thank Sankalpa Community Pharmacy, Sankalpa Foundation for providing its medical database for writing this case study.

References

- eHealthMe - Real World Drug Outcomes. (2012) Could Levofloxacin cause abdominal pain? A study of 155 users. Available at <http://www.ehealthme.com/ds/levofloxacin/abdominal+pain> accessed on 4 Nov 2012.
- Ganske, C.M., Horning, K.K., 2012. Levofloxacin-induced tendinopathy of the hip. *Ann. Pharmacother.* 46, e13.
- Kafle, K.K., Karki, S.B., Rajhbhandari, V., 2007. Report on Consumption of Antibiotics and Other Medicine. Department of Drug Administration, Kathmandu, Nepal.
- Lacy, C.F., Armstrong, L.L., Goldman, M.P., Lance, IL., 2010. *Drug Information Handbook with International Trade Names Index*. 18th ed.. Lexi-Comp.
- Mandel, L., Tillotson, G., 2002. Safety of fluoroquinolone: an update. *Can. J. Infect. Dis.* 13 (1), 54–61.
- McCaffery, M., Pasero, C., 1999. *Pain: Clinical Manual*, 2nd ed. Mosby, St. Louis, MO.
- Naranjo, C.A., Busto, U., Sellers, S.M., et al, 1981. A method for estimating the probability of adverse drug reactions. *Clin. Pharmacol. Ther.* 30, 239–245. <http://dx.doi.org/10.1038/clpt>.
- Nicki, R.C., Walker, B.R., Ralston, S.H., 2010. *Davidson's Principles and Practice of Medicine*. Churchill Livingstone Elsevier.
- Poole, M., Anon, J., Paglia, M., et al, 2006. A trial of high dose short course levofloxacin for the treatment of acute bacterial sinusitis. *Otolaryngol. Head Neck Surg.* 134, 10–17.
- Rosenfeld, R.M., Andes, D., Bhattacharyya, N., et al, 2007. Clinical practice guideline: adult sinusitis. *Otolaryngol. Head Neck Surg.* 137, S1–S31.
- Treato Pharma. (2012) What patients are saying about Levofloxacin and Abdominal Pain. Available at <http://treato.com/Levofloxacin,Abdominal+Pain/?a=s>. Accessed on 4 Nov 2012.