

Review

Loss of menstruation associated with furazolidone: A case report and review of literature

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A 48-year-old Chinese female is described, whose menstruation disappeared after taking furazolidone for 3 years and we review complications associated with furazolidone. It is suggested that clinicians should be aware of various complications unexpectedly associated with furazolidone.

Key words: Furazolidone, complications, menstruation.

INTRODUCTION

Furazolidone is a synthetic nitrofuran with a broad spectrum of antimicrobial action and has been widely used in the treatment of gastrointestinal infections. It has been proposed as an agent to treat *Helicobacter pylori* and is commonly used in some third-world countries. A variety of adverse reactions of furazolidone were reported with its continued clinical application.

This article describes a patient who suffered from stomach disease, who experienced loss of menstruation after taking furazolidone for three years. In order to learn the adverse effects of furazolidone, a comprehensive literature search was performed on Medline, Embase and China National Knowledge Infrastructure (CNKI, China), with adverse events, complication, safety and furazolidone as search terms.

CASE REPORT

A 48-year-old Chinese female was admitted for lumbar disc herniation in our hospital. She said that she had no menstruation when she was 39 years old. When asked detailed medical history, she told us that she started taking furazolidone (0.1 g tid) because of gastrohelcoma with *H. pylori* infection at the age of 36. Menstruation disappeared and severe limb numbness appeared after she took furazolidone for 3 years. She said that she did

not take any special drug within these 3 years. She was told the numbness was associated with furazolidone when she went to see doctors in a local hospital, and that her uterine ultrasound and abdominal computed tomography (CT) showed normal. It was considered that the disappearance of menstruation was associated with furazolidone too and she stopped taking it. However, her menstruation did not resume any more.

DISCUSSION

Furazolidone has a wider antibacterial spectrum; it is more extensively applied in the poor areas because of low-cost. Some patients often buy it themselves. In clinic, there were various complications induced by furazolidone reported (Table 1). The main side effects of the drug are nausea, vomiting and other gastrointestinal reactions and multiple neuritis. Generally, it is considered that taking long-term or large doses furazolidone easily lead to multiple neuritis (Zhidong, 2003), but it appeared in short-term medication (Wenx, 1997; Xiaohuang et al., 1996). Jiming et al. (1997) observed electromyography (EMG) of 13 patients who suffered from peripheral neuropathy associated with furazolidone. It showed earlier onset with higher dose and positive correlation between degree of neuromuscular electrical abnormalities and duration of medication. Pathogenesis is the inhibition of enzyme system of glucose metabolism and the glucose metabolism disorders. It injuries, the motor or sensory fibers, leads to inflammation in the peripheral nervous

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Table 1. Complications associated with furazolidone.

| First author | Year published | Number of cases | Complications | Country |
|----------------|----------------|-----------------|----------------------------|---------|
| Zhidong H. | 2003 | 11 | Peripheral neuritis | China |
| Wenxi Q. | 1997 | 1 | Peripheral neuropathy | China |
| Xiaohuang Z. | 1996 | 2 | Polyneuritis | China |
| Cortez L. M. | 1972 | 1 | Pulmonary hypersensitivity | America |
| Collins J. V. | 1973 | 1 | Pulmonary reaction | England |
| Zielonka T. M. | 1997 | 1 | Pulmonary reaction | Poland |
| Kowalski T. J. | 2005 | 1 | Pulmonary hypersensitivity | America |
| Suling R. | 1998 | 2 | Insanity | China |
| Zijie W. | 2003 | 1 | Mental disorder | China |
| Lifang Z. | 1999 | 1 | Mental disorder | China |
| Qianyi S. | 1991 | 2 | Mental disorder | China |
| Suhong W. | 1999 | 2 | Mental disorder | China |
| Guozheng X. | 1996 | 78 | Acute hemolysis | China |
| Peiqian P. | 1996 | 24 | Acute hemolytic anemia | China |
| Yuhua A. | 1988 | 19 | Acute hemolytic anemia | China |
| Zhenyu H. | 1997 | 1 | Acute hemolytic anemia | China |
| Teqiang L. | 1998 | 15 | Acute hemolytic anemia | China |
| Lianhui L. | 1997 | 1 | Acute hemolytic anemia | China |
| Supan L. | 2003 | 5 | Hemolytic anemia | China |

system finally, because of disruption of energy sources of nervous tissue.

Pulmonary hypersensitivity to furazolidone was reported earlier by Cortez and Pankey (1972). There were another three papers which reported pulmonary reaction to furazolidone (Collins and Thomas, 1973; Zielonka et al., 1997; Kowalski et al., 2005). Pulmonary hypersensitivity due to furazolidone manifests with fever, hypoxia, interstitial infiltrates on chest X-ray and eosinophilia during or shortly after administration of the drug. All patients initially received antibiotics for presumptive infectious pneumonitis and had favorable clinical outcomes following removal of the offending drug. The mechanisms of pulmonary reaction due to drugs of the furadantin group may involve both type III and IV reactions (Collins and Thomas, 1973).

There were some sporadic cases reported in China about mental disorders associated with furazolidone, and they showed symptoms of mental disorder of manic type. The mechanisms are because furazolidone is a monoamine oxidase inhibitor, and it leads to hyperthyroidism of monoamine after taking furazolidone for a long-term. According to "amine hypothesis" of mental illness, it is considered that monoamine release increasingly by inhibiting monoamine degrading enzymes-monoamine oxidase activity. The concentration of effective medium in receptor site increases the excessive functional activity of brain monoamine, so that the patients excite (Suling, 1998; Zijie and Yizu, 2003; Lifang, 1999; Qianyi and Guangbo, 1991; Suhong and Chenggen, 1999).

Acute hemolytic anemia was also a kind of complication associated with furazolidone, particularly in children. Guozheng (1996) reported that 78 children showed acute hemolysis, because they took furazolidone orally, and all patients were Hakka. She thought that Hakka should be careful to a category of drugs which has antioxidant effect. Peiqian (1996) and Yuhua and Zhongling (1988) reported each 24 and 19 cases who mainly come from village, suffered from acute hemolytic anemia due to furazolidone. In addition, there were several reports that described acute hemolytic anemia associated with furazolidone too (Zhenyu, 1997; Teqiang, 1998; Lianhui, 1997; Supan and Juan, 2003) It is considered that patients suffered from acute hemolytic anemia because they have heredity G-6-PD deficiency. The drug can turn oxyhaemoglobin into methemoglobin and make lots of reduced glutathione into oxidized glutathione. It cause red cell membrane changed and obstruct red blood cells metabolism. Meanwhile, red blood cells become stiff when glutathione is reduced into oxidation.

In this case, the patient suffered from loss of menstruation and multiple neuritis after taking furazolidone for three years. Now numbness relieves, her menstruation did not resume and the mechanism why furazolidone is associated with menopause is not clear, but it take her great hurt.

CONCLUSION

Conclusively, we think there are various complications unexpectedly associated with furazolidone. Clinician

should be aware of complications associated with furazolidone and restrict patients from taking furazolidone for long-term because of various complications unexpectedly.

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