Department of Veterans Affairs
Office of Inspector General

Healthcare Inspection

Quality of Care of Two Deceased West Virginia Veterans

Report No. 08-01377-185 **August 14, 2008**

VA Office of Inspector General
Washington, DC 20420

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Executive Summary

The VA Office of Inspector General (OIG) was asked by Senator Rockefeller to review the care of two West Virginia combat veterans who were being treated for severe post-traumatic stress disorder (PTSD) and who died in their sleep. The Senator asked that the review take into account the medications prescribed and explore the possibility of any pattern in these tragic deaths.

We reviewed these patients' medical records and visited the Huntington VA Medical Center (VAMC), Charleston Community Based Outpatient Clinic and Vet Center, and the Cincinnati VAMC PTSD Residential Program. We interviewed the families of the patients and the providers at each site who had been involved in the care of these patients. We reviewed the autopsy and toxicology reports for both patients and discussed the findings with the Chief Medical Examiner for the State of West Virginia. We concluded that the care provided for these patients at the Charleston community based outpatient clinic, and the VA facilities in Huntington and Cincinnati met community standards of care.

VA's Pharmacy Benefits Management Services program and its Center for Medication Safety (VAMedSAFE) conducted a nationwide data pull of all-cause mortality during 1998–2008 for patients prescribed the combination of quetiapine, paroxetine, and clonazepam. Additional analyses examined other combinations of mental health medications, including an analysis by age of patients with and without PTSD. There was no apparent signal to indicate increased mortality for patients taking the combination of quetiapine, paroxetine, and clonazepam when compared with patients taking other similar combinations of psychotropic medications. The direct impact of non-prescribed medications in these patient deaths cannot be determined. VA mental health providers describe the use of non-prescription medications as growing area of concern in the treatment of young veterans.

Returning war veterans may have multiple mental health conditions in addition to PTSD. Restriction of admission to the Clarksburg Residential PTSD Program for patients taking clonazepam and related medications may decrease access to appropriate treatment. We recommended that management evaluate exclusion criteria for admission related to medications for newly-diagnosed patients to the Residential PTSD Program.

DEPARTMENT OF VETERANS AFFAIRS
Office of Inspector General
Washington, DC 20420

TO: Director, Veterans Integrated Service Network (10N4)

SUBJECT: Healthcare Inspection – Quality of Care of Two Deceased West Virginia Veterans

Purpose

The VA Office of Inspector General (OIG), Office of Healthcare Inspections was requested by Senator Rockefeller to review the care of two West Virginia combat veterans who were being treated for severe post-traumatic stress disorder (PTSD) and who died in their sleep. The Senator asked that the review take into account the medications prescribed and explore the possibility of any pattern in these tragic deaths.

In addition, patients' families expressed the following:

- Patients worsened while on medications and an inappropriate dose of a medication was prescribed.
- Physical complaints and medication side effects were not adequately addressed.
- The PTSD Residential Program at Clarksburg, West Virginia, did not accept patients who were taking certain medications.

Background

In 2008, two veterans (Patient A and Patient B) unexpectedly died in their sleep. Both were men under the age of 35 who had recently served in Iraq. Prior to their deaths both patients had been taking three prescribed psychiatric medications—paroxetine, clonazepam, and quetiapine.

Scope and Methodology

We interviewed the families of Patient A and Patient B. We visited the Huntington VA Medical Center (VAMC), Charleston Community Based Outpatient Clinic (CBOC) and Vet Center, and the Cincinnati VAMC PTSD Residential Program. We interviewed providers at each site who had been involved in the care of these patients. We reviewed the autopsy and toxicology reports for both patients and discussed the findings with the

Chief Medical Examiner for the State of West Virginia. We also reviewed VA medical records and Vet Center progress notes. For Patient A, we interviewed his private psychiatrist and the non-VA psychiatrist who cared for him during hospitalization at a state hospital; we also reviewed non-VA medical records.

In May 2008, in response to media reports of the death of these patients, the Veterans Integrated Service Network (VISN) 10 patient safety officer asked mental health clinic managers to review the medical records of patients who were currently prescribed the combination of quetiapine, paroxetine, and clonazepam to determine if any adverse drug events had occurred. We reviewed the facility responses and interviewed the psychiatrist who had performed these chart reviews for the patients at the Cincinnati VAMC.

In response to these deaths, VHA conducted an analysis of all deaths from any cause among patients who were prescribed the medications addressed in this report, and we reviewed that analysis in detail. We also searched the medical literature for reports of unexpected deaths in young adults related to these medications and general studies on accidental drug-related deaths.

We conducted the inspection in accordance with *Quality Standards for Inspections* published by the President's Council on Integrity and Efficiency.

Case Histories

Patient A

Patient A was initially seen for a mental health evaluation at the Charleston CBOC in 2007. The patient had served a 9-month tour of duty in Iraq in 2005. After this deployment, he experienced chronic depression, severe anxiety, social withdrawal, feelings of emotional distance, hyper-vigilance, sleep disturbance, intrusive thoughts of combat, poor anger control, alcohol misuse, and inability to maintain stable employment. Prior to evaluation at the CBOC the patient's family physician had prescribed an antidepressant, but this was discontinued after one week due to sedation. At the CBOC, the patient was treated with citalopram and trazodone for depression, anxiety, panic, and insomnia. Because of nausea, citalopram was discontinued after one week and paroxetine was prescribed. Trazodone was felt to be ineffective and was discontinued. He subsequently presented with suspiciousness, agitation, irritability, and insomnia, and quetiapine was prescribed.

Although paroxetine was somewhat effective, after a few months it was discontinued because of side effects and mirtazapine was prescribed. After he reported tearfulness, poor sleep, nightmares, and feeling that his "medicines were not right," mirtazapine was discontinued and paroxetine was re-started. Several weeks later, the patient reported extreme anxiety and admitted having had past thoughts about killing himself.

Clonazepam was prescribed to be taken at bedtime and quetiapine was discontinued. At a subsequent conversation, the patient admitted that he was still taking the quetiapine and his psychiatrist agreed to continue/re-start the medication.

By the fall of 2007 the patient on his own increased his dosage of quetiapine to 1200 milligrams (mg). At that time he was also taking paroxetine 40 mg per day and clonazepam 3 mg per day. His psychiatrist documented "…reinforced the plan to eventually become med. free, although will allow him [the patient] to play a major role in determining when. I did inform him that there are limits to the amount of medication he can depend upon."

In late 2007 and early 2008, the patient saw a private psychiatrist. His psychiatrist increased the paroxetine dose to 60 mg and later to 80 mg; he also increased quetiapine to 1600 mg and clonazepam to 4 mg per day. Valproic acid was started by the private psychiatrist for irritability and explosive outbursts. Although he was reportedly less irritable and his anger was better controlled, he also reported diarrhea and valproic acid was discontinued.

Subsequently, the patient was reportedly non-compliant with medications. He displayed increasing irritability and isolation and spent an excessive amount of time alone in his room. During that time, he presented to a non-VA facility. He became agitated after waiting several hours in the emergency department and was involuntarily admitted to a state hospital for two weeks. During that hospitalization, the patient was treated for a bipolar disorder with psychotic features and PTSD. Paroxetine was discontinued, escitalopram was initiated, the quetiapine dose was reduced to 800 mg per day, and clonazepam was discontinued. In addition, while at the state hospital he was started on oxcarbazepine.

On the day after discharge from the state hospital, he was seen by a psychologist and a psychiatrist at the Huntington VAMC. The psychiatrist noted that the "…Pt. and his mother believed he was responding better to former medications so I agreed to return him to previous medications." In addition, the patient had apparently developed a tremor after initiation of oxcarbazepine. The oxcarbazepine dose was tapered off, clonazepam was restarted, the quetiapine dose was continued at 800 mg, escitalopram was discontinued, and paroxetine was re-started. A week later the patient was seen by a Huntington VAMC psychologist for individual therapy. At that visit he did not report side effects related to his medications and indicated compliance with his regimen. The patient was found dead at his home less than one week later.

The autopsy report of the Chief Medical Examiner of the State of West Virginia stated that the patient died as a result of combined drug intoxication. The involved drugs included paroxetine, quetiapine, and a non-prescribed medication. No contributory natural diseases or physical injuries were identified.

Patient B

Patient B was deployed to Iraq in 2003. After his return home, he attended group sessions at the Charleston Vet Center and in mid-2006 was referred to the Charleston CBOC for mental health evaluation. He reported having nightmares and feeling paranoid, anxious, depressed, and irritable. He endorsed difficulties with anger and feeling constantly on guard. He described himself as a different person since his return home. He was started on paroxetine, quetiapine, and clonazepam. A few weeks later the patient reported feeling better and having a new full time job at a manufacturing plant.

Over the next nine months, the patient's therapist spoke with him by phone noting the patient's concern that the policy of his employer was that new employees were allowed to miss only 3 days of work during the initial year or face termination. The patient re-presented in the summer of 2007. At a mental health appointment with his therapist, he reported feeling "ready to explode." He discussed significant marital stress and complained of headaches. Primary care and psychiatric medication appointments were arranged. Laboratory work was obtained at a primary care appointment. Paroxetine and quetiapine were re-initiated. In the fall of 2007, he was seen by a primary care provider for chronic knee pain. Physical therapy was recommended and he was prescribed gabapentin.

The patient told a provider that he was taking 30 mg of paroxetine a day instead of the 20 mg prescribed. He had also increased his quetiapine dose; the higher dose helped him sleep. The patient was irritable and reported getting into fights. The dose of paroxetine was increased to 30 mg and the quetiapine to 300 mg, and he was continued on clonazepam. At that time, the patient was seeing a social worker at the Charleston CBOC for therapy and attending group sessions at the Vet Center.

The patient experienced difficulty sleeping, and increased nightmares, anxiety, anger, and irritability. He expressed concern that he might lose his temper and end up in jail. He no longer had a job and reported financial stress and feeling desperate to find work. His paroxetine dose was increased and valproic acid was started to target his irritability and anger outbursts. He was seen by primary care because of frequent headaches, and ibuprofen was prescribed. His family reported that he had gained weight and that his face and hands appeared swollen.

In late 2007 the patient entered the 8 week Residential PTSD Program at the Cincinnati VAMC. A nurse practitioner performed a baseline history and physical examination and an electrocardiogram, chest x-ray, urinalysis, and thyroid blood test were obtained. Prior blood work from the Charleston CBOC was reviewed.

His paroxetine dose was increased in week 3 due to ongoing depressive symptoms. The quetiapine dose was reduced several times after the patient reported over-sedation. At

one point, because of ongoing difficulty with sleep and nightmares, the patient re-increased the dose on his own to 400 mg.

Early in the program the nurse practitioner discontinued the gabapentin because it was felt that it might be contributing to dry mouth and the patient did not feel that it had been effective for his chronic leg pain. Later, the nurse practitioner ordered ibuprofen and Tylenol.

The clonazepam dosage was decreased during the first week and then ordered to be given at bedtime only if needed. The valproic acid dose was increased and, during the 6th week of the program, the patient admitted taking more than prescribed when he felt anxious. He was advised against this practice and was told that an extra dose would not provide any immediate benefit.

Also during the 6th week of the program, the patient complained of ongoing difficulty with nightmares and sleep paralysis. He was prescribed prazosin at bedtime and reported resolution of nightmares during the last week of the program. The patient reported some improvement in mood, but more improvement in irritability, energy, interest, and concentration. Toward the end of the program a reduction in PTSD symptoms was noted on the Clinician Administered PTSD Scale (CAPS) and the PTSD Checklist (PCL).

His family reported that when he was home for Christmas, he had tremors; and he appeared tired, heavily medicated, forgetful, and "foggy," with slurred speech at times. In addition, his voice was described as deep and raspy, different from his normal voice.

The patient met with the nurse practitioner a few days before completion of the program to review discharge planning. He reported plans to follow-up with his primary care physician at the Charleston CBOC. Progress notes written during the program do not indicate problems with sedation, hoarseness, cognitive impairment, or nausea.

On the day of discharge, he had a few episodes of vomiting after arriving home. He reportedly took 2 quetiapine pills (dosage unclear) and fell a sleep on the couch, where early the next morning he was found unresponsive.

The autopsy report of the Chief Medical Examiner of the State of West Virginia stated that the patient died as a result of combined intoxication with paroxetine, quetiapine, and two non-prescribed medications "…under circumstances significant for fatal over-use of prescribed paroxetine…" with apparent misuse of non-prescribed medications of uncertain intentionality.

Inspection Results

Issue 1: Quality of Care for Two Veterans:

The care provided for these patients at the Charleston CBOC, Huntington VAMC, and the Cincinnati VAMC met community standards of care.

Patient A

Medical record progress notes indicate that the patient and his providers discussed medication options, dosing, desired and adverse effects, as well as possible drug-drug and food-drug interactions. Providers documented medication side effects.

Food and Drug Administration-approved prescribing information for quetipaine states that in clinical trials "…the majority of patients responded between 400 to 800 mg/day. The safety of doses above 800 mg per day has not been evaluated in clinical trials." However, depending on a patient's presentation, in clinical practice it is not unusual for psychiatrists to prescribe medications in doses above the recommended dose range. In the fall of 2007, the patient's VA psychiatrist agreed to increase the quetiapine dose to 1200 mg after the patient had self-increased the dose. The dose was again increased while the patient was under the care of a non-VA psychiatrist. After hospitalization at the non-VA hospital, the patient was seen again by the VA psychiatrist, at which time the prescribed quetiapine dose was 800 mg.

The patient was seen by a primary care physician at the CBOC and at the Huntington VAMC multiple times, and was evaluated by a non-VA physician in Huntington. He was also seen by a social worker for therapy and case management at the CBOC, and he attended individual and group sessions at the Vet Center.

The patient's social worker reported that he was frequently difficult to engage in the treatment process. Treatment was also complicated by the patient's other mental health issues. The social worker reported that she had frequently suggested hospitalization or at one point admission to the Residential PTSD Program at the Clarksburg VAMC, but the patient declined.

After he was committed to a state hospital, there was discussion between the patient's family and Huntington VAMC staff about possible transfer to a VA hospital. However, the only VA hospital in West Virginia with a locked inpatient psychiatry unit, which the patient required, is in Martinsburg, more than 350 miles away.

During the hospitalization, a Vet Center therapist told a family member that patients taking clonazepam or similar medications would probably be ineligible for admission to the Clarksburg PTSD Residential Program. During the patient's stay at the state hospital, his psychiatrist discontinued the clonazepam after learning that it might interfere with his acceptance in the PTSD program. Ultimately, the patient was not accepted because he

was felt to be not stable enough to participate in the intensive trauma-focused program. Toward the end of his stay at the state hospital, there was discussion about possible admission to another non-VA psychiatric hospital, but the patient declined.

After discharge from the state hospital, the patient was seen by a psychologist at the Huntington VAMC. The psychologist noted that the patient had limited coping skills for self-management of PTSD symptoms; consequently, he planned to see the patient weekly to begin cognitive-behavioral therapy.

The Associate Chief of Staff at Clarksburg verified to the OIG that the Residential Program at Clarksburg historically does not admit patients on benzodiazepine medications (clonazepam is a benzodiazepine).

Patient B

The patient participated in an 8-week Residential PTSD Program at the Cincinnati VAMC. The focus of the program is improvement through structured individual and group evidence-based psychotherapies. Medication is viewed as serving an adjunctive role to reduce symptoms so that patients are better able to engage in therapy. For example, difficulty sleeping not only negatively impacts quality of life but also interferes with participation in therapy. At initial evaluation and as patients progress through the program, staff reported that they aim to eliminate medications, reduce doses, and simplify regimens if clinically appropriate. Our review of treatment records for this patient showed that staff did attempt to reduce medication doses.

Several clinical providers told us that the patient actively participated in therapy, did not appear sedated or ill, interacted appropriately with peers, and appeared committed to recovery. Blood and urine tests, an electrocardiogram, and a chest x-ray revealed no heart or kidney disease.

Issue 2: Role of Medications in Death of Two Veterans

The Medical Examiner found that these patients died from combined drug intoxication involving prescribed and non-prescribed medications. In the presence of PTSD, other mental health conditions, and uncertain use of medications by patients, we are unable to draw conclusions about the relationship between medication regimens and these deaths.

The toxicology report for one of the patients showed a markedly elevated blood level of paroxetine, even though the patient was prescribed an appropriate dose. The patient did not display signs of suicidal ideation in the weeks prior to his death. Paroxetine is not known to be substantially affected by the presence of the other prescribed medications, and genotyping of liver tissue revealed no significant abnormality in the ability of the liver to metabolize paroxetine. Paroxetine can adversely interact with one of the non-prescribed medications. However, the impact of this potential interaction is unclear.

In May 2008, the VISN 10 patient safety officer asked mental health clinic managers to review the charts of patients currently prescribed the combination of quetiapine, paroxetine, and clonazepam for documentation of any adverse drug effects. No deaths or significant adverse events were reported.

VHA's Pharmacy Benefits Management (PBM) Services program and its Center for Medication Safety (VAMedSAFE) conducted a nationwide analysis of all-cause mortality during 1998–2008 for patients prescribed the combination of quetiapine, paroxetine, and clonazepam. Additional analyses examined other combinations of mental health medications, including an analysis by age of patients with and without PTSD. The VA analysis was essentially a series of data queries, and is limited by inability to determine specific cause of death or adjust for medical co-morbidities. There was no apparent signal to indicate increased mortality for patients taking the combination of quetiapine, paroxetine, and clonazepam when compared with patients taking other similar combinations of psychotropic medications.

VHA researchers are studying mortality in elderly patients taking antipsychotic medications in combination with other psychotropic medications. They will be able to determine cause of death using National Death Index data. VHA's VAMedSAFE is working with the primary investigator to expand the study and has recently applied for funding to include younger patients.

Although antipsychotic medications have been identified as possible causes of cardiac rhythm disturbances, a 2001 review in the medical literature found no association with olanzapine, quetiapine, or risperidone and Torsades de Pointes (a fatal arrhythmia) or sudden death. The authors did caution that all antipsychotic medications may cause serious adverse events, and balancing risks and benefits is a challenge for psychiatrists. The authors also recommended that clinicians ask patients if they have had fainting or have relatives who died suddenly at a young age. For elderly patients, especially those with known heart disease or those already taking non-psychiatric drugs that prolong the QT interval (part of the heart electrical conduction cycle), a pretreatment electrocardiogram would be appropriate.[1] In the absence of known cardiac disease, we are unaware of any clinical practice guidelines recommending baseline or periodic electrocardiogram monitoring in young, healthy patients on quetiapine.

Clinicians have described a tendency of young returning veterans to self-medicate using non-prescribed prescription medication obtained from friends, family members, and co-workers. These behaviors have also been observed among non-veteran patients treated for mental health conditions at private facilities. In addition, media reports during the past year describe the use of non-prescribed prescription medications by patients at military treatment facilities.

[1] Glassman, Alexander H.,M.D., and Bigger, Jr., J. Thomas, M.D., Antipsychotic Drugs: Prolonged QTc Interval, Torsades de Pointes, and Sudden Death, The American Journal of Psychiatry, 158: 1774-1782, November 2001.

Conclusions

These two Iraqi war veterans served honorably in Iraq. After returning from the Middle East they suffered with symptoms of PTSD and other mental health conditions. Their deaths are tragic.

The health care provided for these patients met community standards of care.

VHA's Pharmacy Benefits Management Services program and its Center for Medication Safety (VAMedSAFE) conducted a nationwide data pull of all-cause mortality during 1998–2008 for patients prescribed the combination of quetiapine, paroxetine, and clonazepam. Additional analyses examined other combinations of mental health medications, including an analysis by age of patients with and without PTSD. There was no apparent signal to indicate increased mortality for patients taking the combination of quetiapine, paroxetine, and clonazepam when compared with patients taking other similar combinations of psychotropic medications. The direct impact of non-prescribed medications in these patient deaths cannot be determined.

Returning war veterans may have multiple mental health conditions in addition to PTSD. Restriction of admission to the Clarksburg Residential PTSD Program for patients taking clonazepam and related medications may decrease access to appropriate treatment.

VA mental health providers describe the use of non-prescription medications as growing area of concern in the treatment of young veterans.

Recommendation

We recommend that the VISN Director ensure that the Clarksburg VAMC Director evaluate exclusion criteria for admission related to medications for newly-diagnosed patients to the Residential PTSD Program.

Comments

The VISN and Medical Center Directors agreed with our findings and recommendations and submitted an acceptable improvement plan. (See pages 10–12 for the full text of comments.) We will follow up on the planned actions until they are completed.

(original signed by:)
JOHN D. DAIGH, JR., M.D.
Assistant Inspector General for
Healthcare Inspections

Appendix A

VISN Director Comments

Department of Veterans Affairs **Memorandum**

Date: August 6, 2008

From: Network Director, VISN 4 (10N4)

Subject: **Healthcare Inspection – Quality of Care of Two Deceased West Virginia Veterans**

To: Deputy AIG for Healthcare Inspections (54)

1. Attached please find my approved plan to address recommendations identified by the Office of Inspector General (OIG) to improve the quality of care provided to veterans residing in the State of West Virginia. The action item identified by OIG has been completed.

2. The insights and observations provided by OIG are appreciated and a valuable resource for improving services provided. If you have any questions, please do not hesitate to contact me.

(original signed by Bradley P. Shelton, Deputy Network Director)

MICHAEL E. MORELAND, FACHE

Appendix B

Medical Center Director Comments

Department of Veterans Affairs **Memorandum**

Date: August 6, 2008

From: Director, Louis A. Johnson VA Medical Center, Clarksburg, WV (540/00)

Subject: **Healthcare Inspection – Quality of Care of Two Deceased West Virginia Veterans**

To: Deputy Chief of Staff, VA Central Office, Washington, DC (10B)

Thru: Network Director, VISN 4 (10N4)

1. Attached please find the Louis A. Johnson VA Medical Center's approved action plan to address the recommendation identified by the Office of the Inspector General (OIG) in their draft report regarding Quality of Care to Veterans residing in West Virginia.

2. The insights and observations provided by OIG are appreciated and a valuable resource for improving services provided. If you have any questions, please do not hesitate to contact me at (304) 623-7602.

(original signed by:)

WILLIAM E. COX

Attachment

Louis A. Johnson VA Medical Center, Clarksburg, WV

Director's Comments to Office of Inspector General's Report

The following Director's comments are submitted in response to the recommendations in the Office of Inspector General's report:

OIG Recommendation

Recommendation. We recommend that the VISN Director ensure that the Clarksburg VAMC Director evaluate exclusion criteria for admission related to medications for newly diagnosed patients to the Residential PTSD Program.

Concur **Target Completion Date:** October 1, 2008

Actions:

Louis A. Johnson VA Medical Center has reviewed the admission criteria for PRRTP and is revising the criteria to eliminate barriers to access related to medication profiles. A new policy is being developed and all staff associated with the residential rehabilitation programs will be educated on the revised criteria for admission. We will also inform VA Medical Centers who refer patients to our programs of the changes in admission criteria.

OIG Contact and Staff Acknowledgments

OIG Contact	Michael Shepherd, M.D., Medical Consultant (202) 461-4660
Acknowledgments	Patricia Christ Jerome Herbers Christa Sisterhen

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