

Adverse Reaction To Diazepam; A Case Report

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Citation

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Abstract

Diazepam belongs to the group known as benzodiazepines tranquilizers, anxiolytics, and anti-convulsant agent. Its use as in most drugs has been associated with side effects and adverse reactions. Although a lot of therapeutic goals can be accrued to its use, the case report would highlight an unreported adverse reaction to Diazepam. A 25 years old man had an adverse reaction to diazepam after being administered as a premedication, 10mg intravenously. The observations were tachycardia, blisters all over the body, gross swelling of the right upper limb where the drug was administered, fever, diplopia, headache, as well as sudden hypotension preceded by hypertension. He was managed adequately with steroids, antihistamine, phenergan and intravenous fluid. Notwithstanding surgery for left inguinal hernia was carried-on.

INTRODUCTION

Diazepam belongs to the group of drugs known as benzodiazepines. It is a tranquilizer, anxiolytic as well as anti-seizure drug¹. They are thought to stimulate γ -amino butyric acid receptors in the ascending reticular activating system and they therefore block both the cortical and limbic arousal systems following stimulation of the brain stem reticular formation. They have been shown to depress electrical discharge in septum, amygdala and hippocampus which are components of the limbic system that regulate emotion². Intravenous diazepam or midazolam are used by the majority of endoscopists as premedications. In the UK, the ratio of diazepam to midazolam users is approximately 2:1³.

CASE REPORT

The reported case is about a 25 year old man, a student who was first seen in the surgical outpatient clinic two months prior to surgery with a history of swelling in the left groin of four years duration. The swelling was painful and reducible. He denied any history of trauma, fever, abdominal swelling or vomiting. He was not a known epileptic or diabetic, nor was there a history of drug allergy. He did not take alcohol or take tobacco products in any form, and was the last child in a family of four.

Examination revealed a young man, not pale nor jaundiced, with a pulse rate of 76 beat per minute, regular and good volume.

His blood pressure was 110/70mmHg, and the heart sounds were normal.

Abdominal examination revealed a reducible left inguinal hernia.

Rectal examination revealed no abnormality.

A diagnosis of left reducible inguinal hernia was made. Pre-operatively, His packed cell volume was 40%, Hemoglobin concentration of 14g/dl. The white blood cell count and urinalysis done were normal. He was booked for herniorraphy. As a premedication for ketamine anesthesia, he was given intravenous diazepam 10mg slowly through infusion line. As the drug was being administered, the patient complained of severe pains on the limb and within seconds, he began to complain of tightness' in the chest, dizziness, severe headache and double vision. He became restless and physically aggressive. On examination, he was restless, acyanosed, conscious but disoriented in time, person and place. The pulse rate was 120 beat per minutes, bounding but regular. His blood pressure was 180/110 mmHg. Heart sounds were normal. An impression of adverse reaction to diazepam was made. Intravenous hydrocortisone 200mg and intramuscular 50mg phenergan were given and then the infusion changed from normal saline to dextrose water. Thereafter patient calmed down, the pulse was still 120 beats per minute. The blood pressure dropped to 160/ 100mmHg. However, the operation was

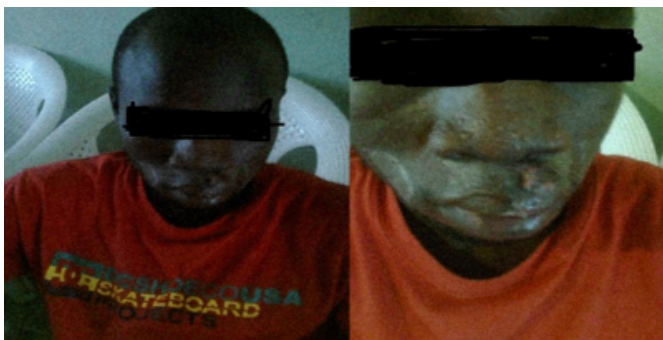
carried-out using local infiltration with xylocaine-adrenaline. The operation lasted for about 30 minutes.

In the immediate post-operative period, the pulse remained high at 130 beat per minutes while the blood pressure then crashed to 60/20mmHg. He was resuscitated with normal saline, plasma expanders, phenergan and hydrocortisone. He also had pain relief with pentazocine. His immediate postoperative pack cell volume was 40% and he was making adequate amount of urine. On the first post-operative day, he was calm and conscious but however, the headache continued, and he developed a high grade fever of 39.5 degree Celsius. The pulse was 130 beat per minutes, the blood pressure remained low at 60mmHg systolic and diastolic unrecordable.

The right upper limb where the diazepam was given was grossly swollen and markedly tender to touch. He developed blisters all over the body, which were worse on the mouth, nose, and the right upper limb. The resuscitation continued using fluid, steroid, and antihistamine. He was also treated for malaria, and was commenced on antibiotics - ampicloxacin and metronidazole.

Figure 1

Figure A :Facial view of patient / Fig B: blisters over lip and nostrils



On the second post-operative day; the headache persisted, blisters had not regressed, though limb edema was subsiding. The pulse was 88 beats per minute, blood pressure has returned to 120/80mmHg, and he was making adequate amount of urine.

On the third post-operative day; he had made remarkable improvement. The hand edema began to subside, and the blisters were disappearing. Both the pulse and blood pressure became normal and stable. The patient made remarkable improvements, thereafter stitches were removed on the sixth post-operative day. The wound was cleaned and he was discharged home seventh post operative day.

DISCUSSION

Idiosyncrasies or peculiar mannerism is an abnormal reaction of a person to otherwise normal substance in abnormal manner. This was clearly demonstrated in this case. The common reactions to diazepam include dizziness, thrombophlebitis, venous thrombosis⁴, apnea, hypotension, circulatory and respiratory depression³, drowsiness, sedation and ataxia. Rare adverse effects include headache, vertigo, hypotension, gastrointestinal upset, skin rashes, visual disturbance, change in libido and urinary retention. Others such as blood dyscrasias, jaundice and hallucination have been reported. There is a report that hemodynamic effects following diazepam infusion depend on dosage, rapidity of administration, concomitantly administered drugs, and basal physiologic state of the patient⁵. Also for subjects without known cardiovascular disease, induction of anesthesia with intravenous diazepam (0.45 mg/kg) was reported to have no significant effect on mean arterial pressure (MAP)⁶ while larger diazepam induction doses (0.8 mg/kg) decreased MAP and cardiac output⁷. This may have been responsible for the hypotension the patient experienced. However the patient's pulse rate remained high throughout the period. The occurrence of thrombophlebitis and venous thrombosis has been reported⁴. However, there were no suppurations of the limb in the indexed case. The gross edema of the limb that followed the drug administration could not be completely explained but may be as a result of vasodilators released, leading to extravasation of fluid massively from the vessels into surrounding tissue. The tightness of the chest he experienced may suggest some cardio-vascular problems, which could not be supported by other investigations. The patient had no past history of allergic drug reactions. Reflex tachycardia⁸ is known as one of the effect of diazepam. This may account for the tachycardia observed as was observed in this case. Tachycardia is a reflex counter mechanism to sudden hypotension.

The fever he developed could have been due to malaria been in an endemic area or as a part of the drug reactions. Also, he had persistent headache but there was no obvious neurological deficit. The blisters disappeared without leaving a trace and gross edema of the limb subsided before his discharge. Immediate hypersensitivity and asthma like reaction to intramuscular and intravenous diazepam⁹ has been reported. Thrombocytopenic purpura¹⁰ and conjunctivitis¹¹ to due to oral diazepam has also been reported.

Ghosh¹² reviewed that hypersensitivity reaction to Diazepam

and other benzodiazepines are rare and have not been fully documented.

A look at drug ampoule confirmed that it was not expired and came from the same batch of drug used for other patients for the same procedure without such reactions. Idiosyncratic reactions are not to be overlooked while using medications as exemplified by diazepam. Close watch and preparedness to manage adverse reactions need to be emphasized because not all persons are constitutionally alike in terms of response to the same drug. It is important for all to be aware that patient can react to any drug despite how safe the drug may be.

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