

## Hyperamylasemia After Over Purchase of Clonazepam

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### Abstract

Clonazepam is an anticonvulsant connected with high affinity to benzodiazepine receptors and effective through GABA (Gamma-aminobutyric acid) and serotonin. Poisoning related to Clonazepam is frequently encountered in the literature. However, cases described a hyperamylasemia have not been reported. In this case, we presented clonazepam overdose with suicidal intent of the 31-year-old female patient who developed hyperamylasemia and reviewed in the light of recent literature.

**Keywords:** Clonazepam; Emergency; Hyperamylasemia; Poisoning

### Introduction

Animal experiments and electroencephalographic studies in humans demonstrated that clonazepam has direct inhibitor activity on cortical and subcortical focuses and inhibits generalized convulsive activity. Clonazepam, therefore, is useful in focal epilepsy and primary generalized seizures [1]. Clonazepam strengthens the pre and postsynaptic inhibitory effects of  $\gamma$ -aminobutyric acid in central nervous system. Excitations due to excessive compensation, physiological activity of neurons without any negative feedback through a devastating impact lightened [2].

Hyperamylasemia developed by the poisoning secondary to valproic acid, other antiepileptic drugs, tricyclic antidepressants, atypical antipsychotics and organophosphates have been frequently reported [3-8]. However, hyperamylasemia and clonazepam poisoning relation have not been reported. In the presented case; Hyperamylasemia resulted by clonazepam overdose is discussed and reviewed in light of the recent literature.

### Case

Thirty-one year old woman as was unconscious, unresponsive to painful stimuli brought to our emergency department in committed suicide about two hours after ingestion of clonazepam overdose. She has been treated for her opiate addiction for two years, 1 year ago. There was no other drugs prescribed to her before intoxication and she had not used any opiates for 1 year since the end of her addiction therapy. Her alcohol consumption was not mentioned by her husband and we did not find alcohol in her blood samples. She was found with empty clonazepam boxes by her husband. When patient was admitted to the emergency room the vital signs were as follows; the arterial blood pressure: 110/70 mm-Hg, pulse: 108/min, body temperature: 36.7°C, respiratory rate: 18/min and Glasgow coma scale (GCS) 3 (E1, M1, V1), respectively. The blood sugar measured by finger stick was 145 mg/dl.

The patient was intubated for safety of airway and 4 lt/min oxygen was started over endotracheal tube. Nasogastric tube was inserted, after gastric irrigation, at a dose of 1gr/kg activated charcoal was given. Patient's taken electrocardiography were unremarkable other than sinus tachycardia (QTc: 0.40 sec, QRS: 0:08 sec PR: 0.12 sec, respectively). Complete blood count and biochemistry tests were taken at the time of the patient refer to the emergency room were within normal limits. Arterial blood gas analysis was as follows, pH: 7.38 HCO<sub>3</sub>: 22 mEq

/ L, pCO<sub>2</sub>: 40 mmHg, pO<sub>2</sub>: 85 mmHg and SaO<sub>2</sub>: 96%, respectively. The cranial computed tomography taken when patient was brought to emergency department unconsciously was normal. At the 48th hour of hospitalization, GCS was 7 and high serum value of amylase 1287 iu/l was found (Table 1). Blood samples were obtained from the patient for lipase analysis and contrasted abdominal CT scan was planned. Lipase levels were within normal limits and no abnormal signs suggestive of pancreatitis was seen on the contrasted abdominal CT scan and it was assessed as normal. At 72th hours of her admission GCS was 13 and blood amylase was in a downward trend and at 96th hours of hospitalization GCS was 15 and blood amylase were within normal limits. The patient was started orally and on 4th day of hospitalization vital signs remained stable and the patient was discharged.

### Discussion

Varying levels of benzodiazepines have sedative, hypnotic, amnesic, anxiolytic, anticonvulsant and muscle relaxant properties,

HOSPITALIZATION dAYS	1 <sup>ST</sup>	2 <sup>ND</sup>	3 <sup>RD</sup>	4 <sup>TH</sup>	5 <sup>TH</sup>
WBC (X 1000/mm <sup>3</sup> )	7.03	25.74	21.51	15.38	13.16
Hb (gr/dl)	13.9	13.8	13.4	13.1	13.1
PLT (X 1000/mm <sup>3</sup> )	366	388	351	356	407
Amylase (U/L)	46	1287	574	72	32
Glucose (mg/dl)	127	173	118	105	98
ALT (U/L)	21	20	14	11	10
AST (U/L)	23	18	17	14	10
LdH (U/L)	178	393.7	197.9	185	182

**Abbreviations:** WBC: White blood count, Hb: Hemoglobin, PLT: Platelet, ALT: Alanine amino transferase, AST: Aspartate amino transferase, LDH: Lactate dehydrogenase.

**Table 1:** Hospitalization days according to the laboratory values.

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and unless taken with CNS (Central Nervous System) depressants such as barbiturates and alcohol death is rare [9]. Within 12-36 hours the majority is fully awake. The therapeutic concentration of clonazepam is 27-75 ng/ml and the toxic concentration on the intake should be over 80 ng/ml [10].

Acute pancreatitis associated with use of atypical psychotic drugs particularly clozapine and olanzapine has been observed, especially in the last 6 months of therapeutic use. More rarely, cases can apply with diabetic ketoacidosis, hyperglycemia and hyperlipidemia [5-8,11].

Gropper and Jackson have identified three cases who developed pancreatitis after the use of quetiapine, and two of three cases were using valproate known as a cause of pancreatitis [12].

In the review metaanalysis published by Koller's, haloperidol treatment has been associated with the development of pancreatitis. In addition, half of the patients were using antipsychotic drugs together with Haloperidol [13].

Lee WC and colleagues reviewed retrospectively 159 cases of organophosphate poisoning in their study, found in 44 patients (36%) serum amylase and lipase levels were higher but that high level of serum amylase and lipase levels were not synonymous with acute pancreatitis had been stated [14]. Hyperamylasemia and hyperlipasemia due to intraductal pressure increment, cholinergic stimulation resulted in acute pancreatitis had been shown in organophosphate poisoning [14-16].

Pezzilli et al reported a case report; on the 2nd days of clinical course of the 30 year old female patient taken amitriptyline at total doses of 800 mg for suicidal purposes, the serum amylase level 823 U/L and lipase level 1054 U/L were found and no any pathology was found in pancreas on the abdominal ultrasonography. On the 4th day pancreatic enzymes have a peak, but no any pathology was found on control ultrasonography. The patient was discharged on 8th day of admission to hospital without sequelae and on the 15th day amylase 403U/L, lipase 239 U/L were found, and the control ultrasonography found to be without any pathological findings. In this case the authors had concluded that over dose of TCA (Tricyclic Antidepressant) may cause damage in the pancreas [17].

In our case, although elevation of leukocytes, LDH (Lactic Dehydrogenase) and amylase refer acute pancreatitis, contrast enhanced computed abdominal tomography was normal. The patient was evaluated as a case of hyperamylasemia and any other reasons of hyperamylasemia including polypharmacy were excluded. As a result of investigations and physical examination of the patient no other reason of hyperamylasemia was detected.

In conclusion, clonazepam overdose is another reason of hyperamylasemia and serum pancreatic enzymes should be determined in patients with clonazepam overdose in order to detect possible pancreatic involvement.

## References

1. Riss J, Cloyd J, Gates J, Collins S (2008) Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. *Acta Neurol Scand* 118: 69-86.
2. Cohen LS, Rosenbaum JF (1987) Clonazepam: new uses and potential problems. *J Clin Psychiatry* 48: 50-56.
3. Gerstner T, Bell N, König S (2008) Oral valproic acid for epilepsy- long term experience in therapy and side effects. *Expert Opin Pharmacother* 9: 285-292.

4. Gertsner T, Büsing D, Bell N, Longin E, et al. (2007) Valproic acid induced pancreatitis: 16 new cases and a review of the literature. *J Gastroenterol* 42: 39-48.
5. Bayard JM, Descamps OS, Evrard S, et al. (2005) Case report: Acute pancreatitis induced by clozapine. *Acta Gastroenterol Belg* 68: 92-94.
6. Collin A, Clevenot D, Moulin P, Macebeo C, et al. (2009) Acute pancreatitis induced by olanzapine. *Ann Fr Anesth Reanim* 28: 907-909.
7. Frankenburg FR, Kando J (1992) Eosinophilia clozapine and pancreatitis. *Lancet* 340: 251.
8. Huang YJ, Lane HY, Liao CH, et al. (2009) Recurrent pancreatitis without eosinophilia on clozapine rechallenge. *Prog Neuropsychopharmacol Biol Psychiatry* 33: 1561-1562.
9. Mc Evoy GK (1994) AHFS Drug Information 94. Bethesda: American Society of Hospital Pharmacists: 1353-1355.
10. Browne TR (1976) Clonazepam. A review of a new anticonvulsant drug. *Arch Neurol* 33: 326-332.
11. Kerr TA, Jonnalagadda S, Prakash C, et al. (2007) Pancreatitis following olanzapine therapy: A case report of three cases. *Case Rep Gastroenterol* 1: 15-20.
12. Gropper D, Jackson CW (2004) Pancreatitis associated with quetiapine use. *J Clin Psychopharmacol* 24: 343-345.
13. Koller EA, Cross JT, Doraiswamy PM, et al. (2003) Pancreatitis associated with atypical antipsychotics: from the Food and Drug Administration's MedWatch surveillance system and published reports. *Pharmacotherapy* 23: 1123-1130.
14. Lee WC, Yang C, Deng JF, et al. (1998) The Clinical significance of hyperamylasemia in organophosphate poisoning. *J Toxicol Clin* 36: 673-681.
15. Dressel TD, Goodale RL, Arneson MA (1979) Pancreatitis as a complication of anticholinesterase insecticide intoxication. *Ann Surg* 189: 199-204.
16. Singh S, Bhardwaj U, Verma SK, et al. (2007) Hyperamylasemia and acute pancreatitis following anticholinesterase poisoning. *Hum Exp Toxicol* 26: 467-471.
17. Pezzilli R, Melandri R, Barakat B, Broccoli PL, Miglio F. (1998) Pancreatic involvement associated with tricyclic overdose. *Ital J Gastroenterol Hepatol* 30: 418-420.