A long-term overdose use of clonidine in a peritoneal dialysis patient: A case study

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Abstract

Clonidine is an alpha-adrenergic receptors and used in the treatment of hypertensive. We described a 22-year-old man with end-stage renal disease and hypertension overdose use for 7 years in a peritoneal dialysis patient do not cause severe toxicity except exhilarate.

INTRODUCTION

Clonidine is an antihypertensive agent that is thought to stimulate alpha-adrenergic receptors in the central nervous system. It is used as an alternative antihypertensive agent (0.2-0.9 mg/d) and it is safe in this recommend dosage. To our knowledge, this is the first case report illustrate clonidine overdose use for 7 years in a peritoneal dialysis patient not to cause severe toxicity.

CASE REPORT

A 22-year-old man with end-stage renal disease and hypertension for 3 years, these conditions were controlled on Peritoneal Dialysis regularly, and Nifedipine 30 mg bid, Metoprolol 47.5 mg bid, Telmisartan 80 mg bid and Clonidine 0.075 ug qid irregularly. he had headache repeat for 1 year and brought to the hospital's kidney department.

On admission. The patient shows paleness, dropsy. Level of consciousness was normal and there were no motor or sensitive alterations. blood pressure was 120/80 mmHg, heart rate was 80 beats/min, temperature was 37 and respirations were 20/min and normal. The abdominal evaluations were within normal limits. The Laboratory evaluation was remarkable for anemia and markedly abnormal serum electrolytes, including a serum K^+ 3.4 mmol/L, Cl^- 92.4 mmol/L and phosphate 2.73 mmol/L. The serum creatinine 1342 umol/L, uric acid 59 umol/L. Other chemistries were normal as was the chest film. He was diagnosed uremia, hypertension and chronic kidney disease associated with anemia, and was treated with oral Valsartan and Amlodipine 80 mg/5 mg bid, Metoprolol 47.5 mg qd, Clonidine 0.075 ug tid. On the second day, he had headache and was relieved by Sublingual Nifedipine10 mg. His BP was maintained at 100-180/70-143 mmHg. He was given Compound Reserpine and Triamterene tablet (Hydrochlorothiazide 12.5 mg, Triamterene12.5 mg, Dihydralazine Sulfate 12.5 mg and Reserpine 0.1 mg) 1# qn, Nimodipine 30 mg tid, Clonidine 0.15 mg tid. On the third day, he had headache accompany with hypertension. His BP was maintained at 140-180/100-140 mmHg. He was given Doxazosin Controlled Release Tablets 4 mg qn. There were no additional significant abnormalities in his brain CT scan and renal artery CTA. On the seventh day, he was given Irbesartan 150 mg bid, Clonidine 0.15 mg qid. The ambulatory blood pressure results on the seventh day as follows: The lowest pressure was 90/55 mmHg, the highest pressure was 170/127 mmHg, average pressure was 142/104 mmHg, average heart was 78 beats/min. the ECG showed Sinus rhythm and ST-T change. Seven days after treatment, the patient complained fatigue, dizziness (upright obviously) and agitation or anxiety. However, A clinical pharmacist found he took Clonidine for a long period and increased dosage to

1.875-7.5 mg/d by himself about 6 months. After he admitted to hospital, Clonidine usage was 0.225-0.45 mg/d, so he appears the discontinuation syndrome as well as his complaint. He was instructed to reduce the clonidine dosage gradually: reduce the dose by half every 2-3 days, and reduce to the normal dose after 6-10 days. At the same time, he was given oral trazodone 50 mg qn and diazepam 5 mg qn. After one month, his clonidine dosage reduced to 1.875-3.75 mg/d. After three years, his clonidine dosage reduced to 1.125-1.5 mg/d. The ECG showed Sinus rhythm and ST-T change. The ambulatory blood pressure results as follows: the average SP was 119 66mmHg. the average DP was mmHg. After seven years, his clonidine dosage reduced to 1.125-1.5 mg/d. the ECG showed Sinus rhythm and ST-T change.

DISCUSSION

Clonidine derived from imidazoline. It stimulated adrenergic (α2) presynaptic receptors, when it overdose use seems to produce depressed mental status, bradypnea, bradycardia, and hypotension[1].Other clinical symptoms include early hypertension, followed by hypotension, hypothermia and respiratory depression. Geoffrey et al reported 133 adults took clonidine overdoses (clonidine >200 ug, median dose taken was 2100 ug) cause persist but not life-threatening clinical consequent with less bradycardia and more CNS depression[2]. It is similar to a large case series from Stein et al who reported 37 adult overdoses from the National Poison information service in London[3].However, in this case, he did not show bradycardia, hypotension and lethargy. A study of adult clonidine ingestion showed that bradycardia was relatively begin persisting for a mean of 20 h[2], A recent study of pediatric patient with clonidine exposure shows that bradycardia was also begin though they do not determine the bradycardia duration[4]. This possibly suggests that he did not show bradycardia due to he took clonidine overdose for a period time.

The clinical findings in the 52 patients were hypotension(n=11), bradycardia(n=44), this indicated that hypotension was not clinically significant[4]. Children with clonidine ingestion usually arouse when stimulated and become unresponsive when left alone. In this case, as an adult, he did not show somnolent. The possible reason is that Clonidine overdose increased parasympathetic outflow but not increase vagal tone.

Clinically abrupt withdrawal of clonidine may result in a rapid increase of systolic and diastolic BP, with associated clinical effects, such as nervousness, restlessness, agitation, insomnia, anxiety, headache, palpitation, sweating. Increased heart rate, muscle pain, hiccups, increased salivation, stomach pain, nausea and flushing[5]. he complains headache repeat 1 year, and when he 7 days after admission, he complains fatigue, dizziness (upright obviously) and agitation or anxiety. Because he takes clonidine for a long time and increases/decrease the dosage by himself, so his clinically symptoms were similar to withdrawal of clonidine. the mechanism involved in the abruptly withdrawal of clonidine therapy has not been precisely determined and several attractive theories were proposed. The management of the discontinuation syndrome has been as follows: patient reinstitution of the clonidine, and decreased dosage follow the doctor's order gradually, and took trazodone 50 mg qn and diazepam 5 mg qn. After 7 yeas, he kept blood pressure steady and decrease clonidine 1.125-1.5 mg/d. he has no other symptoms except exhilarate.

The present case indicates that clonidine overdose use for 7 years do not cause life-threatening clinical effects including CNS syndrome for example exhilarate. As clinical pharmacist, we need consider patient medication history and medication education to avoid abuse drug by patient.

This case is the first reported case of clonidine overdose use for 7 years in a peritoneal dialysis patient not to cause severe toxicity. Our experience suggests that careful attention should be given to patients taking clonidine, especially for those need for long-term use, since they may be show poor compliance.

COMPETING INTERESTS

Authors declare no conflict of interests.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Reference

1 Toce MS, Freiman E, O'Donnell KA, Burns MM. Clinical Effects of Pediatric Clonidine Exposure: A Retrospective Cohort Study at a Single Tertiary Care Center. *J Emerg Med* 2021; 60:58-66[PMID: 33036823 DOI:10.1016/j.jemermed.2020.09.018]

2 **Isbister GK** , Heppell SP, Page CB,Ryan NM.Adult clonidine overdose: prolonged bradycardia and central nervous system depression, but not severe toxicity. *Clin Toxicol (Phila)*2017;55:187-**192[PMID: 28107093 DOI:10.108** 0/15563650.2016.1277234]

3 **Stein B** ,Volans GN. Dixarit overdose: the problem of attractive tablets.*Br Med J* 1978;2:667**-668[PMID: 698654 DOI:10.1136/bmj.2.6138.667**]

4 **Seger DL** ,Loden JK.Naloxone reversal of clonidine toxicity: dose, dose, dose.*Clin Toxicol (Phila)* 2018;56:873-879[PMID: 29544366 DOI:10.1080/15563650.2018.1450986]

5 **Karachalios GN,** Charalabopoulos A, Papalimneou V, Kiortsis D, Dimicco P, Kostoula OK,Charalabopoulos K.Withdrawal syndrome following cessation of antihypertensive drug therapy.*Int J Clin Pract*2005;59:562-57**0** [**PMID: 15857353 DOI:10.1111/j.1368-5031.2005.00520.x**]