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Chlorpropamide Poisoning Induced Atrio-Ventricular Block and Sino-Atrial Block

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KLORPROPAMİD İNTOKSİKASYONUNA BAĞLI ATRİO-VENTRİKÜLER BLOK VE SİNO-ATRİAL BLOK

Özet

İntihar amacıyla 40 tablet Diabinese (10 g klorpropamid) alan 28 yaşındaki erkek hasta hipoglisemi komasıyla acil servise yatırıldı. Çekilen EKG'sinde A-V tam blok saptandı. A-V tam blok giderek yüksek derece, II. ve I. derece A-V bloka geçiş gösterdi. EKG'nin I. derece A-V blok gösterdiği dönemde zaman zaman sino-atrial bloklar gözlenen hastanın ilacı almasından yaklaşık 48 saat sonra EKG bulguları tamamen normale döndü.

Literatür incelemelerinde, bir olguda 40 tablet Diabinese (2500 mg klorpropamid) alınmasını takiben atrial bigeminal erken atımlar ve artial fibriloflatter, diğer bir olguda ise testi sırasında sık ventriküler erken atımlar bildirilmiştir. Klorpropamid intoksikasyonuna bağlı atrio-ventriküler blok ve sino-atrial blok olgusuna ilk kez rastlanması nedeniyle bu olgunun yayınlanmasının uygun olduğu düşünüldü. Ayrıca, klorpropamidin intihar amacıyla kullanılabilen bir drog olması nedeniyle, adli otopsilerde ve adli toksikolojiyle ilgili çalışmalarda, hastane belgelerinde atrio-ventriküler ve sino-atrial blok saptanan olguların klorpropamid tayini açısından da gözden geçirilmesi uygun olur görüşündeyiz.

Summary

A 28 year-old man was admitted to the emergency department of our hospital because of attempted suicide with 10 g chlorpropamide (forty tablets of Diabinese). He was in profound hypoglycemia and his ECG revealed complete A.V. block changed to high grade, second and finally first degree A.V. block. After 48 hours of his drug ingestion ECG turned to normal. In the literature we have found two case reports in relation to this subject. One of them had bigeminal atrial premature beats and atrial flutter-fibrillation after the ingestion of 2500 mg of chlorpropamide.

The other case was about frequent ventricular premature beats during a tolbutamidee test. We haven't found any case report about chlorpropamide induced A.V. block and S.A. block in the literature.

In conclusion we think that it can be of great help to bear in mind chlorpropamide poisoning can induce A.V. block.

Key words : *Suicide - Chlorpropamide poisoning - ECG findings - Atrio-ventricular block - Sino-atrial block*

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CASE REPORT

C. S., a 28-yr-old, male, born in Yugoslavia. On June 2nd, 1988, the patient was taken to a private hospital by his relatives 7-8 hours after attempting suicide with 10 g chlorpropamide (40 tablets of Diabinese). He was unconscious and had apparently taken some amount of alcohol before attempting suicide. In this hospital 20 % dextrose perfusion was started without evaluating the blood glucose level. After some time, the patient was sent to our hospital.

At the time of admission to our hospital, he was unconscious but responsive to painful stimulus. His pupils were isochoric and little miotic and the Babinski's sign was bilaterally positive.

His deep tendon reflexes were found to be hyperactive. The patient perspired a lot, his blood pressure was 110/80 mm Hg, his pulse rate was 44/minutes and arrhythmic, and heart auscultation was normal and nothing pathological could be found in the respiratory and gastrointestinal system examination. His blood glucose level was 40 mg %.

The patient was internalized in the emergency service with a diagnosis of hypoglycemic coma.

Laboratory Findings (June 3rd, 1988)

Htc: 41 %, white blood cell count: 4000/mm, Blood smear: young blood cell 2 %, neutrophils 88 %, eosinophils: 1 %, lymphocytes 9 %. Platelet count: 160000/mm. Blood electrolytes: Na: 137 mEq/L, K: 4.6 mEq/L, Cl: 100 mEq/L, Inorganic phosphorus: 1.48 milimoles/L, Ca: 2.43 milimoles/L. Blood CO_2: 24 milimoles/L, BUN: 2.1 milimoles/L, creatinine: 71 milimoles/L, total protein: 7.05 g/L, albumin: 44.7 g/L, alkaline phosphatase: 102 units/dl, SGOT: 27 units/dl, SGPT: 33 units/dl, total bilirubin: 0.28 mg/dl, direct bilirubin: 0.14 mg/dl.

10 % dextrose perfusion was started immediately and 30 % dextrose injections were also given from the same vessel at certain time intervals. A gastric lavage was employed with the aid of a nasogastric tube. The patient was conscious again 2 hours later. The ECG taken 2 and 4 hours later still revealed complete A.V. block, and the ECG taken at 22 hour later was still the same. The blood glucose levels taken at two-hour intervals were found to be between 45 mg % and 110 mg %. The patient had 2 more hypoglycemic attacks in the first 24 hours. The complete A.V. block changed gradually to high grade, second and finally first degree A.V. block.

Second Day (June 3rd, 1988)

The ECG revealed first degree block. PR length: 0.22 cm. Laboratory findings were as follows: Blood Na: 138 mEq/L, K: 3.4 mEq/L. Blood pressure: 110/60 mm Hg, pulse rate: 60/minutes. Blood glucose: 100 mg %. The patient was conscious and his chest X-ray was normal. The blood glucose level at 16.00 hr of the same day was 54 mg % and the PR length in the ECG was 0.20 cm. Sinoatrial blocks appeared occasionally. Parenteral glucose and electrolyt infusion was continued.

Third Day (June 4th, 1988)

The PR length at 16.00 hr was found to be 0.16 cm. The blood glucose levels as well as the ECG and the biochemistry findings on the following days were at normal ranges.

DISCUSSION

The cardiotoxicity of hypoglycemic drugs of sulfonylurea group is a subject long known and discussed upon. It has been reported that microgranulomas appeared on the heart muscles of patients being treated with these drugs (1,2). *Hildner* et *al* (3) observed that a tolbutamide injection during cardiac catheterization produced an inotropic effect in 5-15 minutes on nondiabetic people. However, *Crockett* et *al* (4) reported that, although this positive inotropic effect can be established in vitro, it is not seen in vivo.

Nonetheless, there are reports about the increase in the inotropic effect on heart muscle and automaticity on Purkinje's fibers after the use of tolbutamide (5) and about

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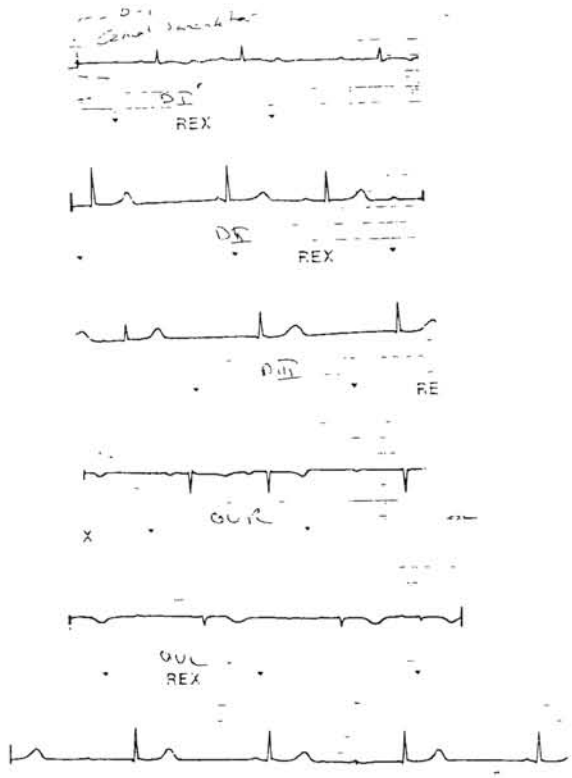

Figure 1. Artio-ventricular block of the patient.

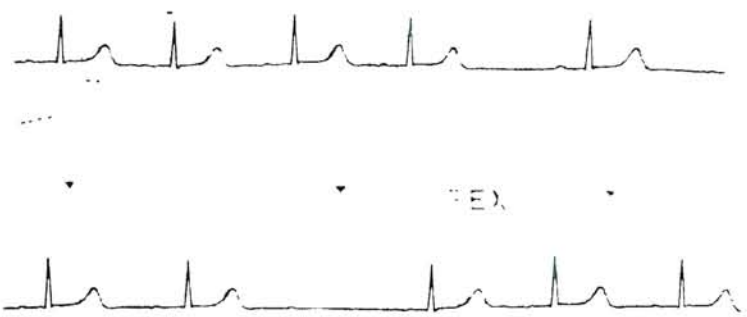

Figure 2. It was shown partial sinoatrial block and second grade AV block in upper and below ECG.

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the increase in ventricular fibrillation rate in diabetic patients who use oral hypoglycemic drugs (6).

In the literature, there were two cases in relation to this subject one of them was a 58 years old patient who had frequent ventricular premature beats during an intravenous tolbutamide test (7). The other case was about a 63 years old patient who had bigeminal atrial premature beats and atrial fibrilloflatter after ingestion of 2500 mg chlorpropamide (10 tablets of Diabinese) (8). In our patient ECG revealed complete A.V. block and his blood glucose levels were below normal; there was a cold perspriation due to reflex sympathic activation, and his deep tendon reflexes were hyperactive. Although tachycardia would be expected, his pulse rate was 44-50/minutes. The cardiothoracic index on his chest X-ray was in the physiological range, and there wasn't an eosinophilic infiltration, although it is possible after ingestion of chlorpropamide. The neutrophilic dominance in the periferic blood smear did not reveal an infiltration, and there was nothing interesting besides the neutrophilic dominance on the periferic smear. Since it has been reported that drugs from the sulfarulurea group lead to microgranulomas on the myocardium (1,2), we thought that this A.V. block could be due to the microgranulomas formed on the excitation and conduction routes on the myocardium. The complete A.V. block gradually changed to high grade, second and finally first degree A.V. block in the second day.

During these days, also sinoatrial blocks appeared occasionally. The ECG findings returned completely back to normal approximately 48 hours after the ingestion of the drug. This is slightly over the half life of the drug which is 36 hours. The patient had not taken any other drugs. Chlorpropamid induced cardiotoxicity and atrial ventricular premature beats have been reported up to now. However, high grade A.V. block has never been reported. In this case the patient's ingestion of alcohol may have increased the cardio toxic effects of chlorpropamide.

We think that it can be of great help to bear in mind that drugs from the sulfonylurea group, especially at high doses, can cause several rythm and conduction abnormalities, and that blocks in old people with arteriosclerosis and increased vagal tonus can be more severe.

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