Case Report

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Ticagrelor Intoxication: Overdose in a Suicidal Attempt

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Abstract

Ticagrelor is one of the new generation antiplatelet agents, which acts by reversibly binding to P2Y12 platelet receptors. Literature-related data on overdose intake of ticagrelor is quite limited. Here, we report a 23-year old male patient, who presented to our emergency clinic with the complaint of suicidal intake of 15 tablets of 90 mg ticagrelor (Brilinta® 90 mg tablet, Astra Zeneca Pharmaceuticals, Istanbul). Ticagrelor is one of the new generation antiplatelet agents that is currently being used in the treatment of acute coronary syndrome in our country. The overdose use of the drug for suicidal purpose or accidentally, is a relatively new issue for emergency physicians. According to our knowledge, suicidal ticagrelor overdose intake is a case that has not been reported in the literature previously. In this article, we shared the asymptomatic process of a case with 1350 mg ticagrelor toxicity. With the increased use and prevalence of the drug in our country, we think that the emergency physicians may encounter ticagrelor poisoning at higher rates. Therefore, in ticagrelor poisoning, emergency physicians need to be aware and familiar with the drug

Key Words: Emergency medicine, suicide, ticagrelor, intoxication

Özet

Ticagrelor, P2Y12 trombosit reseptörlerine geri dönüşümlü olarak bağlanarak hareket eden yeni nesil antiplatelet ajanlarından biridir. Tikagrelorun aşırı doz alımı ile ilgili literatürle ilgili veriler oldukça sınırlıdır. Bu yazıda acil servise, intihar girişimi amacıyla 15 adet 90 mg ticagrelor içeren tablet(Brilinta® 90 mg tablet, Astra Zeneca Pharmaceuticals, İstanbul) alma şikayeti ile başvuran 23 yaşında bir erkek hasta sunuldu. Ticagrelor, ülkemizde akut koroner sendrom tedavisinde kullanılan yeni nesil antiplatelet ajanlardan biridir. İlacın intihar amaçlı veya kazayla aşırı dozda kullanılması, acil durum doktorları için nispeten yeni bir konudur. Bilgilerimize göre intihar amaçlı ticagrelor doz aşımı alımı, daha önce literatürde bildirilmemiş bir durumdur. Bu yazıda 1350 mg ticagrelor toksisitesi olan bir olgunun asemptomatik sürecini paylaştık. Ülkemizde ilacın kullanımının ve yaygınlığının artması ile acil hekimlerin tikagrelor zehirlenmesiyle daha yüksek oranda karşılaşabileceğini düşünüyoruz. Bu nedenle, tikagrelor zehirlenmesinde acil durum doktorlarının ilacı bilmesi ve tanıması gerekir

Anahtar kelimeler: Acil tıp, intihar, ticagrelor, zehirlenme

Introduction

Ticagrelor is one of the new generation antiplatelet agents, which acts by reversibly binding to P_2Y_{12} platelet receptors. Different from thienopyridines (clopidogrel and prasugrel), binding to receptors is reversible and it is thought to act faster than clopidogrel[1]. Due to its platelet-inhibition effect, it is recommended in the treatment of both non-ST elevation acute coronary syndromes (NSTE-ACS) and myocardial infarction with ST segment elevation (STEMI)[2, 3]. Literature-related data on overdose intake of ticagrelor is quite limited. Here, we report a 23-year old male patient, who presented to our emergency clinic (ER) with the complaint of suicidal intake of 15 tablets of 90 mg ticagrelor (Brilinta® 90 mg tablet, Astra Zeneca Pharmaceuticals, Istanbul), and who was discharged from the clinic uneventfully following a 48-hour surveillance. According to our knowledge, no previous case in the literature is present related to suicidal overdose intake of ticagrelor.

Case Report

A 23-year-old male patient presented to the ER declaring that he had ingested 15 tablets containing 90 mg ticagrelor about 20 minutes previously in a suicide attempt. He noted that he had not taken any other substance or drugs except ticagrelor. In his history, there was no chronic disease and he had a history of 1 pack/day smoking and alcohol intake 2-3 times a month. The patient had no complaints upon presentation to the ER. On his physical examination, the vital signs of the patient were recorded as follows: pulse: 87 beats/min, rhythmic, blood pressure: 140/ 90 mmHg, respiratory rate: 14 breaths/min, room air oxygen saturation: 98% and body temperature: 37.1 °C. The patient's general condition was good, The Glasgow Coma Scale was 15; he was conscious, fully cooperative and orientated. He had no active bleeding. A vascular access was established for the patient he was monitored in the ER; orogastric lavage was planned, but the procedure failed because the patient was unable to tolerate it.

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Activated charcoal of approximately 1 gr/kg dose was given orally to the patient. A normal sinus rhythm with 90 beats/min was observed on the electrocardiogram. On the laboratory analyses, the hemoglobin, hematocrit, platelet count values and the blood glucose, renal and liver function tests, uric acid levels and electrolyte levels were within normal ranges. No metabolic acidosis was detected in the venous blood gases. The patient with admission values of PT:12.9 (9.1-12.1) and INR: 1.12 (0.89-1.06) was followed-up at the ER toxicology unit. The patient was asymptomatic on the follow-up, with 24th hour values of PT:13.7 and INR:1.19. The patient's continuously repeated examinations revealed no headache, chest pain, dyspnea, palpitations, nausea, vomiting, any bleeding symptoms and ecchymosis, or any other complaints. His vital signs were stable. On the 2nd day control examinations, the increased PT and INR values were found to be within normal ranges, as 11.8 and 1.03, respectively. This PT and INR elevation, which lasted for about 48 hours, had no clinically significant outcomes. The patient was informed that this condition was the side effect of the drug he had taken. The patient was referred to the psychiatry clinic for his suicidal thoughts, and was discharged from the ER uneventfully and asymptomatic for about 2 days after his application.

Discussion

Today, the recommended treatment dose of ticagrelor for acute coronary syndromes is generally 180 mg loading dose and 180 mg daily maintenance regime[2, 3]. The case we have presented attempted suicide by taking 1350 mg of a total dose at one time. The drug binds reversibly to P_2Y_{12} ADP receptor, has a half-life of about 7 hours, has biliary excretion and binds to plasma proteins at a rate of over 99%[4]. In the DISPERSE-2 study, which has investigated the efficacy and safety of ticagrelor compared to clopidogrel in NSTE-ACS population, the more common side effects seen in ticagrelor group have been listed as nausea, dyspepsia, hypotension and dyspnea. Again, ventricular pauses were observed more frequently in the ticagrelor group (sinoatrial exit block in 7 patients and complete heart block in 4 patients)[5]. In our case, the vital signs were stable throughout the follow-up period at the ER and he had no complaints of dyspnea or palpitation.

Again, in the PLATO study, which is a large, randomized, double-blind, multi-center study that has investigated the efficacy and safety of ticagrelor compared to clopidogrel in both NSTE-ACS and STEMI populations, ticagrelor has been found to be superior in reducing the mortality rates of vascular origin, compared to clopidogrel; however, intracranial hemorrhage and dyspnea were identified at higher rates in the ticagrelor group[6]. No signs of bleeding were observed in our case. In our asymptomatic case, the slightly increased PT and INR values that lasted for about 2 days did not have a clinically significant outcome. It has been stated that ticagrelor-related dyspnea is mostly milder and moderate, mostly occurs in the first days of the treatment, and in a very small percentage of the patients, the drug requires discontinuation[6, 7, 8]. The mechanism of ticagrelor-related dyspnea is still not clear, and the increase in adenosine levels in the pulmonary vagal C fibers due to the inhibition of reuptake of adenosine has been blamed as the cause[4, 8].

Ventricular pauses are one of the side effects that are determined at higher rates, against ticagrelor in PLATO study[6]; however, most patients are stated to be asymptomatic. Drug-related common side effects apart from these have been reported as increased uric acid levels, atrial fibrillation, hypertension, bradychardia, headache, dizziness, hypokalemia, diarrhea, increase in serum creatinine levels and coughing[9]. In our patient, the uric acid and creatinine levels remained normal for 2 days and no electrolyte imbalance was determined.

Due to the fact that ticagrelor is metabolized via the CYP3A4 system[4], the use of other drugs that use this enzyme system along with ticagrelor or overdose use as in our presented case, may cause more serious and long-term side effects. Examples of such drugs may include ketoconazole, clarithromycin, ritonavir, rifampicin and carbamazepine[4]. The presented case had a lucky situation of not using any other drug or substance.

There is no specific antidote that can be used in ER treatment of overdose of ticagrelor[9]. We also applied the general toxicology and support measures to our patient and followed the vital signs and possible complications.

Conclusion

As a result, ticagrelor is one of the new generation antiplatelet agents that is currently being used in the treatment of acute coronary syndrome in our country. The overdose use of the drug for suicidal purpose or accidentally, is a relatively new issue for ER physicians. According to our knowledge, suicidal ticagrelor overdose intake is a case that has not been reported in the literature previously. In this article, we shared the asymptomatic process of a case with 1350 mg ticagrelor toxicity. With the increased use and prevalence of the drug in our country, we think that the ER physicians may encounter ticagrelor poisoning at higher rates. Therefore, in ticagrelor poisoning, ER physicians need to be aware and familiar with the drug.

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