

Which is Responsible for Bradycardia in Woman Treated for Incomplete Abortion and Thrombocytopenia? Intravenous Immunoglobulins, Methylprednisolone or Clindamycin

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ABSTRACT

Clindamycin, IVIg, and corticosteroids are widely used in medicine. In this study, we represent an unusual case of sinus bradycardia following the administration of these drugs. The patient was a 31-year-old woman who presented a complaint of vaginal bleeding at Shahid Motahhari Hospital, Urmia, Iran. Vaginal examination revealed active bleeding. Laboratory tests reported a positive HCG level. Ultrasonography was performed, and the results showed the presence of retained products of conception. The patient became a candidate for curettage. The initial pulse rate was tachycardia. Laboratory data were reported, platelet count of 16000. Corticosteroids and IVIGs were started. Due to the possibility of infectious abortion, Clindamycin and Gentamicin was started. About 24 hours after curettage and 4 hours after starting clindamycin, the patient felt dizziness. Vital signs were obtained that PR: 38-40. We concluded that clindamycin and IVIg can result in severe bradycardia, even in patients with no previous cardiac history, especially when combined with corticosteroids. As a result, we recommend physicians be more cautious when administering these medications.

Keywords: Bradycardia, Clindamycin, Corticosteroids, Intravenous immunoglobulins



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Introduction

Clindamycin, with the structure of 7(s)-chloro-7-deoxy lincomycin, is a semisynthetic, lincosamide antibiotic. Clindamycin is one of the favored antimicrobial agents in the treatment of female genital area infections, some cases of pelvic inflammatory disease (PID), infections of the post-hysterectomy vaginal cuff, post-cesarean section endometritis, and septic abortions (1-3). Several side effects and complications have been reported after the administration of clindamycin. These adverse events include maculopapular rash, nausea, vomiting, diarrhea, flatulence, esophagitis, metallic taste, erythema multiforme, anorexia, fever, hematopoietic, and some rare cases, cardiopulmonary problems (4). Intravenous immunoglobulin (IVIg) is a blood product that is a therapeutic compound of polyclonal immunoglobulin G and is extracted from the plasma of many donors (5). Initially introduced as replacement therapy for patients with immune deficiencies, IVIGs is now used to treat many autoimmune and systemic inflammatory diseases (6). Although IVIg is usually being tolerated well, sometimes adverse events may occur. Most of these adverse effects are mild and reduced after infusion withdrawal, but some of the rare

side effects are severe, including aseptic meningitis, renal impairment, thrombosis, and hemolytic anemia (7). Corticosteroids have a wide range of applications and benefits, mostly related to their powerful anti-inflammatory and immune-modulating effects. Although various side effects of intravenous steroid infusion are well determined in medical studies, corticosteroids are mainly considered to have a good safety record (8). All these drugs are widely used in medicine and may be associated with adverse events. There are case reports about the link between these drugs and sinus bradycardia, but comprehensive information is not available. The purpose of this case report is to demonstrate the possible role played by clindamycin, IVIg, and corticosteroids in the onset of bradycardia in a patient without previous cardiac history.

Case Report

The patient was a 31-year-old woman, gravida 4, para 2, abortion 1, who presented vaginal bleeding and pain in the hypogastric region at Shahid Motahhari

Hospital (Urmia, Iran). She had been suffering from abdominal pain for two hours before going to the hospital, followed by vaginal bleeding. The initial vital signs at the time of arrival to the hospital emergency center were a blood pressure of 90/60 mmHg (obtained from both left and right upper limbs in a supine position), a pulse rate of 100 /min without any arrhythmia, a respiratory rate of 20/min, a body temperature of 37.8 c (axillary), and body mass index (BMI) of 29. Her features were pale. In the bimanual examination of the abdominal area, an enlarged uterus with an estimated age of 12 weeks was revealed. The abdomen was tender in reaction to the physician's touch. In the vaginal examination, there were signs of active bleeding, dilation of the external cervical Os equal to one finger with excretion products of conception. The patient had no history of diseases, for example, heart disease, and was not taking medication. Her last child was born four years prior the incidence following a cesarean section. After that, she underwent curettage about last year due to an incomplete abortion in this center. There was no problem in the history of previous hospitalizations. Her menstrual cycle was regular but had started again after a delay of 12 weeks. Laboratory tests reported a positive HCG level indicating the pregnancy. Ultrasonography was performed at the patient's bedside and showed the presence of retained products of conception. A primary laboratory test was sent urgently, and due to severe vaginal bleeding, an emergency evacuation curettage was prepared in the operating room. The vital signs in the operating room were as following, blood pressure: 90/60 mmHg, pulse rate: 110/min, respiratory rate: 18/min, and O₂ saturation: 98%. Laboratory investigations were reported after curettage and were as following, hemoglobin 10.5 gm/dL, White blood cell count of 9900 /mm³ with 35 % neutrophils, platelet count of 16000, and all electrolytes were reported to be

in their normal range of expected amounts. Emergency consultation was provided with the internal service. Peripheral blood slides were examined, and additional tests were sent. The patient was transferred to the intensive care unit where two units of pack cell and ten units of platelets were transfused. According to the internal service instructions for the patient, corticosteroids and Intravenous immunoglobulins (IVIg) were started. Due to the possibility of infectious abortion, Clindamycin 900 mg and Gentamicin 80 mg every 8-hour intravenously started. About 24 hours after curettage and 4 hours after starting clindamycin, the patient felt dizziness. Vital signs were obtained that included blood pressure: 100/60 mmHg, the pulse rate: 38-40 (bradycardia), respiratory rate: 18/min, saturation O₂: 98%. Electrocardiogram (ECG) showing sinus bradycardia ([Figure 1](#)). The patient did not report any other problems such as chest pain or dyspnea. Because of the pulse rate of 40 bpm, 4 mg of intravenous atropine was administered. An emergency consultation was performed with a cardiologist. The values of Troponin I and creatine kinase-MB were in the normal range. Echocardiography showed an ejection fraction of 50%, and any structural problem was seen in the heart wall and valve function. The cardiologist ordered the IVIG to behold and theophylline to be started every 12 hours. The patient had received one dose of IVIG, then the next dose was held, but theophylline did not start. Due to the start of clindamycin was began bradycardia, this drug also was discontinued. She underwent continuous cardiopulmonary monitoring. Prednisolone due to internal service's order was started 500 mg/daily to control vital signs then after three days tapered to 50 mg/daily. After three days of discontinuation of IVIG and clindamycin, the patient's bradycardia improved, and similar symptoms did not recur. [Figure 2](#) shows the ECG which taken after recovery.

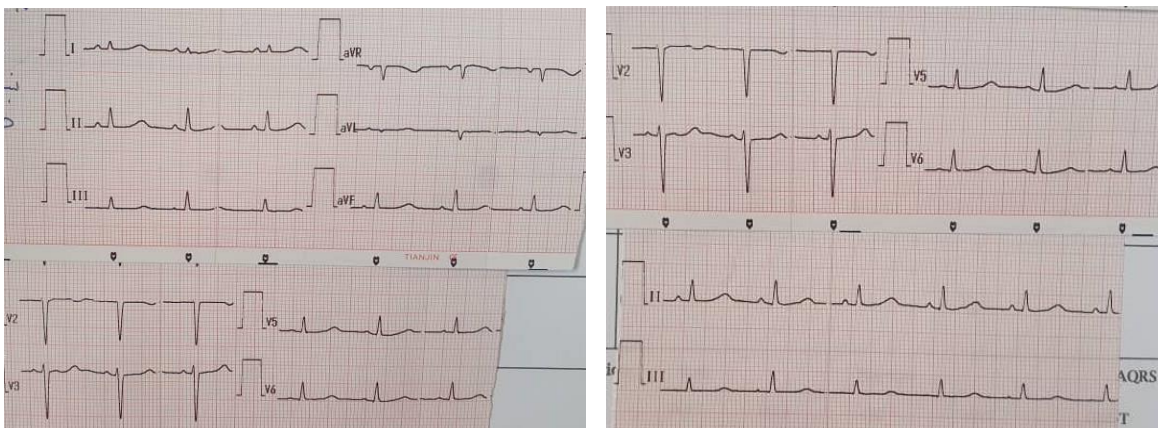


Figure 1. The first electrocardiogram

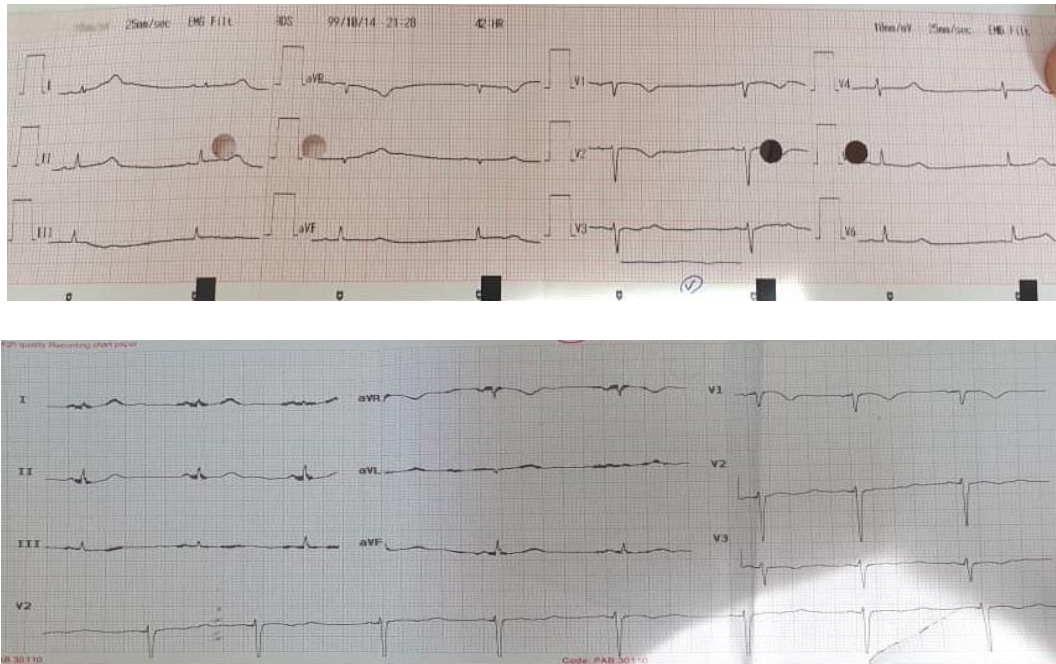


Figure 2. The electrocardiogram which was taken after recovery

Discussion

There have been case reports of bradycardia and association with administration of high-dose corticosteroids or clindamycin or immunoglobulin, but the data are incomplete. Clindamycin administration is the treatment of severe infections caused by anaerobic bacteria since it is very effective against gram-negative and -positive organisms, cocci, and anaerobic bacteria like *Chlamydia trachomatis* (9). Clindamycin can cause gastrointestinal discomfort, nausea, vomiting, diarrhea, hepatotoxicity, maculopapular rash, anorexia, flatulence, drug fever, and Stevens-Johnson syndrome, some of its common side effects (10, 11). A higher liver transaminase level, monoarthritis, hematopoietic effects such as neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura, cardiopulmonary arrest, hypotension, and excessive bleeding are less common adverse events (9-14). Sinus bradycardia is an adverse effect of clindamycin which is reported less frequently. In their case report, Sedigheh Ghasemian *et al.* reported that sinus bradycardia could be a side effect of Clindamycin in the treatment of septic abortion (15). In this case, symptomatic bradycardia occurred four hours after the start of clindamycin and improved three days after discontinuation. The administration of IVIG seems to be promising in clinical practice. While IVIG is usually tolerated well, there have been several reported adverse reactions, most of which are transient and mild, including flushing, headache, malaise, fever, chills, fatigue, and lethargy. However, some rare side effects may present as severe, including renal impairment, thrombosis, arrhythmia, aseptic meningitis, and hemolytic anemia (16). In therapy with IVIg, F. D'Andrea *et al.* reported a case about sinus bradycardia

in a patient with bacterial meningitis (17). Steven Douedi *et al.* likewise have reported a case that IVIG infusion can result in severe bradycardia, even in patients with no previous cardiac history. These patients are asymptomatic and don't require any treatment (18). In this case, too, the patient showed symptomatic bradycardia after receiving one dose of IVIg.

In practice, high-dose intravenous corticosteroid therapy, also known as pulse steroid therapy (PST), is frequently used. Hyperglycemia, gastrointestinal intolerance, minor infections, and psychiatric symptoms are the most common adverse effects of high-dose PST (19). The following are examples of minor adverse effects that can occur: transient facial flushing, a short disturbance of taste, distal paresthesia, insomnia, and mild weight gain (8). In general, high-dose corticosteroid therapy is associated with cardiac arrhythmias (atrial fibrillation/flutter, ventricular tachycardia, and sinus bradycardia) in 1% to 82% of patients (19-20). One of the rare adverse effects of PST is bradycardia which is usually asymptomatic. A case report by Alessandro Soderò *et al.* has described a 48-year-old woman with inflammatory myelitis who developed severe and symptomatic sinus bradycardia after five days of PST (21). Amartya Kundu described a woman during her treatment for multiple sclerosis who showed acute sinus bradycardia after receiving the pulse dose of steroids (22). In a study by Tvede *et al.*, five patients who were being treated for rheumatoid arthritis received high-dose intravenous methylprednisolone. All five of them experienced sinus bradycardia, although only one patient was

symptomatic with chest tightness. The sinus bradycardia was self-limiting in all of them, but for the heart rate, it took as long as seven days to return to normal (23). The temporal association between the IVIg and clindamycin and development of bradycardia and also in our patient according to continued use of corticosteroids, suggest the clindamycin and IVIg maybe this etiology.

Conclusion

In our limited experience, clindamycin can result in severe bradycardia, even in patients with no previous cardiac history, especially when combined with IVIg and corticosteroids because these medications may have potentially induced severe bradycardia. It is suggested that monitoring of general conditions and vital signs during treatment is recommended for the possible causal link between clindamycin or IVIGs and bradycardia, especially in the case of simultaneous administration of corticosteroids. Further studies are needed to verify this relation.

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Conflict of Interest

The authors declared no conflict of interest.

Ethical Approval

This article was extracted from a research project approved by the Ethics Committee of the Urmia University of Medical Sciences, receiving the code: IR.UMSU.RE.1400.176.

Informed Consent

Written informed consent was obtained from the patient.

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