Asystolic cardiac arrest: an unusual reaction following *iv* metoclopramide

[L'asystolie : une réaction inhabituelle à l'administration iv de métoclopramide]

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Purpose: To describe a case of sinus arrest after *iv* metoclopramide.

Clinical features: A 66-yr-old diabetic female with no cardiovascular disease was anesthetized for a partial mastectomy. While in the postanesthesia care unit, she suffered two episodes of asystole after *iv* metoclopramide 10 mg. The first episode lasted ten seconds and corrected spontaneously while the second episode, lasting less than one minute required closed chest massage and atropine *iv* 0.8 mg. The cardiac investigation that followed was inconclusive for ischemia and the patient did not experience any other episodes of dysrhythmia. No formal investigation was done to disclose diabetic autonomic neuropathy. However, based on the results of dipyridamole myocardial single photon emission computed tomography, if diabetic autonomic neuropathy was present, it was very mild.

Conclusion: The patient sustained two episodes of asystole after *iv* metoclopramide 10 mg in the immediate postoperative period in the absence of any predisposing cardiac history or medication. Diabetes, even without overt autonomic neuropathy, may have been a predisposing factor for sinus arrest after *iv* metoclopramide.

Objectif : *Décrire un cas d'arrêt sinusal suivant l'administration iv de métoclopramide.*

Éléments cliniques : *Une femme diabétique de 66 ans, sans maladie cardiovasculaire, a été anesthésiée pour une mastectomie partielle. Une fois dans la salle de réveil, elle a subi deux épisodes d'asystolie après avoir reçu 10 mg iv de métoclopramide. Le premier a duré dix secondes et s'est corrigée spontanément tandis que le second, de moins d'une minute, a nécessité un massage cardiaque externe et l'injection iv de 0,8 mg d'atropine. L'investigation cardiaque n'a pas permis de conclure à une ischémie et la patiente n'a pas subi d'autre dysrythmie. Aucune exploration formelle n'a été faite pour confirmer une neuropathie diabétique autonome. Cependant, d'après les résultats de la tomographie d'émission monophotonique myocardique, avec dipyridamole, si une neuropathie diabétique autonome était présente, elle était peu importante.*

Conclusion : *La patiente a subi deux épisodes d'asystolie après avoir reçu 10 mg iv de métoclopramide immédiatement après l'opération en l'absence de tout antécédent cardiaque ou médicament prédisposants. Le diabète, même sans neuropathie autonome patente, peut avoir été le facteur favorisant l'arrêt sinusal.*

METOCLOPRAMIDE is widely used to prevent or treat postoperative nausea and vomiting. Although it is generally considered safe, problems have been reported following its administration to patients with cardiac abnormalities.[1,2] We report a case of repeated episodes of asystole after two *iv* boluses of metoclopramide to a patient without known cardiac disease.

Case report

The patient was a 66-yr-old female with no previous history of dysrhythmia, coronary disease, syncope, or postural dizziness. She suffered from type II diabetes that was treated with metformin for the past three years. She had a previous partial mastectomy two years ago without any reported adverse event and was returning for a second partial mastectomy. The electrocardiogram (ECG) done a few minutes before surgery showed a normal sinus rhythm at a rate of 92 beats·min^{-1}, a PR interval of 124 msec and a QT interval of 370 msec. Her preoperative blood pressure was 120/70. Anesthesia was induced with *iv* fentanyl 250 µg, thiopental 400 mg, and rocuronium 50 mg followed by isoflurane for maintenance. She did not require reversal of neuromuscular blockade at the end of the one hour procedure.

Upon arrival in the postanesthesia care unit (PACU), the patient's pulse, blood pressure, and oxygen saturation were 41 beats·min^{-1}, 175/80 mmHg, and 97% respectively. Thirty-three minutes later, her

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TABLE Previous case reports of metoclopramide and cardiac dysrhythmias

Reference	*Patient and setting*	*Comorbid conditions*	*Metoclo-pramide*	*Other medications*	*Dysrhythmia*
Shaklai *et al.* 1974	55-yr-old woman ER	vomiting, no cardiac history	10 mg *im*	none reported	multifocal SVB
Withington 1986	54-yr-old man ICU	total pancreatectomy, postop pneumonia, PE, septicemia and jaundice	10 mg and 5 mg postop	dopamine < 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$	complete heart block, asystole
Bevaqua 1988	37-yr-old woman OR	vaginal delivery, no cardiac history, preop laparoscopic tubal ligation	10 mg	none reported	SVT 170 $beats \cdot min^{-1}$
Midttun and Øberg 1994	62-yr-old man ICU	atrial fibrillation 100–110 $beats \cdot min^{-1}$, multiple PE	2.5 mg and 5 mg postop	digoxin	complete heart block
	71-yr-old man ICU	incarcerated femoral hernia, CLL, circulatory failure, ATN	3 doses of 10 mg postop	dobutamine, norepinephrine, dopamine	bradycardia 50 $beats \cdot min^{-1}$
Malkoff *et al.* 1995	51-yr-old woman ICU	Guillain-Barré syndrome, severe dysautonomia, respiratory failure, gastroparesis	5–20 mg q6hr	dopamine 10–20 $\mu g \cdot kg^{-1} \cdot min^{-1}$, phenylephrine 100 $\mu g \cdot kg^{-1} \cdot min^{-1}$, nitroprusside 5–20 $mg \cdot hr^{-1}$	bradydysrhythmias, transient sinus arrest
Baguley *et al.* 1997	37-yr-old woman OR	preop advancement of thigh flap, no cardiac history	10 mg preop	ondansetron 4 mg	bigeminy + ST segment depression
	34-yr-old man OR	palpitations, removal of calcaneal hardware	10 mg intraop	propofol, lidocaine, fentanyl, succinylcholine induction; desflurane maintenance; ondansetron 2 mg	sinus bradycardia, junctional rhythm 30 $beats \cdot min^{-1}$ with PVB

All drugs were given intravenously unless specified otherwise. ER = emergency room; ICU = intensive care unit; IM = intramuscular; intraop = intraoperative; OR = operating room; PE = pulmonary embolus; postop = postoperative; preop = preoperative; PVB = premature ventricular beat; SVB = supraventricular beat; SVT = supraventricular tachycardia.

pulse rate was 80 $beats \cdot min^{-1}$ and she received metoclopramide 10 mg *iv* for treatment of nausea. One minute later, the patient experienced ten seconds of asystole without loss of consciousness. The PACU nurse summoned the attending anesthesiologist, who requested a cardiology consultation, an ECG and a chest roentgenogram. By this time, the patient had reverted to a normal sinus rhythm at 81 $beats \cdot min^{-1}$ with a PR interval of 156 msec and a QT interval of 370 msec. While the cardiologist was in the PACU, 53 min postoperatively, the patient complained of nausea again and received another dose of metoclopramide 10 mg *iv*. Eight minutes later, she experienced a second episode of asystole. Closed cardiac massage was initiated and atropine 0.8 mg *iv* was given. Again the episode lasted less than a minute. A transcutaneous pacemaker was applied and kept on standby. The patient was transferred to the coronary care unit (CCU) for further surveillance. She had no further episodes of bradycardia or asystole while in the CCU.

Subsequent cardiac investigation failed to identify a cause. Repeated cardiac enzyme levels were not elevated. Repeated ECGs were all described as normal, as was an echocardiogram. The exercise stress ECG was suspicious for ischemia, with 0.9 to 1.5 mm ST-depression or downsloping in the inferior leads, when the heart rate and blood pressure were 147 $beats \cdot min^{-1}$ and 185/70 mmHg respectively. Dipyridamole myocardial single photon emission computed tomography (SPECT), done after hospital discharge, was inconclusive for ischemia with a resting heart rate of 102 $beats \cdot min^{-1}$ and a peak heart rate of 167 $beats \cdot min^{-1}$ (peak-basal heart rate ratio 1.64).

Discussion

Metoclopramide treats vomiting by blocking dopaminergic receptors in the central nervous system (CNS) and by direct action on the digestive tract, possibly by the peripheral release of acetylcholine.[3] Although its molecular structure resembles procainamide, metoclopramide seems devoid of any significant antiarrhythmic or local anesthetic activity.[4] Hence, most reported side effects (extrapyramidal symptoms, drowsiness, agitation and anxiety) reflect CNS activity.[5–8] Hypotension[9] and ventricular bigeminy[10] have been reported following prophylactic metoclopramide administration during general anesthesia. Hypotension, associated with metoclopramide, have been described also in healthy, conscious volunteers.[11]

Cardiac dysrhythmias associated with metoclopramide have been reported in the critical care, perioperative, and emergency room settings (Table).

Withington reported a case of asystole and bradycardia in a jaundiced postoperative patient receiving dopamine.[1] Jaundice was suggested as the predisposing factor. Midttun and Øberg described two cases of complete heart block after *iv* metoclopramide.[2] The first patient had been treated with digoxin for atrial fibrillation and the second patient had been treated for circulatory failure. Other authors have reported supraventricular dysrhythmias following the administration of metoclopramide.[12,13] Baguley *et al.* reported two cases of perioperative dysrhythmias after combined administration of metoclopramide and ondansetron and warned against this combination.[14] Malkoff *et al.* reported a case of sinus arrest after *iv* metoclopramide in a woman with Guillain-Barré syndrome and severe dysautonomia and suggested that autonomic dysfunction could be a risk factor for metoclopramide-associated dysrhythmias.[15]

Our patient did not have any predisposing cardiac history nor did she receive any cardiac medications prior to her episodes of asystole. She had not received ondansetron. Her only potential predisposing factor was diabetes. Diabetes is associated with autonomic neuropathy and cardiovascular involvement.[16] The clinical and laboratory characteristics of diabetic autonomic neuropathy have been reviewed elsewhere.[17] A peak-basal heart rate ratio less than 1.2 on dipyridamole myocardial SPECT has been suggested as an indicator of cardiac autonomic dysfunction in diabetes.[18] Our patient did not undergo standardized diagnostic tests for diabetic autonomic neuropathy or any formal assessment of her heart rate variability. Her peak-basal heart rate ratio on SPECT was well above the suggested threshold for cardiac autonomic dysfunction. Still, in the absence of other tests, the possibility of autonomic neuropathy cannot be completely excluded.

In summary, we report a case of repeated asystole after *iv* metoclopramide in the immediate postoperative period. Diabetic autonomic neuropathy could be a contributing factor.

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