Insulin-overdose- A Potential Trigger of Ventricular Fibrillation with Takotsubo Cardiomyopathy?

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Article ID: WMC00851
Article Type: Case Report
Submitted on: 01-Oct-2010, 12:52:14 AM GMT Published on: 01-Oct-2010, 06:30:25 AM GMT
Article URL: http://www.webmedcentral.com/article_view/851
Subject Categories: EMERGENCY MEDICINE
Keywords: Insulin, Hypoglycemia, Ventricular Fibrillation, Takotsubo Cardiomyopathy, Cardiopulmonal Reanimation

How to cite the article: Balga I. Insulin-overdose- A Potential Trigger of Ventricular Fibrillation with Takotsubo Cardiomyopathy? . WebmedCentral EMERGENCY MEDICINE 2010;1(10):WMC00851

Source(s) of Funding:
I have no source of funding for my article.

Competing Interests:
I have no conflict of interest.
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Abstract

A 46 years-old diabetic man lost consciousness because of an insulin-overdose (Glasgow Coma Scale 3, blood-glucose 1.5 mmol/L). He regained consciousness after infusion of glucose 5% 100ml/10minutes (Glasgow Coma Scale 15, blood-glucose 3.8 mmol/L). An additional infusion of glucose 5% 100ml/10minutes was given (blood-glucose 5.2 mmol/L). 5 minutes after the end of glucose infusion, he suddenly lost consciousness because of ventricular fibrillation and immediate cardiopulmonary reanimation for 15 minutes restored a sinus rhythm. The cardiac catheterization proved a takotsubo cardiomyopathy without significant coronary artery stenosis. A hypokalemia of 2.5 mmol/L, presumably caused by the insulin-overdose, was present. Perhaps, insulin-overdose may trigger ventricular fibrillation with takotsubo cardiomyopathy, has not been reported in this context, but may surprise medical stuff working in and out of hospital. Consequently, these patients need quick hospital admission, cardiovascular monitoring, echocardiography and cardiopulmonary reanimation on standby until normalization of all dysrhythmic factors. More case reports or a study in the future are necessary to support this hypothesis.

Introduction

Takotsubo cardiomyopathy (TC) may be caused by hypoglycemia\textsuperscript{10-12}. Hypoglycemia may produce a proarrhythmic state\textsuperscript{13-15}. VF with TC after insulin-overdose has not been reported in this context. The case of a diabetic patient, who survived ventricular fibrillation (VF) with TC after insulin-overdose is reported.

Case Report(s)

Prehospital case report

The ambulance team, an anesthetist and a paramedic, was called for an unconscious 46 years-old patient (weight 85kg, height 170cm) at a snack-bar. On arriving, the man lied on the floor. The observers told, that the man came by car, suddenly lost consciousness before eating and was caught up without injuring himself. The first physical examination showed a normal spontaneous breathing (oxygen saturation 99% in air), a regular radialis pulse 117/minute, a blood pressure 120/70mmHg, a Glasgow Coma Scale (GCS) 1/1/1 and ischorous, mid-dilated pupils reacting normally to light. The measured blood-glucose was 1.5 mmol/L (27 mg/dl). After fractional intravenous (iv) glucose 5% 100ml/10minutes, the man regained consciousness (GCS 15) and a blood-glucose of 3.8 mmol/L (68 mg/dl). Additional iv glucose 5% 100ml/10minutes was given, then a blood-glucose of 5.2 mmol/L (94 mg/dl) was measured. The history revealed a non-compliant diabetic (type II) patient. He had injected himself estimating 40U of short-acting instead of long-acting insulin one hour ago. The patient negated to suffer from a heart disease, angina pectoris or dyspnoea. The cardiac and pulmonary auscultation was assessed inconspicuously. The man denied to be hospitalized. The ambulance team tried to convince the man, that a hospitalization in his case was mandatory. 5 minutes after the end of glucose-infusion, the man suddenly lost consciousness, stopped breathing and no carotid pulse was felt. The electrocardiogram (ECG) presented VF as first rhythm and one biphasic shock of 200J was fired (Illustration 1). Then pulseless electrical activity followed. Three times 1 mg iv epinephrine was applied each 5 minutes. Following differential diagnosis came into consideration: hypokalemia, hypoglycemia, acute myocardial infarction, pulmonary embolism\textsuperscript{1}. It was not possible to gain a blood drop for blood-glucose measurement during the CPR. Because of possible rebound hypoglycemia, 50 ml iv glucose 5% was blindly administered. After 15 minutes of successful CPR, a tachycardia sinus rhythm (Illustration 2) was restored and the patient reflexlessly intubated (capnography, initial CO2 6.2 kPa). During intubation, regurgitation was seen. Blood-glucose was measured 16.6 mmol/L (299 mg/dl) after CPR and 10 minutes later 11.5 mmol/L (207 mg/dl). The patient was brought without further complications and without the need of vasopressive drugs to the intensive care unit.

Hospital case report
All laboratory results of the patient are summarised in Illustration 3. The cardiac enzymes were in the normal range on admission. Laboratory data revealed a hypokalemia 2.5mmol/L and a slight hypocalcemia. Other laboratory data from blood, coagulation, liver and kidney were in the normal range. In the thoracic radiography a bilateral pulmonary edema was visible. The abnormal ECG, a ST-elevation in the wall-leads V2-V4 and III (Illustration 4) was the indication of an immediate cardiac catheterization to exclude a myocardial infarction. The coronary angiography uncovered akinesia in the anterior, apical and septal wall segments of the left ventricle (apical ballooning, Illustration 5 and 6), only a moderately diminished ejection fraction 52%, coronary artery sclerosis without a relevant coronary stenosis (a 30% stenosis in the left anterior descending artery and in the right coronary artery) and no pulmonary embolism or other cardiac pathologies (Illustration 3) could be found. With these clinical findings a TC was diagnosed. The patient suffered from following side diagnoses: arterial hypertension, strong nicotine abuse, depression, restless legs syndrome and psoriasis vulgaris. His daily drugs included: padma, pregabalin for knee pain, long-acting insulin (glargin, 40U) and fast-acting insulin (insulin aspart). A therapy with acetylsalicylic acid, lisopril, atorvastatin, torasis, magnesium as needed, potassium substitution was begun. The pulmonal edema disappeared rapidly and the patient was extubated the next morning (GCS 4/4/6). The cardiovascular support with low-dose norepinephrine could be stopped the next day. On day 3, the patient could be transferred to the ward with a telemetric surveillance. On day 4, a transthoracic echocardiography demonstrated a disorder of relaxation, a moderate diminished ventricular function (ejection fraction 47%), a hypokinesia apical and distal posterior. One week after CPR, no ischemic infarctions appeared in the head computertomography. All pathological diagnostic findings normalized without cardiovascular complication.

**Discussion**

The diabetic patient in a hypoglycemic comatose state ranks as a common daily prehospital emergency. The most part of hypoglycemic patients recover rapidly without complications after administration of iv glucose. Hypoglycemic coma, neurological disturbance and death from hypoglycemic encephalopathy counts among the well known complications from insulin-overdose. In this case, letal complications as VF with TC were produced after insulin-overdose and glucose treatment. Prodrome symptoms and significant coronary artery stenosis lacked. As electrolyte disturbances, a hypokalemia and a slight hypocalcemia were present. Which pathological mechanisms in this case might have triggered off VF and TC ?

A hypoglycemic stress reaction resulted from insulin-overdose and might have contributed for developing a TC. TC may arise from stress, elevating plasma catecholamines, of different causes and hypoglycemic stress of other origin than insulin has been published. Otherwise, hypoglycemia induces epinephrine secretion augmenting the intracellular potassium-shift, prolongs the QT-time and intensifies a proarrrhythmic state. Insulin shifts serum-potassium into the muscle and fatty cells. The intracellular potassium-shift produced a rapid fall in serum-potassium up to 2.5 mmol/L and was estimated as the main cause of VF. In addition, the glucose infusion as enough substratum may have favoured the common intracellular glucose-potassium-shift. TC as stunned heart may predispose to arrhytmiasor to sudden cardiac arrest. The patient suffered from psoriasis vulgaris, a skin disease, that can be associated with hypoaalbuminemia and hypocalcemia. Hypocalcemia is able to prolong QT-time and predispose to arrhythmias. Perhaps, the more triggering proarrrhythmic factors are available, the higher the risk of VF. The speed and duration of proarrrhythmic factors may also play a major role: maybe, the quicklier they develope and the longer they act, the higher the risk of VF. Diabetic patients with a coronary artery disease have a greater risk to develope cardiac arrhythmias. As main mechanism in this case, insulin-overdose presumably produced several, rapid triggering proarrrhythmic factors like stress, hypoglycemia, stunned heart and precipitated VF and TC. Several pathological mechanisms of TC has been discussed, but the exact origin of TC has not been revealed up today.

An other important problem was, that the patient rejected to be hospitalized. Some institutions accept the patient’s desire with his signature and he will not be hospitalized. Every institution or hospital should confirm the rules, how to deal with such complex patients and wich patients must be hospitalized, not to conflict with the law. A well clearing up for such patients and patience in certain cases are necessary. For paramedic people working without a medical doctor or without the chance of asking a medical doctor’s advice, a gradation of patients account to illness in “must be hospitalized” or “must not be hospitalized”, may be helpful.
Beside good instructions concerning the insulin therapy, especially a possible cardiac arrest after insulin-overdose and what to do, should be mentioned to diabetic patients and their relatives. In this case, a diagnostic bedside test of serum-potassium and the therapy of hypokalemia are not available for out-of-hospital. Maybe, some medical prehospital institutions with long transport-times have the capacity. Therefore, a quick hospitalisation and monitored care for patients with insulin-overdose is indispensable. A defibrillator should be within one’s grasp for medical stuff and in case of cardiac arrest, the rules of ACLS should be followed. What could we do anything else, if lethal arrhythmias occur and hypokalemia as obvious cause is suspected, but neither diagnostic bedside test nor treatment of hypokalemia is disposable out-of-hospital? If indicated, we may facilitate intubation with succinylcholine, provided that no contraindications exist and the patient has reflexes. At this point, an anecdote by experience will be told: a 50-years-old man (GCS 15, angina pectoris) presented with a ventricular tachycardia (VT). The ambulance team decided first an intubation with succinylcholine because of aspiration risk, then to treat electrically the VT. The VT converted spontaneously into a sinus rhythm after muscular fasciculations have stopped and before laryngoscopy (Illustration 7). An extracellular serum-potassium shift due to succinylcholine was assumed. Everybody working out-of-hospital should know the drugs elevating serum-potassium he has at his disposal and these drugs may help in an emergency situation (other drug-example: magnesium).

Conclusion

Every patient with obvious insulin-overdose could potentially suffer from VF with TC. Prodrome symptoms and significant coronary artery stenosis may lack. Perhaps, the risk of lethal arrhythmias augments with the number, speed and duration of proarrhythmic factors. Consecutively, these patients may need a quick hospital admission, a mandatory cardiovascular monitoring, bedside echocardiography, CPR on standby until all proarrhythmic causes are corrected. But this is only one case report and in the future, further similar case reports or studies are necessary to support this hypothesis.

Abbreviations(s)

TC: takotsubo cardiomyopathy
VF: ventricular fibrillation
GCS: Glasgow Coma Scale
iv: intravenous
CPR: cardiopulmonal reanimation
ECG: electrocardiogram
VT: ventricular tachycardia

Authors contribution(s)

The author is responsible for the whole manuscript.

References

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Illustrations

Illustration 1

The ECG shows VF on the left side and the biphasic shock on the right side.

Illustration 2

Tachycardia sinus rhythm was restored after the CPR and blood pressure 96/76mmHg measured.
Illustration 3

Results from blood sample and cardiac catheterization on admission.

<table>
<thead>
<tr>
<th>Laboratory data</th>
<th>normal range</th>
<th>patient’s results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin T</td>
<td>&lt; 0.1 μg/L</td>
<td>0.02</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>&lt; 110 μg/L</td>
<td>116</td>
</tr>
<tr>
<td>Creatine kinase-MB</td>
<td>≤ 5 μg/L</td>
<td>5.0</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>&lt; 195 U/L</td>
<td>85</td>
</tr>
<tr>
<td>B-type natriuretic peptide</td>
<td>&lt; 33 ng/L</td>
<td>18</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.4-4.5 mmol/L</td>
<td>2.5</td>
</tr>
<tr>
<td>Calcium total/ionized</td>
<td>2.15-2.55/1.15-1.35 mmol/L</td>
<td>2.07/0.98</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.70-1.05 mmol/L</td>
<td>1.03</td>
</tr>
<tr>
<td>Alcohol</td>
<td>&lt; 0.1 %</td>
<td>&lt; 0.08</td>
</tr>
<tr>
<td>thyroid-stimulating hormone</td>
<td>0.27-4.20 mU/L</td>
<td>2.13</td>
</tr>
<tr>
<td>Blood-glucose</td>
<td>3.9-6.4 mmol/L</td>
<td>15</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>&lt; 5 mg/L</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>Body temperature</td>
<td>°C</td>
<td>34.2</td>
</tr>
<tr>
<td>pH</td>
<td>7.370-7.450</td>
<td>7.173 arterial</td>
</tr>
</tbody>
</table>
### Diagnostic values of the cardiac catheterization (patient intubated, ventilated)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCO2</td>
<td>4.70-6.10 kPa 8.39 arterial</td>
</tr>
<tr>
<td>pO2</td>
<td>9.50-13.90 kPa 10.4 arterial</td>
</tr>
<tr>
<td>Base excess</td>
<td>-2-+3 mmol/L -7.3 arterial</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>21.0-26.0 mmol/L 18.5 arterial</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>95.0-98.5 % 92 arterial</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>70-75 % 69.1 venous</td>
</tr>
<tr>
<td>Lactate</td>
<td>0.5-1.6 mmol/L 5.7</td>
</tr>
</tbody>
</table>

### Left ventricular volume
- **Endsystolic/Enddiastolic**: 115/55 ml

### Left ventricular pressure
- **Endsystolic/Enddiastolic**: 127/16 mmHg

### Aortic pressure
- **Systolic/Diastolic/mean**: 105/70/84 mmHg

### Right ventricle
- **Endsystolic/Enddiastolic**: 34/10 mmHg

### Pulmonary artery pressure
- **Systolic/Diastolic/mean**: 30/17/22 mmHg

### Right atrial pressure
- **Mean**: 8 mmHg
Illustration 4

12-lead ECG. ST-elevation in the wall-leads V2-4 (>2mm) and III (>1mm) was detected.

Illustration 5

Cardiac catheterization, left ventriculography. The illustration 5 shows the heart during diastole.
Illustration 6

Left ventriculography. The illustration reveals an apical ballooning during systole, a TC.

Illustration 7

VT (left side) converted spontaneously into a sinus rhythm (right side) after iv succinylcholine.
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