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Possible sitafloxacin-induced dysglycemia: Case report

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Abstract

A 93-year-old diabetic patient was prescribed sitafloxacin (100 mg, bid, po) for 8 days to treat a pulmonary infection. Prior to the treatment with sitafloxacin, his blood sugar was well controlled, but during treatment, his blood sugar showed abnormal biphasic dysregulation, with a downward trend in the early stages of treatment (d1-3) and an upward trend in the late stages of treatment (d4-8), and the dysglycemia persisted for about 20 days after treatment. Sitafloxacin, like other fluoroquinolones, may be strongly linked to glucose homeostasis abnormalities in this case, necessitating clinical medical staff vigilance, particularly in patients with high-risk diabetes.

Keywords: Sitafloxacin; Adverse drug reaction; Dysglycemia.

Introduction

Fluoroquinolones, such as levofloxacin, ciprofloxacin, moxifloxacin, and gatifloxacin, have been linked to dysglycemia, resulting in hypo- or hyperglycemia, as well as biphasic changes in blood glucose, indicating the risk of hypo- and hyperglycemia coexisting [1,2]. This is especially true in diabetics, where abnormal blood glucose occurs earlier and more severely. Sitafloxacin (DU-6859a, STFX), a new generation of broad-spectrum fluoroquinolone antibiotics [3], is used in clinics for severe respiratory and urinary tract infections caused by susceptible bacteria [4,5], but little is known about its effect on blood glucose homeostasis. Here in, we present a case of blood glucose dysregulation caused by oral sitafloxacin in anelderly diabetic patient. By retrospectively analyzing the patient's glycemic changes before, during and after the administration of sitafloxacin with instantaneous scanning glucose monitoring system (ISGMS, Abbott), as well as insulin doses, we aim to explore the effect pattern of sitafloxacin on blood glucose and provide reference for blood glucose monitoring and management in diabetic patients while using this drug.

Case report

The 93-year-old patient has been in the hospital since June 9, 2019, due to frequent aspiration pneumonia caused by swallowing dysfunction and gastroesophageal reflux. Enteral nutrition has been used since a gastrostomy was performed two years ago. He had type 2 diabetes for 13 years and was taking sitagliptin phosphate (100 mg qd, po), metformin hydrochloride (250 mg bid, po), insulin glargine (34 units, qd, sc), and insulin aspart (8~12 units, tid, sc). Under the supervision of ISGMS, his blood glucose was well-controlled. The patient had several chronic diseases, including chronic obstructive pulmonary disease, coronary heart disease, heart failure with preserved ejection fraction, and so on.

On February 28, 2002, the patient developed a fever with a maximum temperature of 37.5°C, and the laboratory inflammatory indicator increased as well. He was diagnosed with pulmonary infection and given ceftriaxone sodium (2 g, qd, iv gtt) for two days, but the results were disappointing. On March 2, the treatment was upgraded to cefoperazone-sulbactam (1.5 g, tid, ivgtt) and sitafloxacin (Gracevit, 100 mg, bid, po) for 8 days,

with favorable results. During treatment, the nutrition plan was not changed, the patient's blood sugar was closely monitored, and the insulin dosage was adjusted in timely manner under the supervision of skilled medical professionals. We collected and analyzed the following data in the blood glucose report monitored by ISGMS from 7 days before the treatment to 20 days after the treatment, including average blood glucose, maximum and minimum blood glucose, time in range (TIR, defined as the percentage of time that glucose remained within the target range of 3.9 ~ 10.0 mmol/l within 24 hours), Time Below Range (TBR), Time Above Range (TAR), and total insulin dosage (units/day) [6]. Prior to sitafloxacin treatment, blood glucose was well controled; the daily average blood glucose, maximum and minimum blood glucose levels were all within the safe range, TIR reached 64%, and the average daily insulin comsumption was 70 units. During the first three days of the sitafloxacin treatment, the average glucose and Time of glucose Below Range (TBR) increased, while the daily insulin consumption was significantly reduced by 5 units compared to before treatment; in contrast, during the d4-8 sitafloxacin treatment, the blood glucose has an ascending trend, and the daily insulin dosage has also increased by nearly 6 units; these changes persisted for about 20 days. The daily minimum blood glucose levels did not differ significantly between the four groups. Table 1 and Figure 1 contain more information. Though the skilled doctor regulated the use of insulin based on blood glucose changes, glucose Time In Range (TIR) was only 22.2 percent during sitafloxacin treatment, significantly lower than before treatment. Though TIR gradually increased to 50% after treatment, but the whole blood glucose level still higher than before treatment; meanwhile, TAR was the highest during treatment, significantly different from other three duration groups. Figure 2 and Table 1 depicts this.

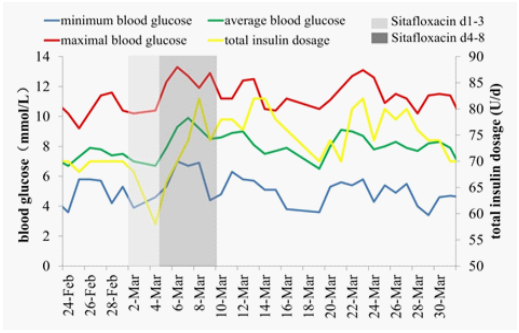

Figure 1: Trends of blood glucose and insulin consumption peri-sitafloxacin treatment.

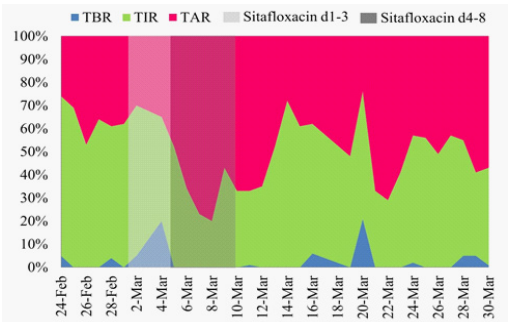

Figure 2: Trends of blood glucose control metrics peri-sitafloxacin treatment.

Table 1: Comparison of blood glucose control metrics and daily insulin usage in different periods of sitafloxacin treatment.

	Before treatment (7d)	During treatment (d1-3)	During treatment (d4-8)	After treatment (20d)	P
Daily average blood glucose (mmol/L, $\bar{X}$±s)	7.39±0.41	7.20±0.6^{2c}	9.10±0.5^{7ab}	8.05±0.7^{1ab}c	<0.001
Daily maximum blood glucose (mmol/L, $\bar{X}$±s)	10.57±0.81	10.97±1.1^{6}c	12.4±0.8^{4a} b	11.41±0.9^{0a} c	0.012
Daily minimum blood glucose (mmol/L, $\bar{X}$±s)	4.96±0.91	4.60±0.7^{0} c	5.96±1.25 b	4.95±0.81 c	0.118
Daily total insulin dosage (U/d, $\bar{X}$±s)	69.71±0.76	64.00±5.29^{ac}	75.6±4.56^{ab}	76.20±4.15^{ab}	<0.001
TBR (IQR)	0.00(0,0.04)	0.05(0,0.05)	0.00(0,0.00)	0.00(0,0.04)	0.182
TIR (IQR)	0.64(0.57,0.69)	0.52(0.45,0.52)	0.33(0.22,0.38)	0.51(0.37,0.56)	0.001
TAR (IQR)	0.36(0.30,0.39)	0.35(0.30,0.35)	0.67(0.62,0.79)	0.47(0.40,0.59)	0.003

[a]vs before treatment, P<0.05; [b]vs during treatment d1-3, P<0.05; [c]vs during treatment d4-8, P<0.05. IQR: Inter-Quartile Range; TIR: Time In Range; TBR: Time Below Range; TAR: Time Above Range

Discussion

We reported a possible sitafloxacin-induced dysglycemia in an elderly diabetes patient, and analyzed the changes of blood glucose before, during and after treatment. The results showed that the effect of sitafloxacin on blood glucose had a biphasic change, meaning that blood glucose had a downward trend in the early stages of treatment (d1-3) and an upward trend in the late stages of treatment (d4-8), and the abnormal blood glucose persisted for approximately 20 days after treatment. Even though the patient's blood sugar was closely monitored, and the insulin dosage adjusted simutanously, and despite the absence of symptomatic hypo- and hyperglycemia in the clinic, the blood sugar variation was nevertheless significant. It is clear that the effect of sitafloxacin on blood glucose, like that of other fluoroquinolone drugs, necessitates clinical medical staff vigilance, particularly in patients with high-risk diabetes. Due to the limited clinical application of sitafloxacin, similar cases have not been retrieved. As far as we know, this is the first case of sitafloxacin-induced glucose dysregulation in a very elderly man who suffers from multiple chronic conditions, and concurrently takes a variety of medicines. Although the causal relationship with the application of sitafloxacin cannot be determined, in the whole process, except for cefoperazone-sulbactam, only sitafloxacin is a newly prescribed drug, and there are more re-

ports of abnormal blood glucose caused by fluoroquinolones when compared to cephalosporins [1]. Therefore, we speculate that the glucose homeostasis abnormalitiesin this case is highly related to sitafloxacin.

The precise mechanism of sitafloxacin-induced dysglycemia is not fully understood; it might be fluoroquinolones'direct effect of the on glucose metabolism or the result of the combined action of multiple factors [7]. Animal studies show that the mechanism of fluoroquinolone induced hypoglycemia is to promote insulin secretion by blocking ATP sensitive potassium channels in pancreatic beta cells [8,9]. According to clinical research, levofloxacin and ciprofloxacin may contribute to aberrant blood glucose levels by impairing cells' GLUT1 and glucose transport mechanisms [10]. Also, gatifloxacin can also trigger the vacuolation of pancreatic beta cells, leading to reduced insulin levels and hyperglycemia. In an in vitro experiment using mouse pancreatic cells, gatifloxacin can stimulate insulin secretion and reduce blood glucose in the short term, while inhibit insulin biosynthesis and increase blood glucose in the long term [11]. That's why in some cases, hypoglycemia followed by hyperglycemia developed during gatifloxacin therapy [9]. Further evidence is required from studies on blood glucose caused by sitafloxacin.

The effect of fluoroquinolones on blood glucose has individual differences, and elderly patients and those with diabetes are more vulnerable to major abnormal blood glucose episodes [12]. The elderly are frequently associated with age-related renal dysfunction, occult diseases, or the use of blood glucose-affecting drugs, making them a high-risk group for drug-induced abnormal blood glucose. Furthermore, the physiological function of the elderly is reduced, as are the functions of the anterior pituitary and adrenal cortex. When abnormal blood glucose occurs, the normal anti-regulatory function is compromised, and the hormone that regulates blood glucose cannot be secreted in a timely manner. As a result, the consequences of abnormal blood glucose are often more serious. Therefore, fluoroquinolone use should be more careful in this population.

Conclusion

To summarize, we described a case of abnomal blood glucose caused by sitafloxacin. Our findings have significant clinical implications. In clinical applications, physicians should be aware of the risks of dysglycemia caused by sitafloxacin. It is critical to closely monitor blood glucose changes, timely adjust the dose of hypoglycemic drugs, and address the signs of hypoglycemia or hyperglycemia in time to avoid the occurrence of adverse events.

Declarations

Conflicts of interest: none.

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