Pancreas tissue concentration and pharmacokinetics analysis of vancomycin for severe acute pancreatitis: a case report

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Abstract

Antibiotic concentration in pancreas tissue is very important for the treatment of severe acute pancreatitis (SAP) with infection. We report a case of a 44-year-old female with SAP on treatment of vancomycin. The time courses of vancomycin concentration in serum and pancreas tissue of the patient was described. This case demonstrated that it took about 30 minutes for vancomycin to get through from serum to pancreas tissue and about 76% of vancomycin could move into pancreas tissue for SAP patients.

RESULTS——CASE PRESENTATION

A 44-year-old female was diagnosed with SAP in February 2018 because of her clinical manifestations (abdominal pain, nausea, emesis and fever), imaging work-up (ultrasound and computed tomography) and laboratory parameters (serum amylase and lipase to be three times of the upper limit) with Acute Physiology and Chronic Health Evaluation II (APACHE II) score of 12, Balthazar CT score of 6 and Marshall score of 3. Since hospital admission, she was constantly in fever with intermittently elevated white blood cell (WBC) and neutrophil percentage (N%). On February 28th, the patient's WBC and N% rose to 30.17*10ˆ9/L and 96% respectively, which can be explained with aggravation of infection. As she underwent trachea intubation because of hypoxemia on the same day, stress response or the effect of glucocorticoid after trachea intubation couldn't be excluded. To control the infection better, the patient was operated percutaneous drainage and vancomycin was prescribed empirically on the basis of imipenem/cilastatin. The primary dosage regimen of vancomycin was 0.5g thrice daily, which was calculated using SHIONOGI-VCM-TDM S1-1[26] according to her age (44 year), weight (60 kg), and serum creatinine (89 $\mu mol \cdot L^{-1}$). On March 2nd, when vancomycin concentration was assumed to achieve steady state, we got the drainage and blood for vancomycin concentration measurement simultaneously. The sampling time was at 0.5 hours before administration and 1.5, 2, 3, 5, 7 hours after administration of the seventh dose. And the concentration was determined using chemiluminescent microparticle immunoassay assay (CMIA) method[27]. On March 12th, the patient's temperature, WBC and N% returned to normal.

Figure 1 showed the result of vancomycin concentration in serum and pancreas tissue. It could be seen that the time to peak concentration (T_{max}) of pancreas tissue fell behind T_{max} of serum about 30 minutes, which means it took time for vancomycin to get through from serum to pancreas tissue. And we calculated the area under curve (AUC) of these two curves to estimate the amount of vancomycin in pancreas tissue by trapezoidal rule. The $AUC_{0\text{-}8h}$ of time-tissue concentration and time-serum concentration was 117 and 154 respectively. The ratio of the two was 76%, which means about 76% of vancomycin could move into pancreas tissue. Besides, the pharmacokinetic parameters were calculated using first-order conditional estimation method[28] with NONMEM version 7.3.0 software (ICON Development Solutions). One- and two-compartment models with first-order absorption and linear elimination were investigated to determine the optimal structural model. Because we only had one patient, the inter-individual variability was fixed as 0 and no covariate

was retained in the final model. The two-compartment model was chosen finally as it well described the data. The results were shown in Table 1.

DISCUSSION

Antibiotic concentration in pancreas tissue is very important for the treatment of SAP patients with infections. Previous studies show that quinolones and carbapenems have high pancreatic tissue levels and aminoglycosides fail to penetrate into the pancreas in sufficient tissue concentrations[22-25]. However, there are limited data with respect to vancomycin. This case indicated the good penetration ability of vancomycin in human pancreatic tissue, which provides evidence for the prescription of vancomycin in SAP patients.

This result was inconsistent with another published animal study[29], which concluded only 9% of vancomycin can penetrate into pancreas tissue. The reason may be the difference between human and animal studies or the difference of concentration between drainage and tissue. Besides, it can also be explained as the increased permeability to pancreas tissue of vancomycin under the pathological inflammation state[30].

As for the dosage regimen, only renal function was considered for this patient. Twice measured trough steady state concentration was 11.9 $mg{\cdot}L^{-1}$ and 15.7 $mg{\cdot}L^{-1}$ respectively, which were within the therapeutic window of 10-20 $mg{\cdot}L^{-1}$[19]. $AUC_{0\text{-}24h}$ was three times of 154, which was also during the range of 400-600 recommended as the pharmacokinetics/pharmacodynamics target of vancomycin[20]. And the patient's outcome was good. As a consequence, the dosage regimen for this patient was acceptable.

A previous study of the pharmacokinetics of vancomycin in patients with SAP[31] shows the trough concentration is relatively low, and the clearance is relatively high. However, the clearance (Table 1) of this patient is similar to the description of vancomycin pharmacokinetics characteristic in package insert[32]. But the pharmacokinetic parameters need to be validated with more future studies since we only have one patient.

CONCLUSION

Simultaneous measurement of pancreatic tissue and serum concentrations have demonstrated that vancomycin can rapidly penetrate into pancreas with acceptable amount, implying that vancomycin can be prescribed for SAP patients without worrying about its penetration ability.

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COMPETING INTERESTS

There are no competing interests to declare. The patient has consented to publication.

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Table1. Pharmacokinetic parameters estimated for vancomycin.

Parameter	Value
CL	2.56 L/h
Q	6.1 L/h
V_c	8.66 L
V_p	12.3 L

CL: clearance; Q: intercompartmental clearance; V_c: central compartment volume of distribution; V_p: peripheral compartment volume of distribution.

Figure legend

Figure1. The vancomycin concentration-time profiles of serum and pancreas tissue in the patient.