PB2325 APPLICATION AND COMPARISON OF TWO PHARMACOKINETIC DETECTION METHODS IN CHILDREN WITH HEMOPHILIA A—AN INSPECTION REPORT FROM SINGLE CENTER

Topic: 33. Bleeding disorders (congenital and acquired)

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Background: Personalized prophylaxies for moderate and severe hemophilia A and B are based on personal pharmacokinetics (PK), half-life (T1/2). While classical method for personal PK needs multiple blood collections, at least 5 points collections for children and 11 points for adults, and expensive for testing and leads low compliance. Popular PK based on pupolar data can have a less blood collections but a rough data (range) is recommended for reference. One-chamber model may also have a less blood collection 2-3 collections for PK detection.

Aims:

Objective: To analyze and compare the half-life (T1/2) results of Factor VIII (FVIII) calculated by modified one-chamber model by “CAI's” hemophilia pharmacokinetic calculation tool and WinNolin software (five-point sampling), non-av model, and to explore the reliability and clinical application value of “CAI's” hemophilia pharmacokinetic calculation tool.

Methods: A total of 30 patients with moderate and severe hemophilia A were treated with FVIII (50IU/Kg) after the 72-hour elution period. Peripheral blood samples were collected at five time points before and after FVIII injection (0h, 1h, 9h, 24h, 48h), and FVIII activity was detected by one-stage method. The T1/2 of FVIII was calculated by WinNolin software. Two of the three time points of FVIII activities (9h~24h, 9h~48h, 24h~48h) were used to calculate the FVIII T1/2 by “CAI's” hemophilia A pharmacokinetic calculation tool, and the results were compared with those of WinNolin software, and the correlation analysis was conducted.

Results:

1. 30 cases of T1/2 of FVIII calculated by WinNolin software was from 5.55 hs to 12.5 hs.

2. Compared with WinNolin software (five-point method, the results of T1/2 of FVIII caculated by "CAI's" hemophilia A pharmacokinetic calculation tool) at 9h~24h, 9h~48h and 24h~48h showed that the detection periods with highist consistent T1/2 were 9h~48h, 24 out of 30, 80.0%, while 9h~24h 6 out of 30, 20.00%;

3. Correlation analysis shows that there is a good correlation between the T1/2 of the modified one-chamber model and the results of WinNolin's calculation in all three time periods, but the correlation/consistency is the highest in the period of 9h~48h (see fig 1);

4. Analysis of the FVIII T1/2 results of 9h~24h, 9h~48h and 24h~48h we found that there were 8 out of 30 cases (26.67%) of T1/2 were basically stable at the same level, while 53.33% (16/30) of the children had significant changes at each time period.
Summary/Conclusion: 1. Compared with the T1/2 results by WinNolin's method and modified ond-chambor model ("CAI’s” tool), the most consistency of T1/2 of blood sampling was 9h~48h. However, for those T1/2 short than 7~8hs, the detection time should be adjusted (the later blood sample taking should be adjust to earlier);

2. Nearly 3/4 of the 30 cases, the T1/2 results fluctuated among three periods (9h~24h, 24h~48h, 9h~48h) in one case, suggesting a standardized test procedures such as specimen collection, sample transportation and detection ect needs to set up to ensure the stability and reliability of test results.

3. The classical pharmacokinetic test requires at least 5 points of blood sample collections, which is difficult to be popularized and applied in clinical practice. If a standardized and standardized testing process is established, the one-chamber model method is relatively simple and easy to be accepted and popularized by patients.

Key words: hemophilia A, pharmacokinetics, children, one-chamber model, non-av-model