

Population Analysis of Densely Sampled Pharmacokinetic Data

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Background: The use of NONMEM software in the analysis of data rich situation such as Phase I clinical trials or bioequivalence studies has been advocated. We report a case comparing PK parameters obtained from densely sampled PK data using the standard two stage (STS) or mixed effect method.

Methods: Plasma concentration data of propofol in twenty patients with intermediate to severe burn and another twenty patients without burn were analyzed using NONMEM. The subroutine ADVAN6 with FOCE interaction method was used to fit the data to 3-compartment models. The PK parameters obtained thereby were compared with those from STS method (WinNonlin Pro.).

Results: In both of burned and unburned patients, the individual PK parameters from the STS method showed much wider range of distribution than those from NONMEM. This was remarkable especially for central (V_1) and peripheral (V_3 - which was smaller than V_2) volumes of distribution and their inter-compartmental clearances.

Discussion: In such a 'rich data from a small number of subjects' environment, between-subject variability (BSV) of PK parameters tends to be greater than it appears in larger population. However, NONMEM-estimated omega values were not large enough to cover the observed BSV and the gaps between the observed vs. estimated BSV were dumped to the residual error side. This example alerts us about the possibility of misled conclusion if the analysis results from NONMEM are not carefully reviewed in comparison with those from STS method.

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Education

- 1986 ~ 1992: M.D., Seoul National University College of Medicine, Seoul, Korea
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Career

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