RETROSPECTIVE ANALYSIS OF PHARMACOKINETICALLY GUIDED BUSULFAN DOSING IN TWO DIFFERENT DOSING REGIMENS IN PATIENTS UNDERGOING CONDITIONING FOR ALLOGENEIC STEM CELL TRANSPLANTATION

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Introduction: Busulfan is a key component of ablative conditioning regimens before allogeneic stem cell transplantation. The aim of our retrospective analysis was to compare the pharmacokinetic parameters of busulfan and the clinical course of patients, and to evaluate two different dosing regimens.
Patients and methods: This is a retrospective analysis of 90 adult patients treated with busulfan as part of the conditioning regimen prior to allogeneic peripheral stem cell transplantation. All patients were diagnosed with acute myeloid leukemia or AML-type myelodysplastic syndrome and underwent a conditioning regimen consisting of 12.8 mg/kg i.v. busulfan along with fludarabine. Busulfan was administered as a once-daily dose in 47 patients, and in a standard divided regimen of four daily doses given every 6 hours in 43 patients. Plasma concentrations of busulfan were monitored in all patients. We evaluated pharmacokinetic parameters and clinical outcomes for all 90 patients. Pharmacokinetic parameters were calculated using the NLME method.
Results: The results showed that the area under the curve (AUC) of busulfan was comparable between two regimens, due to careful dose adjustments targeting an AUC range of 5500–6000 µmol/min/day. The most relevant covariate predicting pharmacokinetics appeared to be the dose adjusted to IBW (ideal body weight) with a 40% correction. No statistically significant differences were found between the two regimens in terms of overall survival, relapse-free survival, or relapse incidence. At 2 years, the predicted overall survival, relapse-free survival, and relapse incidence were 73%, 59%, and 30% respectively for the four-times-daily regimen, and 71%, 58%, and 38% respectively for the once-daily regimen.
In addition, operational impacts were also assessed. The once-daily regimen significantly reduces logistical demands, facilitates plasma level monitoring, and shortens administration time without compromising therapeutic effect. Furthermore, the once-daily regimen allows for a simpler calculation of AUC from measured levels using non-compartmental (trapezoidal) analysis.

Conclusion: Our retrospective analysis demonstrated that once-daily busulfan dosing is pharmacokinetically and clinically comparable to the standard four-times-daily regimen. Additionally, it offers significant operational advantages, simplifies patient care, reduces the time burden on nursing staff, and enables straightforward AUC calculation.