Pharmacoeconomic aspects of dose-banding

Dose-banding (DB) is widely used for outpatient chemotherapy in the UK, and several advantages have been observed with the system, including reduced patient waiting times and reduced stress for staff. A study evaluated DB for inpatient chemotherapy.

For the last 50 years, doses for the majority of anticancer agents have been individualised according to body surface area (BSA) in an attempt to minimise intra- and interpatient variability in therapeutic and toxic effects. In recent years, the scientific validity and clinical value of this practice, which clearly has practical and economic implications for the healthcare system, have been questioned.

Dose-banding (DB) is an approach that has been proposed as a first step to rationalise chemotherapy dosing. In DB, patient-specific chemotherapy doses are fitted to predefined “bands” (dose-ranges), which can be provided with standard doses (band midpoint), using pre-prepared syringes/infusions either singly or in combination. In each “dose-band”, the maximum variation of the adjustment between the “dose-banded” and the patient-specific dose is 5% or less. DB has been widely adopted in the UK, and reports have indicated strong support from oncology pharmacists, primarily because DB reduces preparation urgency and stress, and decreases patient waiting times and hence complaints from patients, nurses and oncologists.

As prefilled syringes are prepared in batches, the system also facilitates quality control (QC) and the possibility to assign pre-determined shelf-lives. Additionally, DB is likely to be more cost-effective than patient-specific dose preparation.

There are significant costs associated with cancer chemotherapy preparation, and patient-specific dose preparation precludes the efficient use of resources and results in substantial amounts of drug wastage due to discarding of partly used vials and deferred doses. In the absence of reports of DB for inpatient chemotherapy, a study was designed to statistically compare DB with the provision of patient-specific doses in terms of chemotherapy provision times, treatment delays and overall costs for inpatient chemotherapy.

Discussion
The study was conducted within the Pharmacy Technical Services Department at Derriford Hospital (Plymouth, UK), which prepares and releases approximately 130 parenteral chemotherapy items per day, both individualised (35%) and DB (65%). Ethics and institutional approvals were obtained.

All stages necessary for the preparation, dispensing and final release of patient-specific and DB chemotherapy items were identified. Timings of every stage, the grade of staff performing each stage, direct costs of drugs, diluents, disposables, labour and QC (for prefilled syringes), together with indirect costs of drug wastage, were assessed at baseline and for DB chemotherapy provision, both for individual drugs and on a per-regimen basis. Timings were logged with time-/date-stamps, costs were based on current institution prices and salary data, and staff had been trained in dispensing and administering DB syringes according to standard operating procedures prior to the study.

The most common regimen in both baseline and DB study periods (both four weeks) was cyclophosphamide/doxorubicin/vincristine/prednisolone (CHOP). For this regimen, the average doses in DB were 0.7% lower (cyclophosphamide) and 1% higher (doxorubicin) than the average doses when each drug was provided with patient-specific doses. For vincristine, there was no change in average dose. The average number of syringes required to provide the dose of each drug in DB was three, except for vincristine, for which a single syringe was used.

Labelling and dispensing of combinations of prefilled syringes required to provide the DB dose of each drug for a patient took approximately 11 minutes for cyclophosphamide, 10 minutes for doxorubicin and 7 minutes for vincristine. In the provision of patient-specific doses, the additional time required for preparation was 18 minutes for a cyclophosphamide dose (requiring reconstitution), 12 minutes for a doxorubicin dose and 13 minutes for vincristine (the latter two were simple draw-up processes). Consequently, the average labour time for dispensing prefilled DB syringes was reduced.
The dose-banding system has been introduced to rationalise chemotherapy dosing by 43 minutes/patient, compared with patient-specific preparation of the CHOP regimen. Obviously, the labour time for the planned batch manufacture of prefilled DB syringes has to be included. For the combination of prefilled syringes required to provide the CHOP regimen for one patient, this average manufacturing time (including QC) was 36 minutes.

Although the total time-saving was not therefore substantially reduced, it was statistically significant (p<0.01). For the average dose and patient, provision of a complete CHOP regimen cost £12 (£17) less with DB than with patient-specific dose provision (p<0.01). This included the cost of drug wastage and QC. These total savings in time and cost may not seem large. However, these data do not give the complete picture, since preparation of prefilled DB syringes is planned and chemotherapy can be dispensed with minimal delay when needed. On the contrary, patient-specific doses prepared on demand may be subject to significant delays before preparation can commence, partly because access to Safety Class II cabinets' isolators is required. Regarding costs, treatment costs for one patient could be saved for every 10 patients treated with DB, using CHOP (which is a low-cost regimen) as an example. On a dose-dependent basis, savings with DB (due to reduced drug wastage) are expected to be larger for more expensive drugs. Drug wastage costs also depend on the availability of different vial sizes and on the size of the oncology unit. Similarly, labour costs depend on which grades of staff perform the different stages in chemotherapy provision.

**Conclusion**

Advantages of DB in outpatient settings may not extrapolate directly to inpatient chemotherapy, where treatment delays are less likely to be due to pharmacy issues. However, the results suggest that DB is more economic and that it facilitates effective planning of time and resources. The possibility of prospective QC with prefilled syringes used in DB could significantly reduce preparation errors, particularly for batches made from pooled drug solution. Ward-based studies are ongoing to evaluate patient complications, medication errors and acceptance of DB by nursing staff.

The acceptability of DB is poor in many countries, due to the fact that exact patient-specific doses are abandoned. However, this current study, as well as additional studies,\(^5\) has shown that variations from prescribed doses using DB were minimal. Nevertheless, the system must be justified in terms of safety and efficacy, and pharmacokinetic crossover studies comparing DB with patient-specific dosing are therefore ongoing.\(^{13\,11}\)

**References**