The impact of high-dose methotrexate management protocol on clinical outcomes among patients with haematological malignancies - a retrospective analysis

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ABSTRACT

Introduction: High-dose methotrexate (HDMTX), defined as Methotrexate doses ≥500mg/m^2, has been an important backbone in the treatment of leukaemia, lymphoma and osteosarcoma. In 2019, a HDMTX management protocol was implemented in Hospital Sultanah Aminah, Johor Bahru (HSAJB). Prior to the adoption of this protocol, clinicians encountered a worrying trend of nephrotoxicity following administration of HDMTX. The purpose of this study was, therefore, to evaluate the impact of the newly introduced protocol on the incidence of delayed methotrexate clearance, appropriate leucovorin use, incidence of nephrotoxicity and length of hospital stay. **Methods:** This was a single-centre, retrospective study. A total of 37 patients received 90 cycles of HDMTX before the protocol implementation (1 January 2018 through 31 December 2018) and 37 patients received 96 cycles of HDMTX after the protocol implementation (1 January 2020 through 31 December 2020). Patient characteristics and primary outcomes were analysed using inferential statistics. **Results:** Both pre- and post-protocol groups showed similar incidence of delayed methotrexate clearance, 22.4% vs. 17.7% respectively (p=0.259). For patients who required leucovorin dose escalation, 14.3% vs. 90.0% were appropriately dosed as per protocol in the pre- and post-group respectively (p=0.001). The incidence of nephrotoxicity was significantly reduced in the post-protocol group 2.1% compared to 10.0% in the pre-protocol group (p=0.022). The median length of stay was reduced, albeit insignificant, in the post-protocol group compared with the pre-protocol group, 5 days vs. 6 days, respectively (p=0.587). **Conclusion:** Among patients who received HDMTX at HSAJB, the implementation of a protocol drives standardisation of practice, thereby, helps reduce the incidence of nephrotoxicity.