Administration of Cyclosporine as an Intravenous infusion every 12 hours Versus a Continuous 24 hour Infusion

Deanne Beck, RN, BSN, CPON – Oncology Intensive Care Unit
CHOC Children's, Orange, CA

PICO Question

In the post allogeneic bone marrow transplant patient does the administration of intravenous (IV) Cyclosporine every 12 hours versus a continuous 24 hour infusion impact the side effects and/or adverse reactions to Cyclosporine?

Discussion

Cyclosporine is the primary of pharmacologic intervention used to prevent graft-versus-host disease (GVHD) in post allogeneic bone marrow transplant patients. It is given prophylactically and is usually started one day prior to the marrow infusion and continued for approximately 6 to 7 weeks post transplant. GVHD continues to be a major concern in allogeneic bone marrow transplant patients. Even though advances have been made in understanding GVHD, this disease remains one of the leading causes of early treatment related mortality. This evidenced based practice review examined the risks and benefits of infusing IV Cyclosporine every 12 hours versus infusing IV Cyclosporine as a continuous 24 hour infusion in the post bone marrow transplant patient. The focus was on studies that assessed the tolerance level of patients who have received Cyclosporine using either modality. This review identified the specific patient characteristics that increased the side effects and/or adverse reactions to IV Cyclosporine given every 12 hours versus as a continuous 24 hour infusion.

Evidence Search

Data base searches for this evidenced based practice review included: CINAHL, PubMed, and Ovid. Reviewed websites included: Joanna Briggs Institute, American Academy of Family Physicians, Cochrane Library, National Guideline Clearinghouse, National Cancer Institute, National Institute of Health, American Cancer Society, American Institute for Cancer Research, and The Children's Oncology Group. Sample size variations included patients with age ranging from 16- 65 years. The measurement of variability was largely heterogeneous in the studies evaluated. In all studies reviewed patients were undergoing allogenic bone marrow transplant as a treatment therapy for their disease state. All patients in the proposed studies were evaluated for their response to Cyclosporine and the incidence of GVHD.

Synthesis of Findings

There was no consensus from the research findings regarding the most beneficial time period over which an administration of IV Cyclosporine should be given. Cyclosporine was actively manipulated as the independent variable; however, none of the studies could conclusively determine a recommended infusion schedule for Cyclosporine.

The risks and benefits of both infusion modalities were widely variable. GVHD was not entirely prevented and patients from both infusion modalities experienced side effects associated with Cyclosporine. While side effects and/or reactions to Cyclosporine were controlled, the findings were inconclusive regarding a safe and effective dose administration schedule to prevent acute GVHD.

Limitations

Limitations were numerous among the studies evaluated. The infusion rate and dosage administered of Cyclosporine was inconsistent from study to study. The concentration target level for Cyclosporine was undetermined by the study researchers. There was no consensus of when target levels of Cyclosporine should be drawn or how they should be drawn. In one study (Oshima, 2008) there was no appropriate definition of standard risk disease. There may have selection bias based on the patient's disease process and exposure to chemotherapy and antibiotics. Pre-existing renal and/or hepatic disease was not determined. Patient participant selection was not standardized in any of the studies reviewed.

Practice Recommendations

- The narrow therapeutic index of Cyclosporine makes it important to evaluate the real Cyclosporine dose a patient is exposed to during the treatment regimen.
- A consistent recommendation in the articles was that, regardless of infusion times, Cyclosporine levels must be drawn to evaluate the efficacy of the medication in the prevention of GVHD while also minimizing adverse side effects (Hendriks, 2006; Miller, 1993; Ogawa, 2004; Oshima, 2008; Tallman, 1988; Yee 1988).
- The benefit of obtaining both a trough and five hour post level of during Cyclosporine therapy was also noted (Izumi, 2007). However, this study could not determine if the five hour sampling point provided the most accurate marker of a peak level. The author showed that having low Cyclosporine concentration levels five hours after infusion was a risk factor for moderate to severe acute GVHD. Their recommendation was that it may be necessary to monitor Cyclosporine concentration levels after the start of therapy to achieve immunosuppressive activity adequately to prevent GVHD (Izumi, 2007).
- Further research is needed to determine the advantages versus disadvantages of short 12 hour twice daily IV infusion versus 24 hour continuous IV infusion of Cyclosporine. The scheduling of Cyclosporine is currently determined by the institution's policy and procedure guidelines.
- Further studies are needed with evaluation of larger numbers of patients with study limitations.
- It may be advantageous to monitor Cyclosporine concentration levels after therapy has begun albeit the most valuable time for obtaining peak concentration levels has yet to be established. Adaptation of obtaining a post Cyclosporine concentration level appears to offer valuable information to the clinician managing patients receiving Cyclosporine during the bone marrow transplant process in the prevention of GVHD.

Literature Cited

Available upon request.

Acknowledgments

- The Evidence-Based Scholars Program was supported by a grant from the Walden and Jean Young Shaw Foundation.
- Vicky R. Bowden, DNSC, RN
  Azusa Pacific University
  EBP Scholars Program Mentor
- Children's Hospital of Orange County Nursing Administration
- Jan Grabowski
  Burlew Medical Library
  St. Joseph Hospital
- Melanie Patterson, MHA, RN
  Director
  CHOC Children's Cancer Institute