DEVELOPING NURSE GUIDANCE FOR IV BUSULFAN CHEMOTHERAPY

This is a summary: the full paper can be accessed at nursingtimes.net

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Busulfan is a major agent used in the conditioning regimens of haematopoietic progenitor cell transplantations. Initially it was only available as an oral preparation but, over the last 5–6 years, it has been increasingly used as an IV infusion. Due to increasing use of the drug in the transplant setting and the change in preparation, it was important to develop clear and concise guidelines for chemotherapy nurses administering it by the IV route.

INTRODUCTION

Blood and marrow transplants (BMTs) offer patients diagnosed with haematological malignancies or acquired conditions (such as aplastic anaemia) high-dose treatment of their disease. In some cases, it may result in a potential cure. There are two types of transplant: autologous, where the cells for the transplant are sourced from the patient; or allogeneic, where the cells come from a donor. Before the cells are infused, patients receive a conditioning regimen. This consists of a combination of chemotherapy, with or without radiotherapy (Leukaemia Research, 2006). Conditioning regimens aim to eradicate residual malignant cells, make space in the bone marrow for the introduction of the transplanted cells/marrow, and, in the case of allogeneic transplants, reduce patients’ immune response to prevent graft rejection. How the conditioning regimen is delivered is a key element in the success of the transplant. Depending on the regimen used, they usually last 1–10 days.

THE NEED FOR GUIDELINES

When the change occurred from the oral to IV preparation, it was difficult to ensure that nurses administering the chemotherapy had all the necessary information. In a literature search, the only guidance identified was a user’s guide by the manufacturer of the IV busulfan preparation (Pierre Fabre Ltd, 2006), which offers only general information. There are also snippets of information in the BNF and chemotherapy administration books. This information is generally inaccessible and does not fully prepare nurses for the administration of IV busulfan, especially clinical aspects.

A project to develop busulfan guidelines specifically for nurses began, in association with the manufacturer. Information was gathered from a variety of sources. The user’s guide was reviewed and relevant information used, advice was gathered from pharmacy technicians, haematology consultants, chemotherapy nurses and from first-hand experience, through clinical work.

GUIDELINE BASICS

Busulfan is a potent cytotoxic alkylating agent, which acts primarily on the granocyte precursors in the bone marrow. It is cell cycle non-specific, working on all phases of the cell cycle and is metabolised primarily in the liver, with a moderate amount excreted in the urine over 48 hours. It also crosses the blood-brain barrier.

Treatment regimens using busulfan

The current allogeneic (sibling and matched unrelated) transplant protocols in clinical use include:

- BUCY – busulfan and cyclophosphamide;
- FBC – fludarabine, busulfan and campath (alemuzumab);
- FB ATG – fludarabine, busulfan and rabbit anti-thymocyte globulin;
- TBI + BUCY – total body irradiation + busulfan and cyclophosphamide.

The current allogeneic (cord) transplant protocol in clinical use is – thiopeta, IV busulfan, fludarabine, and rabbit anti-thymocyte globulin (ATG).

IV busulfan dosage

Dosage should be based on actual body weight. In obese patients dosing should be adjusted to ideal body weight. In renally impaired patients, dose modification is not recommended, as it is only moderately excreted in urine. Busulfan should be used with caution in hepatically impaired patients. In both instances, it is important patients are carefully monitored for any signs of toxicity.

The ideal times to give busulfan are related to the specific regimen the patient is having:

- 0.4mg/kg qds for TBI BUCY 5am, 11am, 5pm and 11pm;
- 0.8mg/kg qds – for BUCY, FBA, FB ATG 5am, 11am, 5pm and 11pm;
- 3.2mg/kg once/day (over three hours) – cord protocol.

If a dose is missed, that is, during four-
BACKGROUND

Busulfan is a potent cytotoxic agent initially indicated as a myeloablative and antileukaemic treatment of chronic myelogenous leukaemia, where it was used as an oral preparation before a BMT. Recently it has been used in conditioning regimens of allogeneic transplants.

Oral administration continued to be used in the transplant setting for many years but clinicians alluded to the need for an IV form to allow precise dosing, and to eliminate problems associated with the oral form, such as veno-occlusive disease.

When the IV form was developed it aimed to address practical and clinical issues associated with emesis, dose assurance, adequate myeloablation and reduction of adverse events (Kashyap et al, 2002).

Preparation and stability

IV busulfan is prepared by the aseptics department within pharmacy and in standard regimens. It will be diluted with 50 or 100ml normal saline (depending on the dose) or 5% glucose. In the cord blood regimen, it will be diluted with 250ml N/saline or 5% glucose. In order to ensure product stability, the volume of the diluent should be 10 times the volume of IV busulfan, ideally making the final concentration 0.5mg/m^2.

Stability after dilution in either glucose 5% or sodium chloride (0.9%) solution for injection has been demonstrated for:

- Eight hours (including infusion time) when stored at 20°C ± 5°C;
- Twelve hours when stored at 2°C–8°C followed by three hours stored at 20°C ± 5°C (including infusion time).

It should be used immediately after dilution to cut microbiological contamination risk. If it is not used immediately, it should be stored in the fridge at 2°C–8°C.

Administration

Busulfan must only be infused centrally (vesicant properties are unknown) and should not be given by bolus or rapid infusion. Practitioners should also not infuse concurrently with any other IV solution.

1. Remove the busulfan bag from the fridge 30 minutes before being administered.
2. Aseptically withdraw 3–5ml from the central line to check line positioning.
3. Flush the line with 10ml N/saline in order to ensure patency.
4. Attach the primed giving set, with N/saline or 5% glucose, depending on diluent.
5. Infuse the entire solution at rate of 50ml/hour (over two hours) or over three hours if following the cord regimen.
6. At completion, flush with 100ml of the same diluent that busulfan has been prepared in.
7. If flushing with 5% glucose, flush the central line with a further 10ml N/saline.

For details on busulfan-associated side-effects and potential drug interactions, see nursingtimes.net.

Laboratory tests required

While a patient is receiving busulfan, certain laboratory tests should be monitored such as:

- Full blood count – daily to check bone marrow function; serum transaminases, alkaline phosphatase and bilirubin – daily until 28 days post-infusion to detect hepatotoxicity, which may herald the onset of hepatic VOD.

Safety

If the solution comes into contact with skin, wash thoroughly in warm water immediately for a minimum of 10 minutes and then seek medical assistance for possible treatment. Complete an adverse incident form.

CONCLUSION

A leaflet for chemotherapy nurses was developed to provide guidance and support on the administration of IV busulfan. The leaflet provides concise, accessible information, in a clear and simple format.

Declarations of interest: The manufacturer of busulfan had no influence over the content of this article apart from providing advice on correct usage of the drug.