Slow Infusion of Vincristine in the Treatment of Refractory Thrombocytopenic Purpura

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Abstract
Eight patients with idiopathic thrombocytopenic purpura (ITP), who were refractory to glucocorticoid therapy, were given slow infusions of vincristine (VCR) over a 4- to 6-hour period at weekly intervals for 4 weeks. Three patients showed a return to normal platelet counts maintained for 3 months or longer. A transient recovery was observed in 1 patient and a partial response was observed in 3 patients. All patients tolerated therapy well, without side effects. In conclusion, therapy with slow infusion of VCR can be effective in refractory ITP.

Introduction
Vinca alkaloids have showed effectivity in the management of refractory idiopathic thrombocytopenic purpura (ITP). The use of vincristine (VCR) as a bolus injection results in a good response in about one third of patients, but this improvement is sometimes transient. Vinblastine-loaded platelets are effective but expensive, require maintenance therapy, and febrile reactions from the use of allogenic platelets are common [1]. After intravenous injection, vinca alkaloids are rapidly cleared from the circulation [2, 3]. Consequently, slow infusions of VCR are been proposed in order to maintain higher plasma concentrations of the drug to enhance uptake by the patient’s own platelets. This article describes the results of therapy in 8 patients with this method of administration.

Materials and Methods
Eight patients with ITP refractory to glucocorticoid therapy were given slow infusions of VCR. None of them had been previously splenectomized. There were 4 men and 4 women with a mean age of 49 years, ranging from 25 to 77 years. Duration of ITP ranged from 2 to 39 months. VCR 1 mg was dissolved in 250 ml of isotonic saline and infused intravenously over 4–6 h. Treatment was repeated at weekly intervals for 4 weeks.
A complete response was defined as a return to normal platelet count. A partial response was defined as an increase in platelet count between \(50 \times 10^9/\text{l}\) and \(140 \times 10^9/\text{l}\). Response was considered sustained when platelet increase was maintained for 3 months or longer, otherwise the response was considered transient.

Results
Responses to slow infusions and clinical details of patients are summarized in table I. Three patients had a prolonged complete response. Three patients had a partial response, which was transient in 2 patients. One patient showed a transient complete response, and another patient had no response. All patients tolerated therapy well, without side effects.

Discussion
In accordance with previous reports by Ahn et al. [4] and Manoharan [5], a considerable rate of response is observed with slow infusions of VCR in refractory ITP. Three of our 8 patients achieved a prolonged complete response. However, in 2 out of 3 patients with prolonged complete response, and 2

<table>
<thead>
<tr>
<th>Table I. Summary of responses to slow infusion of vincristine</th>
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<td>Patient</td>
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with partial response, duration of ITP was less than 6 months, and during this period a spontaneous remission could have occurred. As in the study by Manoharan [5], our patients had not undergone splenectomy, consequently these results confirm that splenectomy is not obligatory in order to obtain a response to vincristine.

Ahn et al. [4] chose an infusion time of 6–8 h and Manoharan [5] gave VCR over a 4-hour period. The infusion time in our study was 4–6 h. It is unknown if the response rate may be increased by prolonging the infusion period. However, periods longer than 6 h are difficult to perform on an ambulatory basis.

In our study, patients received 1 mg of VCR per week, a dose smaller than in previous reports. The positive responses obtained in our patients suggest the effectivity of VCR even in doses as low as 1 mg per week.

This therapy is well tolerated and no side effects have been observed. In Manoharan’s [5] study 2 patients developed VCR neuropathy, however, the VCR doses used were higher than in our study.

In conclusion, therapy with slow infusions of VCR might have a place in the treatment of patients with ITP refractory to steroids, especially when splenectomy is contraindicated.

References