BMC Blood Disorders

Case report

Severe hypomagnesaemia with tetany following ESHAP protocol

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Published: 2 January 2002

BMC Blood Disorders 2002, **2**:1

Received: 1 November 2001
Accepted: 2 January 2002

This article is available from: http://www.biomedcentral.com/1471-2326/2/1

Abstract

Background: One patient with B-cell Non-Hodgkin's Lymphoma developed severe hypomagnesaemia and tetany 15 days after the first course of treatment with ESHAP protocol. This prompted a careful look at the incidence and severity of hypomagnesaemia during treatment with this combination chemotherapy.

Method: This patient and two further patients having the same treatment were monitored for hypomagnesaemia throughout their treatment period.

Result: All three patients developed significant hypomagnesaemia requiring intravenous magnesium infusion in the second and third weeks after treatment though not after every course of chemotherapy.

Conclusions: ESHAP protocol is often associated with significant hypomagnesaemia two to three weeks after treatment. Therefore, serum magnesium level should be monitored throughout the treatment period.

Background

ESHAP protocol [1] is an effective second line treatment for Non-Hodgkin's Lymphoma (NHL). This combination includes etoposide, methyl prednisolone, cytarabine and cisplatin. As cisplatin is known to cause hypomagnesaemia the protocol included daily monitoring of serum magnesium from day 1 to 8 and daily infusion of 10 mmol of magnesium intravenously during the treatment (days 1 to 5) period.

A 56 year old female with low-grade B-cell NHL proved refractory to chlorambucil and CIOP (cyclophosphamide, idarubicin, vincristine and prednisolone) combination and was started on ESHAP protocol. During the first course of treatment her serum magnesium remained within the normal range (750 to 900 µmol/l) and on day 8 the level was 680 µmol/l, slightly below the normal range.

On the day 15 (10 days after completion of treatment) she presented with extreme prostration and tetany involving both hands. Her full blood count, renal function, liver function and serum calcium were normal. Serum magnesium was 313 µmol/l. She was given 10 mmol of magnesium by IV infusion for 3 successive days. After the first infusion all her symptoms disappeared and her serum magnesium level returned to normal after 3 days. However, her serum magnesium level dropped to 460 µmol/l on the day 21 when she required another infusion of magnesium 10 mmol. Thereafter, her serum magnesium level remained within the normal range until the next course of chemotherapy. This episode prompted monitoring of the serum magnesium level of the patients undergoing treatment with ESHAP protocol throughout their treatment period.

Method
Serum magnesium level was assayed twice weekly for three patients who were treated with ESHAP protocol for refractory NHL. Two patients received 4 courses and another patient received 3 courses of ESHAP at 4 weekly intervals (total 11 courses). None of the patients had any renal impairment and were not on any other potentially nephrotoxic drugs. The serum magnesium levels were normal in all three patients prior to each course of chemotherapy.

Result
During these 11 courses of treatment, significant hypomagnesaemia (< 500 μmol/l) was observed after 7 courses, once in the second week and the others in the third week from the starting of the most recent course of chemotherapy. In six of these episodes serum magnesium level fell below 400 μmol/l and on these occasions the patients complained of general weakness, malaise and listlessness. Carpopedal spasm was observed on two occasions in the same patient when serum magnesium level fell to 313 and 271 μmol/l. Each time the serum magnesium level fell below 500 μmol/l, patients were treated with IV infusion of magnesium 10 mmol daily for 3 days which promptly corrected the hypomagnesaemia. On 3 occasions further magnesium infusions were needed at the end of the third week to keep serum magnesium level at a safe level (>500 μmol/l). Following the 4 remaining courses of ESHAP mild hypomagnesaemia was noted in the second and the third weeks after chemotherapy but the serum magnesium level returned to normal in the fourth week without any therapeutic intervention.

Discussion
Hypomagnesaemia is a known complication of cisplatin therapy though it is usually asymptomatic. Hypomagnesaemia often develops in the first 2 weeks after cisplatin therapy when the renal tubular damage is most severe. In these 3 patients hypomagnesaemia developed later than usual probably because of magnesium supplementation during the treatment. However, the degree of hypomagnesaemia was more severe than expected and on two occasions caused carpopedal spasm. On 4 other occasions hypomagnesaemia was associated with non-specific symptoms which responded to magnesium infusion. More serious manifestations of hypomagnesaemia were prevented by magnesium infusion during these episodes. One of these patients, not the one who had tetany, was on long-term oral frusemide therapy for pedal oedema which might have contributed to developing hypomagnesaemia but the other two patients were not on any other drug which might have aggravated the effect of cisplatin.

Conclusion
ESHAP protocol may induce severe and late hypomagnesaemia. Patients receiving ESHAP protocol should have their serum magnesium level monitored twice weekly throughout the course of the treatment as some of these patients would require magnesium supplementation in the second and third weeks after chemotherapy.

Competing interests
None declared

References
1. Velasquez WS, McLaughlin P, Tucker S, Hagemeister FB, Swan F, Rodriguez MA, Romaguera J, Rubenstein E, Cabanillas F: **ESHAP – An effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study,** *J. Clin. Oncol* 1994, **12**:1169-1176