Efficacy of methylcobalamin administered intravenously for chemotherapy-induced peripheral neuropathy (CIPN): A prospective crossover study

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Background
CIPN is a dose-limiting and disabling side effect of oxaliplatin and/or paclitaxel. We prospectively evaluated the efficacy of methylcobalamin intravenously for CIPN.

Methods
Thirty patients with gastrointestinal cancer who were receiving oxaliplatin and/or paclitaxel and had peripheral neuropathy of CTCAE ≥ 2 were enrolled to the trial. Each patient was assessed CIPN on day 3 (T1) and a day before next cycle (T2) of chemotherapy contained oxaliplatin and/or paclitaxel with Chemotherapy-Induced Peripheral Neuropathy Assessment Tool (CIPNAT) for two cycles. Methylcobalamin intramuscularly was for the first cycles and intravenously was for the second cycle in first 15 patients. Injection order was reversed in the latter 15 patients. Mecobalamin 5 mcg/d was given from day 3 to a day before the next cycle. The primary end point was a change of CIPNAT score between T1 and T2.

Eligibility criteria:
• Age 18-75;
• Primary histologically proven gastric or colorectal cancer;
• Receiving chemotherapy of oxaliplatin and/or paclitaxel;
• ECOG 0 to 2;
• Peripheral neuropathy of CTCAE ≥ 2.

Study schema

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<th>Days of CT</th>
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<tbody>
<tr>
<td>First 15</td>
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<td>Latter 15</td>
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CT: chemotherapy; M: intramuscularly; I: intravenously

Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients (N=30)</th>
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<tr>
<td>Median age (years, range)</td>
<td>62 (31-76)</td>
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</tbody>
</table>
| Gender, n(%) | Male 20 (66.7%)
| | Female 10 (33.3%) |
| Primary tumor | Gastric cancer 15 (50%)
| | Colorectal cancer 15 (50%)
| Stage | IB 3 (10%)
| | IIA 1 (3.33%)
| | III 2 (6.67%)
| | IV 24 (80%) |

Conflict of interest:
• No conflicts of interest to this work.

Results
Thirty patients were enrolled and completed the trial. Median age was 62 (range, 31-76), male/female was 20/10. Most primary sites were gastric cancer (n=13), colorectal cancer (n=12). Most regimens were paclitaxel/oxaliplatin/5-FU (n=13), FOLFOXIRI (n=11), FOLFOX (n=3), paclitaxel/5-FU (n=2), nab-paclitaxel (n=1). The cycle of chemotherapy before start methylcobalamin injection was 6 (1-12). The total CIPNAT scores (mean±SD) were 148.90±56.09 for T1, 41.40±37.52 for T2 in the intravenous cycle, 158.90±57.02 for T1, 120.20±56.02 for T2 in the intramuscular cycle. A decline CIPNAT scores (mean±SD) between T1 and T2 was 107.50±42.04 in the intravenous cycle, 38.70±30.33 in the intramuscular cycle (Z=5.715, P<0.001). No significant drug and injection-related side effects were observed in bot groups.

Conclusion
Intravenous methylcobalamin is more effective than intramuscular injection in oxaliplatin and/or paclitaxel induced peripheral neurotoxicity.

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