Coadministration of 5% Glucose Solution and Dexamethasone and Oxaliplatin-Related Vascular Pain Grade: A Case Study

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Agents used in cancer treatment can cause many side effects in patients. Oxaliplatin is a platinum-based cytotoxic agent that is used in the treatment of colorectal cancers, and one of its potential side effects is vascular pain. The current article will discuss the coadministration of dexamethasone and its potential effect on oxaliplatin-related vascular pain.

Oxaliplatin is a platinum-based cytotoxic agent commonly used to treat colorectal cancer (de Gramont et al., 2000). The most commonly reported adverse events related to oxaliplatin are fatigue, nausea, vomiting, diarrhea, and neuropathy (de Gramont et al., 2000). Vascular pain at the site of infusion is a lesser experienced, but significant, side effect. Yoshida et al. (2012) found that the direct addition of dexamethasone (DEX) to oxaliplatin infusion helps control the vascular pain experienced with oxaliplatin administration. Despite following this recommendation, some patients continue to experience vascular pain with oxaliplatin infusion.

Case Report

This case study will discuss two patients who had metastatic colorectal cancer and received oxaliplatin. Both patients reported vascular pain after the administration of oxaliplatin through a peripheral IV catheter placed in the forearm. The patients reported grade 3 vascular pain at the site of infusion, which persisted for five days following infusion. The half-life of oxaliplatin is 14.1 minutes, with disappearance of the drug from the blood vessels about three hours after its administration (Ehrsson, Wallin, & Yachnin, 2002). In the following instances, the oxaliplatin was dissolved in 250 ml of 5% glucose solution and the dose of DEX was 3.3 mg/m². Prior to the onset of any pain, the oxaliplatin was administered with the addition of DEX. DEX was given simultaneously with the oxaliplatin infusion through the same primary IV. Using this method, the patients reported an improvement in their vascular pain (vasculitis) from grade 3 to no pain (grade 1) (see Table 1).

On a subsequent infusion, DEX was added directly to the oxaliplatin. With this method, the pain improved from grade 3 to grade 2 immediately, persisted for several days, and gradually resolved.

The final approach was coadministration of the oxaliplatin and DEX at initiation of infusion. Prior to the onset of any pain, DEX and oxaliplatin were given simultaneously through the same primary IV. The DEX was given in conjunction with the main line using secondary tubing. No vascular pain was experienced with this administration strategy.

Discussion

Vascular pain induced by IV infusion of antineoplastic agents can affect patient ability to complete or continue chemotherapy. A number of methods for preventing antineoplastic agent-associated phlebitis have been reported (Curran, Luce, & Page, 1990); however, none of these are completely effective. Corticosteroids have been suggested to be effective for the prevention of phlebitis (De Cock, Vermeij, & Stijnen, 1984; Kohlhardt, 1994). Tononi et al. (1997) reported that post-treatment with DEX reduced phlebitis caused by vinorelbine. Kohno et al. (2008) suggested that pretreatment with DEX was more effective than post-treatment. Moreover, Jerremalm et al. (2002) reported that the addition of steroids to oxaliplatin is useful in controlling vascular pain.

Oxaliplatin may be given using a peripheral IV, central line (port), or peripherally inserted central catheter (PICC) line. Yoshida et al. (2012) evaluated the effectiveness of DEX for controlling vascular pain caused by the administration of oxaliplatin via the peripheral vein. The study included 47 patients who received XELOX (capecitabine plus oxaliplatin) and bevacizumab for metastatic colorectal cancer. In all the patients, oxaliplatin was administered in combination with
### TABLE 1. Vasculitis by Grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>Effect</th>
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<tbody>
<tr>
<td>1</td>
<td>Asymptomatic; intervention not indicated</td>
</tr>
<tr>
<td>2</td>
<td>Moderate symptoms; medical intervention indicated</td>
</tr>
<tr>
<td>3</td>
<td>Severe symptoms; medical intervention indicated (e.g., steroids)</td>
</tr>
<tr>
<td>4</td>
<td>Life-threatening; evidence of peripheral or visceral ischemia; urgent intervention indicated</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
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DEX via the peripheral vein. In the method of Yoshida et al. (2012), the DEX was in the same IV bag as oxaliplatin. Yoshida et al. (2012) reported that vascular pain developed in 34 patients (72%), and that the direct addition of DEX to oxaliplatin infusion controlled vascular pain caused by the administration of oxaliplatin via the peripheral vein. Despite following this recommendation, some patients continued to experience vascular pain with infusion. Two such patients are discussed in this article. In both, the co-administration of 5% glucose solution and dexamethasone was a useful preventive method for oxaliplatin-induced vascular pain. Yoshida et al. (2012) also reported that the response rate to the chemotherapy combined with the use of DEX indicates that DEX does not exert adverse effects on the therapy.

Many patients have experienced adverse effects such as phlebitis and venous pain that have proved to be related to an unphysiologic low solution pH (Kuwahara, Asanami, Kawauchi, & Kubo, 1999). Oxaliplatin dissolved in a solution of 5% glucose in water had a pH of about 4.8 (Yoshida et al. 2012). Some investigators reported that the addition of steroids to an oxaliplatin drip infusion is useful in controlling vascular pain (Jerremalm et al., 2002; Yoshida et al., 2012). The pH did not exceed 7.4 even when DEX was added to oxaliplatin (Yoshida et al., 2012). Although at pH 7.4, the intermediate only constitutes a minor fraction (maximally 0.7%) of the oxaliplatin concentration, it may rapidly react with essential endogenic compounds resulting in a continuous conversion of oxaliplatin to its monodentate form (Jerremalm et al., 2002). Therefore, most of the oxaliplatin does not appear to be degraded when administered in combination with DEX via the peripheral vein. Dissolving oxaliplatin in a basic solution generally is not recommended because oxaliplatin is unstable under alkaline conditions. In addition, Fokalsrud, Pederson, Murphy, and Beckerman (1968) indicated that neutralizing the pH of the infusion solution to 7.4 significantly reduced the incidence of infusion phlebitis; they concluded that neutralization of the infusion solution was the most significant factor for reducing infusion phlebitis.

In the two cases presented in this article, the patients initially developed vascular pain with infusion of oxaliplatin. When oxaliplatin was administered simultaneously through a peripheral IV in combination with DEX, no vascular pain was detected. Excluding pH, additional causative factors of phlebitis may include osmotic pressure of the solution, size of the vein used, size and material of the catheter, and infusion periods (Kuwahara, Asanami, & Kubo, 1998). Additional studies are needed to determine the efficacy of this method.

### Conclusion

The use of DEX can be helpful in relieving infusion-related vascular pain. This report is the first to describe the co-administration of 5% glucose solution and dexamethasone as a preventive method for oxaliplatin-induced vascular pain. The authors recommend this approach on subsequent administrations if patients experience pain, but not on all administrations. However, given the small sample size, additional investigation is needed. A randomized study is needed to compare the frequency and degree of vascular pain.

### References


