Oxaliplatin and pH

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Oxaliplatin, a platinum-based chemotherapeutic agent, has showed marked efficacy for the treatment of advanced colorectal cancer [1,2]. Chemotherapy for colorectal cancer has advanced remarkably with the introduction of folic acid, fluorouracil, and irinotecan (FOLFIRI); and folic acid, fluorouracil, and oxaliplatin (FOLFOX); therapies, which require a central venous (CV) port. With the recent development of capetabine plus oxaliplatin (XELOX) therapy, capetabine plus irinotecan (XELIRI) therapy and irinotecan plus S-1 (IRIS) therapy involving oral administration of drug preparations, etc., implantation of a CV port can be now avoided. However, vascular pain occasionally requires switching of the drip infusion route during XELOX therapy by the administration of oxaliplatin via the peripheral vein.

Vascular pain and phlebitis induced by intravenous infusion of antineoplastic agents reduces the completion or continuation of chemotherapy. The causative factors of vascular pain and phlebitis include the pH and osmotic pressure of the solution, size of the vein used, size and material of the catheter, and infusion periods [3]. A number of methods for avoiding phlebitis have been reported [4,5]; however, none of them are completely effective. Thus, there is an urgent need to develop new methods to prevent and alleviate phlebitis. 5% glucose in water containing oxaliplatin had a pH of approximately 4.78 [6]. Many patients have experienced adverse effects such as phlebitis and venous pain, which have proved to be related to an unphysiologically low solution pH. Kuwahara et al., [7] reported that phlebitis was less likely when the solution of Plas- amino was neutralized to pH 5.93 when given to rabbits, and was nearly eliminated when the pH was increased further to 6.49 [7]. Thus, the tolerance pH for the peripheral vein is about 6.5, i.e. an infusion solution does not cause phlebitis due to acidity if the pH is not lower than the tolerance pH. Some investigators reported that addition of steroids to oxaliplatin drip infusion is useful in controlling vascular pain [8]. However, the pharmacological use of steroids can make oxaliplatin unstable due to the elevation of pH; further, the effectiveness of oxaliplatin in this therapy is unknown because of lack of published data in this regard. The kinetics of the alkaline hydrolysis of oxaliplatin has been evaluated. Even though, at pH 7.4, the intermediate only constitutes a minor fraction (maximally 0.7%) of the oxaliplatin concentration, it might rapidly react with essential endogenous compounds resulting in a continuous conversion of oxaliplatin to its monodentate form [9].

We recently reported that the effectiveness of dexamethasone (DEX) for controlling vascular pain caused by the administration of oxaliplatin via the peripheral vein during XELOX therapy [6]. Furthermore, we found that co-infusion of DEX to oxaliplatin may be a useful preventive method for oxaliplatin-induced hypersensitivity. However, further studies will be needed to determine the efficacy of this method.

References

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