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Oxaliplatin

Updated: January 20, 2014.

OVERVIEW

Introduction

Oxaliplatin is an intravenously administered platinum containing alkylating agent which is used for the treatment of advanced colorectal cancer. Oxaliplatin therapy is associated with a low rate of transient serum aminotransferase elevations, but is commonly associated with sinusoidal and vascular injury to the liver which can lead to sinusoidal obstruction syndrome and to nodular regenerative hyperplasia with noncirrhotic portal hypertension.

Background

Oxaliplatin (ox al" i pla' tin) is a cisplatin analog with a tetravalent platinum molecule which is referred to as a platinum coordination complex. Oxaliplatin acts as an alkylating agent causing cross linking between and within DNA strands leading to inhibition of DNA, RNA and protein synthesis and the triggering of programmed cell death, mostly in rapidly dividing cells. Oxaliplatin was approved for use in cancer chemotherapy in the United States in 2002. Its current indications are colorectal carcinoma and it is usually administered in combination with other agents such as 5-fluorouracil (5-FU), irinotecan or capecitabine. Oxaliplatin is available in an aqueous solution for injection in 50, 100 and 200 mg vials in generic forms and under the brand name Eloxatin. The platinum based antineoplastic agents have similar toxicities, including nausea and vomiting, diarrhea, bone marrow suppression, as well as neuro-, oto- and nephrotoxicity. They are also mutagenic, teratogenic and carcinogenic, and their use has been associated with an increased risk of secondary leukemias.

Hepatotoxicity

Mild and transient elevations in serum aminotransferase levels are found in an appreciable proportion of patients taking oxaliplatin, but their relationship to oxaliplatin is often unclear. Chemotherapy with oxaliplatin has been associated with histological changes in the liver marked by sinusoidal dilatation, congestion and centrolobular necrosis. These changes are usually not clinically significant during the acute phase, but they can progress to clinically apparent sinuosidal obstruction syndrome or, with chronic therapy, to nodular regenerative hyperplasia with splenomegaly, thrombocytopenia and esophageal varices. Nodular regerative hyperplasia typically requires 6 to 18 months to develop and arises after repeated cycles of chemotherapy with oxaliplatin. Serum enzyme and bilirubin elevations are minimal, the major laboratory finding being a progressive and persistent thrombocytopenia reflecting the development of splenomegaly and portal hypertension. The first clinical evidence of nodular regenerative hyperplasia may be ascites, esophageal variceal hemorrhage or hepatic encephalopathy. Attempts at hepatic resection, severe gastrointestinal bleeding and septicemia may trigger hepatic decompensation and liver failure. Interestingly, nodular regenerative hyperplasia and portal

hypertension tend to improve slowly once chemotherapy is stopped, but the long term consequences of the changes are not well defined.

Mechanism of Injury

The cause of sinusoidal dilatation and central congestion after oxaliplatin therapy is unknown, but probably relates to injury to sinusoidal endothelial lining cells. While described largely after oxaliplatin therapy, similar changes may occur after therapy with the other platinum coordination complexes.

Outcome and Management

The majority of instances of sinusoidal dilatation, vascular injury and congestion found histologically after oxaliplatin therapy occur without significant serum enzyme elevations or clinically apparent liver injury. Rare instances of acute onset of sinusoidal obstruction syndrome with ascites and hepatic failure have been described after oxaliplatin therapy, but usually when given in combination with other antineoplastic agents. Repeated cycles of oxaliplatin and chronic therapy have been linked to nodular regenerative hyperplasia which can be associated with portal hypertension and complications of ascites, variceal hemorrhage and hepatic encephalopathy. There is likely to be cross sensitivity to liver toxicities of the various platinum coordination complexes and continued use or rechallenge after clinically apparent liver injury from oxaliplatin should be avoided.

References to the hepatotoxicity of carboplatin, cisplatin and oxaliplatin are given after the Overview section on Platinum Coordination Complexes.

Drug Class: Antineoplastic Agents, Alkylating Agents, Platinum Coordination Complexes: Carboplatin, Cisplatin

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Oxaliplatin – Generic, Eloxatin®

DRUG CLASS

Antineoplastic Agents, Alkylating Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Oxaliplatin	61825-94-3	C8-H14-N2-O4-Pt