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Oxaliplatin induced-neuropathy in digestive tumors

María Sereno [a,*], Gerardo Gutiérrez-Gutiérrez [b], César Gómez-Raposo [a], Miriam López-Gómez [a], Maria Merino-Salvador [a], Francisco Zambrana Tébar [a], Cristina Rodriguez-Antona [c], Enrique Casado [d]

[a] *Medical Oncologist, Medical Oncology Department, Infanta Sofía University Hospital, San Sebastian de los Reyes, Madrid 28702, Spain*
[b] *Neurologist, Neuromuscular Unit, Neurology Department, Infanta Sofía University Hospital, San Sebastian de los Reyes, Madrid 28702, Spain*
[c] *National Center in Oncology Research, Madrid 28015, Spain*
[d] *Medical Oncologist, Chief of Medical Oncology Department, Infanta Sofía University Hospital, San Sebastian de los Reyes, Madrid 28702, Spain*

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Contents

* Corresponding author at: Pico de la Miel Street, no. 13, chalet 46, San Sebastian de los Reyes, Madrid 28708, Spain. Tel.: +34 649002612.
E-mail address: mariasereno75@gmail.com (M. Sereno).

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Abstract

Oxaliplatin is one of the main drugs used in digestive tumors treatment. Peripheral neuropathy is a well-recognized dose-limiting toxicity of OXL. Two types of neuropathy have been described with this agent: acute or transient and chronic or persistent, with different etiology, clinical manifestations and prognosis.

This paper is an exhaustive review about the main aspects of oxaliplatin induced peripheral neuropathy, focus in clinical features, treatment, prevention strategies and future approach.

Keywords: Oxaliplatin; Peripheral neuropathy; Digestive tumors

1. Introduction

Oxaliplatin (OXL) is a third-generation organoplatinum compound with significant activity against advanced or metastatic digestive tumors, mainly colorectal cancer (CRC) [1]. OXL acts by cross-binding of DNA as well as by blocking DNA synthesis and could be administered with 5-fluorouracil (5-FU) and leucovorin (LV) in a combination regimen, known as FOLFOX4 or FOLFOX 6; with capecitabine (XELOX or CAPOX); with Epirubicine (EOX) or Irinotecan (FOLFOXIRI) [2].

Peripheral neuropathy (PN) is a well-recognized dose-limiting toxicity of OXL and typically induces two clinically distinct forms of PN: acute and chronic [3]. Whereas acute form is not dosis dependent, high cumulative doses of OXL are strongly associated with occurrence of chronic peripheral nerve damage [4].

In this paper, we are going to review the main aspects of oxaliplatin induced peripheral neuropathy (OXLIN), focus in clinical features, treatment and revention strategies.

2. Types of neurotoxicity associated with oxaliplatin

As previously we mentioned, the neurotoxicity seen with oxaliplatin (OXLIN) can manifest as either of two distinct syndromes: a transient, acute syndrome that can appear during or shortly after infusion, and a chronic dose-limiting, cumulative sensory neuropathy.

The acute, transient neurotoxicity observed with oxaliplatin occurs in a high rate of patients on treatment with OXL and it usually happens rapidly during or within hours of infusion. The symptoms are typically induced or aggravated by exposure to cold and clinical manifestations included distal sensory and motor toxicity. The sensory component consists of paresthesias and/or dysesthesias in the distal extremities and/or the perioral region. Some patients (around 1–2%) suffer a transient cold-induced pharyngolaryngeal dysesthesia, causing a feeling of difficulty in breathing. Sometimes, these sensory symptoms are paralleled by motor symptoms including: tetanic spasms, fasiculations, and prolonged muscular contractions [5].

The second type of OXLIN is the chronic neuropathy. It is a dose-limiting, defined as a cumulative sensory neurotoxicity, and it is seen in 10–15% of patients. After cumulative doses of 780–850 mg/m^2. Incidence is very variable and depending on the seria. Symptoms include dysesthesias and paresthesias of the extremities non-cold related similar than happens in cisplatin toxicity. Symptoms generally persist between cycles and increase in intensity with cumulative dose. Sometimes, symptoms may be severe enough to limit patients from performing their activities of daily living [6]. In the majority of cases, these symptoms are reversible recovering from grade 3 neurotoxicity to grade 1 or less within 6–12 months of therapy discontinuation, but in a few group of patients these symptoms remain for longer [7]. In a de Gramont et al. 74% of patients recovered from grade 3 to grade 1 or nonneuropathy in 13 weeks [8].