PERIPHERAL NEUROPATHY INDUCED BY OXALIPLATIN: RISK FACTORS

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Background

• Oxaliplatin is one of the main drugs used in digestive tumors treatment.
• Peripheral neuropathy is a well-recognized dose limiting toxicity of OXL.
• The principal predisposing risk factors are: diabetes, chronic alcoholism, number of cycles (cumulative dose), denutrition (variation of Body Mass Index BMI > 10%), history of gastrointestinal surgery (GI) which is the cause of malabsorption of denutrition such as the vitamin B12, anaemia, kidney failure and concomitant neurotoxic medications (paresthesia frequency <1/10 and > 1/100) such as amiodarone, atorvastatine, etc.

Purpose

• The objective is to analyze these RF and to determine a relationship between the number of RF and the cumulative dose, the average cumulative dose (ACD) of OXL, the correlation among RF and PN development, and to determine the differences of the PN’s length according to the these RF.

Patients and methods

• Retrospective 2 years study (2011-2012), n = 96 patients (43 cases with PN, 53 controls without PN).
• The RF mentioned above were identified from cases-patients’ records.
• To explore the association between RF and incidence/severity of oxaliplatin-induced neuropathy, permutation tests were carried out ($\chi^2$).
• From the chemotherapy software Asclepios® we identified the cumulative dose to the onset of PN for each patient, then a Pearson correlation was realized between the cumulative dose and the number of RF.
• The length of PN was described as the median value and was determined using Kaplan-Meier method.
• SPSS software (version 20.00, Chicago) was used for statistical analysis. A p value of ≤ 0.05 was considered to indicate statistical significance.

Results and Discussion

• The incidence of PN in our sample is 45%.
• The most important RF are:
  1. Antecedents of GI surgery (74%): it’s evident because of adjuvant regimen of OXL (post GI surgery).
  2. Anaemia (65%): it’s a RF widely described in literature; his origins are multiple: tumour, denutrition, GI surgery, and OXL’s toxicity, because after infusion 37% of the dose are irreversible binding to erythrocytes.

The ACD in our sample at the onset of clinical signs is 331 mg/m². According to the Summary of Product Characteristics this ACD at the onset is 850 mg/m². It’s 2.6 times smaller (p<0). It’s inversely proportional to the number of RF ($r = - 0.930$, $< -0.7$: very strong negative relationship) ($p = 0.069$).

• PN development appeared to be positively correlated with GI surgery and the number of chemotherapy cycles.
• Denutrition is significantly non a RF, and other RF are non significant.

• The Kaplan-Meier survival curves showed that the length of neuropathy was significantly longer in patients with anaemia ($p = 0.053$), with number of cures > 6 cycles ($p = 0.006$) and with the presence of GI Surgery ($p = 0.044$) regardless of other RF ($p > 0.05$).

• It has been shown that more the number of RF is higher, the ACD is low. In our simple this ACD is 331 mg/m². According to the literature these RF do not contraindicate the use of oxaliplatin and in practice the reducing or stopping of oxaliplatin is dictated by the clinic of PN.

• A multivariate analysis for RF described before and including the season (winter or other) at the onset of PN, between Cases and Controls will allow to determine the Relative Risk (RR) and Odds Ratio (OR).

Conclusion