Incidence of oxaliplatin hypersensitivity reaction among colorectal cancer patients: A 5-year retrospective study

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Received (first version): 25-Jan-2022  Accepted: 29-Mar-2022  Published online: 31-Mar-2022

Abstract
Background: Oxaliplatin is a third-generation platinum compound that has efficacy against colorectal cancer. Hypersensitivity reactions during oxaliplatin infusion are a key problem during its use, with the varying incidences and deficiencies of clearly identified risk factors. Objective: To determine the incidence, severity and risk factors of oxaliplatin-related hypersensitivity reaction (HSR). Method: This retrospective study investigated 245 colorectal cancer patients (1,690 treatment cycles) receiving care at King Chulalongkorn Memorial Hospital, Thai Red Cross society between January 1, 2015 and December 31, 2019. The patients’ demographic data, laboratory data and clinical features suggesting hypersensitivity reactions to oxaliplatin were reviewed. The Fisher’s Exact test and unpaired t-test were used to determine the differences among patients with and without oxaliplatin HSR. The potential risk factors for oxaliplatin HSR were analyzed for statistical significance by logistic regression. Results: A total of 245 colorectal cancer patients (1,690 treatment cycles) were included in this study. The incidence of oxaliplatin HSR was 37.96%, according to the US National Cancer Institute (NCI)-Common Terminology Criteria for Adverse Events (NTCAE) version 5.0, grade 1, grade 2 and higher grades were 27.35% (67 patients), 6.53% (16 patients) and 4.08% (10 patients), respectively. The proportion of male patients and patients with a history of prior exposure to platinum-based chemotherapy were statistically higher in the HSR group. The eosinophil count and serum creatinine level were also significantly greater in the HSR group. On the contrary, the total lymphocyte count and serum albumin level were significantly lower in the HSR group. The multivariate logistic regression found 5 risk factors with a significant difference. Male gender, prior exposure to platinum-based chemotherapy and elevated eosinophil count were associated with increased risk of oxaliplatin HSR, whereas elevated albumin level were significantly lower in the HSR group. Conclusion: Colorectal cancer patients treated with an oxaliplatin-based regimen with male gender, prior exposure to platinum-based chemotherapy and elevated eosinophil count have a greater risk of oxaliplatin related hypersensitivity reactions.

Keywords: Oxaliplatin; Hypersensitivity reactions; Colorectal cancer; Risk factors

INTRODUCTION
Colorectal cancer (CRC) is the fourth most common cancer and the second leading cause of death due to cancer globally. In Thailand, CRC accounts for 11% of cancer burden, which is the only malignancy with an increased incidence in both sexes. CRC treatment is presently a public health priority and comprised of non-pharmacotherapeutic modalities and pharmacotherapy.

Oxaliplatin is a third-generation platinum compound with a 1,2-diaminocyclohexane carrier ligand, has been approved both for treatment of metastatic colorectal cancer and adjuvant treatment in combination with 5-FU and LV or capecitabine. The National Comprehensive Cancer Network (NCCN) guidelines recommended the FOLFOX or CAPEOX as standard regimens for adjuvant chemotherapy for stage II CRC with high-risk factors and stage III CRC as well as the first-line regimen for metastatic CRC. The modified FOLFOX regimen, comprises of oxaliplatin 85 mg/m² concurrent with LV, 200-400 mg/m² on day 1, followed by a bolus 5-FU, 400 mg/m², on day 1 and a continuous 5-FU, 1,200 mg/m²/day, on day 1 and 2 repeated every 2 weeks for 12 cycles. The CAPEOX regimen consists of oxaliplatin, 130 mg/m² on day 1 and oral capecitabine 1,000 mg/m² twice daily on days 1 to 14 of a 3-week cycle for 8 cycles. The common adverse reactions of oxaliplatin include nausea, vomiting, diarrhea, and peripheral neuropathy. These adverse reactions can be managed by dosage modification or premedication. The serious adverse reactions involve hematologic...
toxicities, presented as neutropenia and thrombocytopenia. Hypersensitivity reaction (HSR) is another serious adverse effect that should be concerned. HSR to oxaliplatin has been less frequently described than cisplatin or carboplatin. At the first use, the incidence of HSR to oxaliplatin was very rare, but after the expanded use of oxaliplatin in clinical practice, we are now encountering a significantly increased incidence of oxaliplatin-HSR. Recent reports have shown that the rate of HSR to oxaliplatin has varied from 8.9% to 23.8%. HSR to oxaliplatin should be of concern, due to its unpredictability, it is potentially life-threatening requiring the subsequent treatment withdrawal. Yu et al. 2021, reported that 85.6% of cancer patients with oxaliplatin-HSR had to interrupt the oxaliplatin course and needed corresponding treatment. Identifying patients with risk of oxaliplatin-HSR is a key clinical issue and several studies have shown supporting risk factors, with various results. Kim BH et al., 2009 retrospectively analyzed patients receiving oxaliplatin and HSR was associated with younger mean age, female gender and with use of oxaliplatin as salvage therapy. Seki K et al., 2011 reported 5 risk factors associated with oxaliplatin-HSR in CRC patients including female, preexisting allergies, lower level of lactate dehydrogenase (LDH), higher neutrophil count and lower monocyte count. Kim MY et al., 2012 reviewed all patients treated with oxaliplatin and HSR correlated with lower dexamethasone doses. Parel M et al., 2014 identified that developing oxaliplatin-HSR increased with women, younger patients and patients with prior exposure to platinum salts. The aforementioned studies were conducted among patients in the United States, France, South Korea, Japan and China which could be different from Thai patients. In this retrospective study, we explored the incidence, severity and risk factors of oxaliplatin-HSR among Thai patients with CRC.

**METHOD**

We conducted a retrospective review of the medical records of colorectal cancer patients treated with oxaliplatin-based regimen at King Chulalongkorn Memorial Hospital, Thai Red Cross society, Thailand between January 1, 2015, and December 31, 2019. This study was approved by the Institutional Review Board (IRB), Faculty of Medicine, Chulalongkorn University (IRB no. 323/61).

All patients received intravenous dexamethasone 8 mg and ondansetron 8 mg as premedication before oxaliplatin infusion. Oxaliplatin-HSR was assessed and classified according to the National Cancer Institute Common Criteria (NCI-CTCAE v5.0) and was noted by attending healthcare staff in the medical records.

**Data collection**

1) Patient characteristics: gender, age, body surface area (BSA), Eastern Cooperative Oncology Group (ECOG) performance status; scale describing a patient’s level of functioning in terms of their ability to care for themselves, daily activity and physical ability, medical conditions and preexisting allergies (allergy to specific food or drug). 2) Cancer and chemotherapy characteristics: type of cancer, purpose of treatment, treatment regimen, oxaliplatin dose administration, prior exposure to platinum-based chemotherapy, the number of cycles administered when the episode occurred and the severity of HSR. 3) Baseline laboratory data were obtained for 1 month before the day of administration of oxaliplatin regimen: serum creatinine, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamate-pyruvate transaminase (SGPT), alkaline phosphatase (ALP), serum albumin, white blood cell (WBC) count, neutrophil count, lymphocyte count, monocyte count and eosinophil count.

In addition, the management, the response to treatment, the mode of prevention used during rechallenging and the final decision (oxaliplatin continuation or withdrawal) were reviewed.

**Data analysis**

Statistical analysis was performed using the SPSS software, version 22 (IBM Corp., Armonk, NY, USA). After collecting the data, we imputed the missing data by using multiple regression. Quantitative data are reported as means and standard deviation and qualitative data are shown as numbers and percentage. Incidence was defined as the number of cases divided by the total number of patients included in the study. The correlations between HSR to oxaliplatin and several background factors were statistically analyzed using Fisher’s exact test or the unpaired t-test. In statistical testing, two-sided p-values ≤ 0.05 were considered statistically significant. The risk factors examined included gender, age, BSA, ECOG performance status, preexisting allergies and pre-exposure to platinum chemotherapy. The results from laboratory test data were also analyzed. To determine risk factors potentially associated with HSR to oxaliplatin, those factors were collected and subjected to univariate and multivariate logistic regression. All variables with p-values < 0.2 were included in the initial multivariate model. Multivariate analysis with backward stepwise elimination was then conducted to develop the final model. The goodness of fit for each stepwise model was compared with Hosmer and Lemeshow test. A p-value of < 0.05 was considered significant.

**RESULTS**

**Patient characteristics**

We retrospectively analyzed the records of 245 colorectal cancer patients (1,690 treatment cycles) who were treated with oxaliplatin-based regimens. The median age was 61 years (range 33-88 years) and 142 (57-96%) were male. Approximately 70% of patients had received capecitabine plus oxaliplatin regimen (CAPEOX). The background characteristics of colorectal cancer patients who had a positive and negative experience of oxaliplatin-HSR and the baseline laboratory data were listed in Table 1.

There were no statistical differences of age, body surface area, dosage regimen, performance status, total infusion course, and history of drug hypersensitivity between the patients without HSR (control group) and with HSR (case group). Compared with women, men had relatively higher susceptibility to HSR
Palapinyo S, Klaewsongkram J, Sriuranpong V, Areepium N. Incidence of oxaliplatin hypersensitivity reaction among colorectal cancer patients: A 5-year retrospective study. Pharmacy Practice 2022 Apr-Jun;20(2):2635. https://doi.org/10.18549/PharmPract.2022.2.2635

(p=0.015). Those patients who had been exposed to platinum compound before this episode of treatment also had higher HSR reports (p=0.009). Baseline biochemical examination of blood showed that the percentage of lymphocytes, eosinophils and serum albumin were statistically different between the 2 groups (p=0.044, 0.012, 0.024 respectively).

### Table 1. Patient characteristics (n=245)

| Parameter                              | Number of patients (%) |   | p-value |
|----------------------------------------|------------------------|---|---------|
|                                        | Patient without HSR (n=152) [Max,Min] | Patient with HSR (n=93) [Max,Min] |       |
| Age (years), mean ± SD                 | 59.34±11.38 [81,33]    | 59.96±11.19 [88,40]    | 0.677  |
| Gender: Male/Female                    | 79 (52.0)/73 (48.0)    | 63 (67.7)/30 (32.3)    | 0.015* |
| Body surface area (m²), mean ± SD     | 1.62±0.19 [2.23,1.12]  | 1.64±0.15 [2.01,1.27]  | 0.370  |
| ECOG Performance Status               |                        |                           |        |
| 0                                      | 1 (0.7)                | 0 (0.00)                  |        |
| 1                                      | 133 (87.5)             | 79 (84.9)                 | 0.574  |
| 2                                      | 18 (11.8)              | 14 (15.1)                 |        |
| Metastasis, yes                        | 88 (57.9)              | 46 (49.5)                 | 0.198  |
| Prior exposure to platinum-based chemotherapy, yes | 18 (11.8)         | 23 (24.7)                 | 0.009* |
| History of drug hypersensitivity, yes  | 13 (5.3)               | 12 (4.9)                  | 0.275  |
| Underlying medical condition, yes      | 97 (63.8)              | 55 (59.1)                 | 0.499  |
| Regimen                                |                        |                           |        |
| CAPEOX                                 | 104 (68.4)             | 66 (71.0)                 |        |
| mFOLFLOX                               | 15 (9.9)               | 16 (17.2)                 | 0.059  |
| FLOX                                   | 33 (21.7)              | 11 (11.8)                 |        |
| Purpose                                |                        |                           |        |
| Adjuvant                               | 81 (53.3)              | 70 (75.3)                 | 0.001* |
| Palliative                             | 71 (46.7)              | 23 (24.7)                 |        |
| Dose (mg), mean ± SD                   | 177.36±45.78 [250,65]  | 183.06±37.51 [250,100]   | 0.290  |
| Dose per body surface area (mg/m²), mean ± SD | 108.71±23.70 [135.80,43.62] | 111.58±21.55 [142.86,55.87] | 0.342 |
| Cumulative dose (mg), mean ± SD        | 1160.53±471.58 [2040,125] | 1234.11±465.85 [2400,180] | 0.235 |
| Total infusion course, median          | 8 [12,1]               | 7 [12,1]                  | 0.844* |
| WBC count (x10³/μL)                    | 6.95±2.26 [14.74,2.19] | 6.78±2.05 [14.07,3.99]   | 0.329  |
| Neutrophil count (cells/mm3)           | 4468.09±1922.92 [12087,1473] | 4414.39±1764.801 [11017,1828] | 0.827 |
| Total lymphocyte count (cell/mm³)      | 1690.83±5914.56 [6222,131] | 1459.30±539.54 [3185,356] | 0.033* |
| Monocyte count (cell/mm³)              | 479.01±192.56 [995.80,37.98] | 444.97±210.39 [1210.02,24.00] | 0.196 |
| Eosinophil count (cell/mm³)            | 142.41±134.24 [716,0]  | 189.45±170.32 [961,0]    | 0.017* |
| Serum albumin (g/dL), n=171             | 3.76±0.46 [4.5,2] n=98  | 3.59±0.54 [5.2] n=73     | 0.024* |
| Alkaline phosphatase (U/L)              | 90.89±94.71 [869,20]   | 96.91±98.82 [573,21]     | 0.635  |
| Serum creatinine (mg/dL)               | 0.78±0.19 [1.3,0.3]    | 0.84±0.28 [2.2,0.5]      | 0.073  |
| - more than 1 mg/dL                    | 14 (9.2)               | 20 (21.5)                 | 0.007* |
| eGFR (ml/min)                          | 83.84±7.22 [199.84,26.22] | 83.23±26.29 [137.67,15.86] | 0.863 |

*p < 0.05, * Mann–Whitney’s U-test
mFOLFLOX: Oxaliplatin plus leucovorin and 5-Fluorouracil every 2 weeks
CAPEOX: Intravenous oxaliplatin 130 mg/m² (day 1) followed by oral capecitabine 1,000 mg/m² twice daily (day 1, evening, to day 15, morning)
WBC white blood cell
FLOX: 5-Fluorouracil plus oxaliplatin on weeks 1,3,5 of 8-week cycle
SGOT: Serum glutamic-oxaloacetic transaminase
SGPT: Serum glutamate-pyruvate transaminase
eGFR: estimated glomerular filtration rate
Incidentes de reacciones de hipersensibilidad a oxaliplato

Durante el seguimiento de 5 años, 93 pacientes experimentaron reacciones de hipersensibilidad a oxaliplato. Según NCI-CTCAE v.5, la incidencia de grado 1 fue del 27.3% (67 pacientes), del 6.5% (16 pacientes) y del 4.1% (10 pacientes), respectivamente. (Tabla 2) La hipersensibilidad a oxaliplato apareció en un promedio de 3 infusiones (1-11). Además, de los 23 pacientes (9.39%) que desarrollaron oxaliplato-HSR en la primera y segunda infusión, 10 (43.48%) habían sido transferidos a agentes platinados antes de esta episodio de tratamiento. Los factores comunes de HSR fueron reacciones cutoanexas como chupeteo, rascado, dolor y pequeña eritema, a menudo en las palmas y plantas. Algunos pacientes presentaron reacciones más severas como cefalea, vómito, diarrea, tos y cambios en la presión arterial. (Tabla 2) Diez pacientes fueron diagnosticados con anafilaxia, con síntomas agudos y severos durante la infusión o comenzaron hasta 30 minutos después de la infusión completa. Diez de estos fueron grado 3 HSR, en el que la infusión de oxaliplato fue inmediatamente suspendida cuando la reacción ocurrió y fue temporalmente interrumpida antes de ser admitido al hospital. (Tabla 3)

| Symptom                | Number of patients (%) |
|------------------------|------------------------|
| Incidence of hypersensitivity | 93 (37.96) |
| Severity               |                        |
| Grade 1                | 67 (27.35)             |
| Grade 2                | 16 (6.53)              |
| Grade 3/4              | 10 (4.08)              |
| Symptom                |                        |
| Cutaneous reactions    | 58 (23.67)             |
| Anaphylaxis            | 11 (4.49)              |
| Digestive symptoms     | 20 (8.16)              |
| Respiratory symptoms   | 17 (6.94)              |
| Blood pressure rising  | 6 (2.45)               |
| Fever/Chill            | 4 (1.63)/6 (2.43)      |
| Palpitation            | 3 (1.22)               |
| Blood pressure lowering| 2 (0.82)               |
| Cycle number at event  | 3 (1-11)               |
| Grade 2, median (range)| 4 (1-11)               |
| Grade 3, median (range)| 2.5 (1-6)              |

Factores de riesgo para reacciones de hipersensibilidad a oxaliplato

Para investigar los posibles factores de riesgo para el desarrollo de oxaliplato-HSR, aplicamos un modelo de regresión logística, en el cual los siguientes factores fueron incluidos: (1) edad, (2) sexo, (3) metástasis, (4) prior platinum exposure, (5) history of drug hypersensitivity, (6) neutrophil count, (7) lymphocyte count, (8) monocyte count, (9) eosinophil count, (10) serum albumin, (11) serum creatinine, (12) oxaliplatin infusion number and (13) total dose of oxaliplatin. A través del análisis univariado, en total 8 factores tuvieron p-values < 0.2 que cumplieron los criterios para inclusión en el análisis multivariado (Tabla 4).

Después del procedimiento de eliminación por pasos hacia atrás, 5 factores finales fueron seleccionados: género, prior platinum exposure, eosinophil count, monocyte count and serum albumin. El cociente de odds ratio (95% Cl) del modelo multivariado se presenta en la Tabla 4. Establecimos que la incidencia de hipersensibilidad a oxaliplato en pacientes con cáncer colorectal tratados con este régimen de base de oxaliplato era:

\[ Y = 3.419 + [0.966 \times \text{Gender}] + [0.818 \times \text{if prior platinum exposure}] + [0.003 \times \text{number of eosinophil count in cells/mm}^3] - [0.002 \times \text{number of monocyte count in cells/mm}^3] - [1.111 \times \text{serum albumin in g/dL}]. \]

DISCUSION

Las reacciones de hipersensibilidad a oxaliplato resultan en la suspendición del tratamiento con la quimioterapia o la reducción del número de opciones terapéuticas. La incidencia de oxaliplato-HSR está aumentando como consecuencia del aumento del uso de oxaliplato en pacientes con cáncer colorectal. La incidencia de oxaliplato-HSR en este estudio fue de 37.96%, relativamente más alta que las tasas descritas en estudios previos (8.9% a 23.8%),12,14,17,22,23 sugiriendo efectos raciales y dosis. El estudio MOSAIC, una gran, fase III trial en países occidentales, mostró que el 10.3% de 1,100 pacientes que recibieron 5-fluourouracil con oxaliplato desarrollaron HSR.21 El informe de pacientes japoneses indicó que el 22.9% de 108 pacientes experimentó hipersensibilidad a oxaliplato.18 Además, la dosis de oxaliplato en el estudio MOSAIC fue 85 mg por metro cuadrado o se redujo a 75 mg por metro cuadrado en el evento de neuropatía periférica,21 pero la media de dosis de oxaliplato en este estudio fue 110 mg por metro cuadrado. Interesantemente, grado 3/4 HSR en este estudio fue similar al estudio previo.21,22,23 En el estudio MOSAIC, el reintroducción de oxaliplato fue realizada después de la prueba de sensibilidad a oxaliplato y 6 pacientes fueron reintroducidos a oxaliplato. El reintroducción de oxaliplato fue realizada después de la prueba de sensibilidad a oxaliplato y 6 pacientes fueron reintroducidos a oxaliplato. El reintroducción de oxaliplato fue realizada después de la prueba de sensibilidad a oxaliplato y 6 pacientes fueron reintroducidos a oxaliplato. El reintroducción de oxaliplato fue realizada después de la prueba de sensibilidad a oxaliplato y 6 pacientes fueron reintroducidos a oxaliplato. El reintroducción de oxaliplato fue realizada después de la prueba de sensibilidad a oxaliplato y 6 pacientes fueron reintroducidos a oxaliplato.
Palapinyo S, Klaewsongkram J, Sriuranpong V, Areepium N. Incidence of oxaliplatin hypersensitivity reaction among colorectal cancer patients: A 5-year retrospective study. Pharmacy Practice 2022 Apr-Jun;20(2):2635.

https://doi.org/10.18549/PharmPract.2022.2.2635

Table 3. Characteristics of the ten patients with grade 3/4 oxaliplatin hypersensitivity

| No., Gender, Age (years) | Prior plt exp | Metastasis | Regimen | Purpose | Dose/BSA (mg/m²) | Cycle # at event | Onset of HSR (minutes) | Total cycle | Treatment | Management |
|--------------------------|---------------|------------|---------|---------|-----------------|-----------------|----------------------|-------------|-----------|------------|
| 1,F,59                   | N             | N          | CAPEOX  | A       | 130             | 5               | 50                   | 5           | 1. CPM 10 mg, Dexamethasone 5 mg IV STAT 2. Hold 30 minutes then slow infusion about 6 hours | Discontinue and adjust to single capecitabine then re-evaluate |
| 2,M,59                   | N             | N          | CAPEOX  | A       | 130             | 2               | 90                   | 6           | 1. Discontinue 2. Hyoscine-N-butyl bromide 20 mg IV STAT and hydration | 1. Add loperamide 2 mg Sig. 2 caps on CMT day 2. Add CPM 10 mg IV pre CMT 3. Rechallenge with prolonged infusion time (4 hours), finally complete total 6 cycles |
| 3,F,60                   | Y             | N          | mFOLFLOX| A       | 85              | 2               | 20                   | 12          | 1. Hold and reduce rate of administration to 80 mL/hr 2. CPM 10 mg, Dexamethasone 5 mg IV STAT 3. Adrenaline 0.3 mg IM | 12 step desensitization protocol, finally complete total 12 cycles |
| 4,F,62                   | Y             | Y          | FLEX    | P       | 80              | 2               | 120                  | 4           | 1. Adrenaline 1 mg IM and hydration | 1. 12 step desensitization protocol with mild HSR through desensitization. 2. Patient requested to discontinue after the 4th cycle |
| 5,M,47                   | N             | N          | mFOLFLOX| A       | 85              | 3               | 110                  | 8           | 1. Discontinue 2. Dexamethasone 10 mg IV STAT 3. Adrenaline 0.5 mg IM | 1. 12 step desensitization protocol, but grade-2 HSR through to the 8th cycle 2. Discontinue after the 8th cycle |
| 6,M,45                   | Y             | N          | CAPEOX  | A       | 100             | 2               | 15                   | 3           | 1. Hold 2. Adrenaline 0.3 mcg IM and hydration 3. Admit and rechallenge oxaliplatin 20-40 mL/hr | 1. Rechallenge with prolonged infusion time (4 hours), grade 2 HSR occurred so discontinue. 2. Skin test: Positive |
| 7,M,47                   | Y             | N          | FLEX    | P       | 85              | 1               | 90                   | 6           | 1. Hold and oxygen therapy 2. Adrenaline 0.5 mg IM and Dexamethasone 10 mg IV 3. Admit and then slow infusion about 4 hours | 1. Skin test: Negative 2. rechallenge (2nd cycle) with prolonged infusion time (6 hours), but mild HSR 2. 12 step desensitization protocol (3rd-6th cycle) |
| 8,M,56                   | N             | N          | mFOLFLOX| A       | 80              | 6               | 80                   | 6           | 1. Hold 2. Symbicort™ (160/4.5) 4 puffs and oxygen therapy 3. CPM 10 mg IV 4. Continue infusion rate 80 mL/hr | Discontinue according to therapeutic plan |
| 9,M,44                   | N             | N          | CAPEOX  | A       | 90              | 6               | 120                  | 6           | 1. Hyoscine-N-butyl bromide 20 mg IV and CPM 10 mg IV STAT | Discontinue according to therapeutic plan |
| 10,F,73                  | Y             | Y          | CAPEOX  | P       | 120             | 3               | 120                  | 3           | 1. Loperamide 2 mg 2 capsules STAT 2. Hydration | Discontinue [Hand foot syndrome grade 3] |

No.=Number  
Prior plt exp= Prior platinum exposure  
Purpose: A=Adjuvant, P=Palliative  
CMT=Chemotherapy  
HSR= Hypersensitivity reaction  
mFOLFLOX: Oxaliplatin plus leucovorin and 5-Fluorouracil every 2 weeks  
CAPEOX: Intravenous oxaliplatin 130 mg/m² (day 1) followed by oral capecitabine 1,000 mg/m² twice daily (day 1, evening to day 15, morning)
al. and Kim et al., studies which suggested that females were at higher risk of oxaliplatin-related HSR,17-19 explained by a possible role of hormonal influences. Several studies have also reported no correlation between gender and HSR.12,28 Our study demonstrated that prior platinum exposure was the independent risk factor that was distinguished from previous studies.

On the other hand, we found that lower monocyte count and serum albumin was significantly associated with the incidence of oxaliplatin-related HSR. Seki et al., also suggested that female, preexisting allergies, lower LDH level, higher neutrophil count and lower monocyte count were associated with the incidence of HSR.18 Serum albumin is commonly utilized as a marker of nutritional status. Malnutrition degrades both the innate and adaptive immune system.29 Low serum albumin level increases vascular permeability and increases interstitial volume, which potentiates immediate HSR.30 However, Nishihara et al., reported that serum albumin level above 4.1 g/dL was the potential risk associated with the incidence of oxaliplatin-related HSR. Oxaliplatin may also act as a hapten: a small molecule which, when combined with a larger carrier such as a protein can elicit the production of antibodies that bind specifically to it, binding to macromolecular carrier proteins, such as albumin.31 A possible reason for the variation of risk factors was the ethnic differences between the participants in this study. Finally, we found that treatment regimen and oxaliplatin dose were not associated with an increased risk of oxaliplatin-related HSR.

Strength and limitations

This retrospective study was conducted to clarify the risk factors for oxaliplatin-related HSR in Southeast Asia and demonstrated the management of severe oxaliplatin-related HSR in the real situation. Limitations of this study include its retrospective design and incomplete clinical data. Some medical records were insufficient, and hypersensitivity symptoms were not actively followed.

Suggestion

Further prospective studies are needed to refine this oxaliplatin-related hypersensitivity prediction model to be more precise and develop the final model as a guide to prevent oxaliplatin-related HSR. Finally, the caregiver team’s vigilance should be improved with males, prior platinum exposure, eosinophil count, monocyte count and serum albumin.

CONCLUSION

Oxaliplatin-related hypersensitivity is a significant potential adverse reaction. The incidence was approximately 38%, with grade 3/4 events in 4% of patients. In this study, males, prior platinum exposure, eosinophil count, monocyte count and serum albumin were the independent risk factors that were associated with the incidence of oxaliplatin-related hypersensitivity.

ACKNOWLEDGEMENT

We would like to acknowledge Stephen Pinder, a native speaking medical English specialist, for conducting a comprehensive English language review of our manuscript.

CONFLICTS OF INTEREST/COMPETING INTERESTS

The authors declare that there are no conflicts of interest.

FUNDING

This research received no specific grant from any funding agency.
Palapinyo S, Klaewsongkram J, Sriuranpong V, Areepium N. Incidence of oxaliplatin hypersensitivity reaction among colorectal cancer patients: A 5-year retrospective study. Pharmacy Practice 2022 Apr-Jun;20(2):2635.

https://doi.org/10.18549/PharmPract.2022.2.2635

AUTHORS’ CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation and data collection were performed by Sirinoot Palapinyo. The data analysis was performed by Sirinoot Palapinyo and Nutthada Areepium. The first draft of the manuscript was written by Sirinoot Palapinyo and all authors commented and edited previous versions of the manuscript.

ETHICS APPROVAL

This study was approved by the Institutional Review Board (IRB), Faculty of Medicine, Chulalongkorn University (IRB no. 323/61).

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www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)
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