ISSN 1695-6141
Revista electrónica trimestral de Enfermería
Nº47
Julio 2017
www.um.es/eglobal/

ORIGINALES

Main complications associated with the administration of intraperitoneal and intravenous chemotherapy in ovarian cancer patients

Principales complicaciones asociadas a la administración de quimioterapia intraperitoneal y endovenosa en pacientes con cáncer de ovario

Mercedes Palmés-Ferrera[1]
Cassandra Ixena Andersson-Vila[2]
Maria del Carmen Barrera-Reyes[1]
Maria del Carmen García-Gigán[1]
María Alba Graells-Piqué[1]
Esther Gómez-Rodríguez[1]

[1]Diploma in Nursing. Institut Clínic de Malalties Hemato-Oncològiques (ICMHO), Hospital Clínic de Barcelona. Spain.
[2]Graduated in Nursing. Institut Clínic de Malalties Hemato-Oncològiques (ICMHO), Hospital Clínic de Barcelona. Spain.

E-mail: mpalmes@clinic.ub.es

http://dx.doi.org/10.6018/eglobal.16.3.260351

Received: 04/06/2016
Accepted: 30/08/2016

ABSTRACT:

Background: Ovarian cancer displays the highest death rates amongst all gynaecologic cancers. Most cases are diagnosed at an advanced stage of the disease and the treatment of choice is generally the combination therapy of intraperitoneal (IP) and intravenous (IV) chemotherapy. While this approach has been shown to prolong survival, multiple associated toxicities have been reported.
Objective: To identify the side effects and complications resulting from IP+IV chemotherapy treatment in stage III and stage IV ovarian cancer patients during the 2007-2015 period.
Methods: A descriptive, longitudinal and retrospective study was performed. A group of 17 women diagnosed with stage III and stage IV ovarian cancer were treated with IP+IV chemotherapy in Hospital Clínic de Barcelona during the period 2007-2015.
Results: Of the 17 patients who were treated with IP+IV chemotherapy, only 5 (29,41%) completed the 6 cycles of treatment. Notably, 12 (70,58%) patients discontinued the treatment due to a series of complications, which were frequently associated with IP reservoir and psychological disorders. The most commonly reported side effects were asthenia, neurotoxicity and abdominal pain.
Conclusions: The majority of patients discontinued their prescribed therapy due to complications associated with IP reservoir and psychological disorders. We believe that the nurse plays a key role, not only in managing the technical aspects of the therapy but also in providing patients with emotional support throughout their journey.

Keywords: Intraperitoneal chemotherapy; nursing care; ovarian cancer; adverse effects; complications; toxicity.

RESUMEN:
Antecedentes: El cáncer de ovario causa más muertes que cualquier otro tipo de cáncer ginecológico. La mayoría de casos se diagnostican en una etapa avanzada de la enfermedad y el tratamiento de elección es generalmente la terapia combinada de quimioterapia intraperitoneal (IP) y endovenosa (EV). A pesar de que esta opción farmacológica ha demostrado alargar la supervivencia, se han reportado múltiples efectos adversos asociados a dicho tratamiento.
Objetivo: Identificar los efectos adversos y las complicaciones derivadas del tratamiento con quimioterapia IP+EV en pacientes con carcinoma de ovario avanzado a partir de estadio IIIC, durante el periodo 2007-2015.
Metodología: Se realizó un estudio descriptivo, longitudinal y retrospectivo. Un grupo de 17 mujeres diagnosticadas con cáncer de ovario a partir de estadio III fueron tratadas con quimioterapia IP+EV en el Hospital Clínic de Barcelona durante el periodo 2007-2015.
Resultados: De las 17 pacientes que recibieron tratamiento con quimioterapia IP+EV, sólo 5 (29,41%) finalizaron los 6 ciclos de tratamiento. De forma notable, 12 (70,58%) pacientes no completaron el tratamiento debido a una serie de complicaciones, que fueron frecuentemente asociadas al reservorio IP y a trastornos psicológicos. Los principales efectos adversos reportados fueron astenia, neurotoxicidad y dolor abdominal.
Conclusiones: La mayoría de pacientes interrumpieron la terapia debido a complicaciones relacionadas con el reservorio IP y trastornos psicológicos. Creemos que la enfermera juega un papel importante, no sólo en el manejo de los aspectos técnicos de la terapia, sino también en el soporte emocional a dichas pacientes durante esta etapa.

Palabras clave: Quimioterapia intraperitoneal; cuidados de enfermería; cáncer de ovario; efectos adversos; complicaciones; toxicidad.

INTRODUCTION

Ovarian cancer is the most common cause of death on women that develops malign gynaecologic tumor[1]. From epidemiologic information of “Sociedad Española de Oncología Médica” (SEOM) in 2012, in Spain it is the fifth most common neoplasm in feminine population with a 3.7% of incidence and a 4.8% of mortality[2].

5-10% of ovarian cancers are inherited as a mutation of genes BRCA1 and BRCA2. As any other malign tumour, the accumulation of genetic disorders are the cause of the uncontrolled growth and proliferation of epithelial cells, unknowing the mechanism that induce such disorders[3].

This neoplasm is the most frequent in postmenopausal woman, with a maximum incidence between the ages of 50-75. More than 75% of the cases are diagnosed in an advanced stage of the illness (stage III-IV)[1,4] worldwide, and this affects in causing peritoneal involvement and an elevated mortality in patients. Mortality increasement is explained by two reasons:

- The absence of initial specific symptoms so the majority of patients present a disseminated disease in the diagnostic moment which is more difficult to cure
- The absence of early detection methods such as screening which are efficient and validated

In these cases Intraperitoneal Chemotherapy (IP) is an appropriate treatment as it allows giving a higher concentration of cytotoxic drug into tumour mass, a drug’s average life higher in comparison with intravenous (IV) administration and the consequent reduction of systemic toxicity [4,5,6,7,8].

Ideal cytoreduction surgery of the tumour (less than 1 cm) constitutes the first line treatment. During this procedure a one-lumen intraperitoneal catheter is introduced and implanted in right or left quadrant of the abdomen, which is tunnelled up to

peritoneal cavity[7]. Afterwards, this catheter is used for IP chemotherapy administration with Cisplatin and Paclitaxel[1].

Several studies show the use of IP chemotherapy increases up to 12 months the survival of patients with ovarian cancer and optimally removed tumour in relation to exclusive IV treatment with chemotherapy[4,6,7,8,9,10,11,12,13,14,15]. Despite that fact, IP chemotherapy causes a higher number of toxicities grades 3 and 4 at all levels and a worse tolerance that ends up to an appreciable number of cases with an interruption of the IP treatment [7].

The first reference of IP chemotherapy appears in the 1950's as a treatment against malign ascitis[16]. Recently several clinical trials, which support the use of this treatment, have been made [13,17,18].

The IP chemotherapy treatment diagram that is being used in Hospital Clínic of Barcelona is divided into 6 cycles. Each cycle consist on administration of Paclitaxel IV 1St day (135mg/m^2) during 3 hours, Cisplatin IP 2nd day (100mg/m^2) and Paclitaxel IP 8th day (60mg/m^2) every 21 days.

IP chemotherapy is administered through a subcutaneous reservoir which we have described beforehand[5]. It is recommended that handling and administration of saline solution through the reservoir must be done by a specialized nurse. During IP chemotherapy and IP administration of saline solution (body temperature)[17] the patient must be absolutely resting in supine and semi-fowler position [5,17,19]. The administration of the treatment will always be by gravity force[19] regardless of the catheter gauge we used to prick subcutaneous reservoir. Once IP administration has finished it is necessary for the patient to carry out postural changes from right to left lateral position every 15 minutes during 1 hour. This way equitant distribution of chemotherapy is done thorough the whole peritoneal cavity [5,19].

OBJECTIVES

Our objectives in this study are:

General:

To identify side effects and main complications resulting from IP chemotherapy treatment in patients that have been diagnosed of advanced ovarian carcinoma from stage IIIC on and that have been treated in Hospital Clínic of Barcelona during the period between 2007-2015.

Specific:

- To identify the reasons of interruption or withdrawal of the treatment with IP chemotherapy
- To know the number of patients that have finished all treatment cycles
- To define nursing care directed towards decrease side effects and complications derivative from treatment

METHODS

It is a descriptive, longitudinal and retrospective study. A group of 17 women diagnosed of stage III-IV ovarian cancer and that have received IP chemotherapy in Hospital Clínic of Barcelona between 2007-2015 have been studied.

Investigation project was submitted to our Hospital Clinic Investigation Ethics Comitee (CEIC) being passed on February 2016. This project does not pose any ethical conflict as no direct intervention has been made. All necessary information was compiled from our hospital data base (SAP) by clinical records written up until now. This is the reason why it is not necessary any informed consent.

Medical and patients' information has been exclusively used as study aim, so have been preserved confidentially as establishes organic law 15/1999 of personal information protection.

Information obtained from patients' clinical records are: age when the diagnosis was made, stage of illness, IP chemotherapy dose that has been administered, reason for treatment stoppage, side effects during and post administration and if any reduction of doses has been made.

Regarding study limitations, as a consequence of the incomplete clinical records, some troubles in key information gathering were detected such as side effects or tolerance during IP chemotherapy administration.

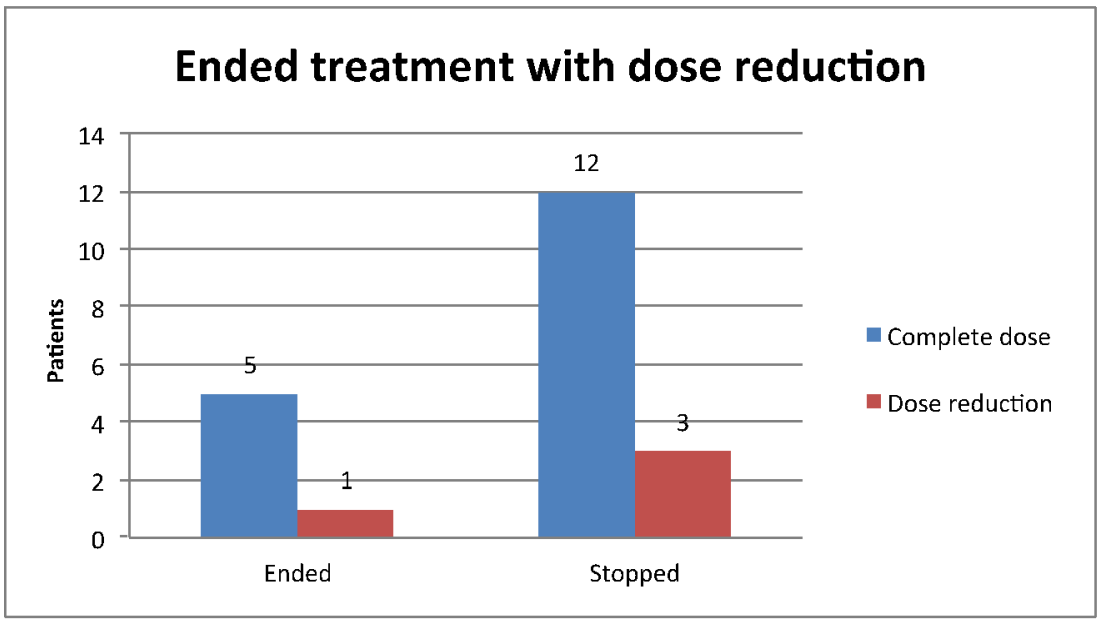
RESULTS

A total of 17 patients with ages between 29 and 66 years old (being the median 50 years old) received IP chemotherapy treatment.

5 patients (29.41%) ended all 6 cycles of the treatment, which consists on IP + IV chemotherapy and 12 patients (70,58%) didn't get to complete them.

From all patients included in this study, 4 of them (23,52%) needed a reduction of IP Cisplatin dose. From this group, 1 patient (25%) completed all cycles and the reminder ones (75%) stopped the treatment; 2 of them because of psychological disorder and 1 for presenting hypomagnesaemia. [Figure 1]. The reason why these 4 patients doses had to be reduced was haematological toxicity in one of them and intestinal toxicity in 3 patients.

Figure 1]



Blue colour shows the number of patients who received IP Cisplatin with no alteration in chemotherapy dose. And red colour shows the number of patients who needed a reduction in IP Cisplatin dose during treatment.

During IP administration, 8 patients (47%) referred abdominal pain or discomfort, which was solved by reducing infusion speed or administering IV analgesic.
Additionally, most frequent side effects post-administration of IP+IV chemotherapy which patients presented were asthenia, neurotoxicity, abdominal pain and diarrhoea [Table I].

Table I.- SIDE EFFECTS

Side effects	**N**	**%**
Asthenia	13	76,47
Neurotoxicity	7	41,17
Abdominal pain	7	41,17
Diarrhoea	6	35,29
Nauseas	5	29,41
Constipation	4	23,52
Anxiety	4	23,52
Haematological Toxicity	4	23,52

omplications that made patients stop IP treatment were most of them associated with IP reservoir and psychological disorder [Table II].

Table II.- CAUSES OF TREATMENT STOPPAGE

Cause of stoppage	N	%
IP reservoir complications	4	33,33%
Psychological disorders	3	25%
Abdominal clinics	2	16,66%
Electrolytic disorders	2	16,66%
Impervious to Cisplatin	1	8,3%

Main cause of stoppage was associated with IP subcutaneous reservoir in contrast to impervious to Cisplatin as the one with less incidence rate.

From all IP chemotherapy programmed doses (N=204; 12 doses per patient) a total of 126 were administered which means 61,76% from the total.

DISCUSSION

The combination of IP and IV chemotherapy increases survival in advanced ovarian cancer diagnosis in comparison with exclusively IV administration[13].

In spite of this clinical advantage, this study highlights the appearance of complications and side effects related with IP+IV chemotherapy that obliged them to stop before reaching the total number of planned cycles.

Comparing this study with modified GOG-172 trial, which uses the same treatment diagram, we observe that the percentage of patients that ended the treatment was 29% in comparison with 42% of GOG-172 trial [8,15,19,20] and 58% from SWOG 8501[8] trial. We must take into account the difference between samples with 17 patients versus 415.

An important limitation in this study is the lack of patients sample treated in only one centre, so multicentre studies would provide statistical significant results.

On the other hand, the number of patients who receive this treatment per year in Hospital Clínic of Barcelona has increased, so there is a possibility to include a higher number of patients in future studies and, as a result, a new evaluation on associated complications.

One of the measures taken to reduce significantly hematologic and intestinal toxicity is changing the dose, especially with IP Cisplatin, which has considerable systemic toxicity[1]. This implies a growth of patients who end the treatment although survival rate can be not that successful.

Most frequent side effect observed in this study is asthenia; which can also be affected by other factors like surgery, pain, sleep disorder, anaemia, gastrointestinal disease and emotional distress. These results agree with the ones obtained in other studies (Herben et al., 1999; Holzner et al., 2002; Holzner et al., 2003; Payne, 2002; Terauchi et al., 2003)[21].

Other detected side effects were neurotoxicity and abdominal pain, which were also described in GOG-172 trial[8].

The main reason to stop the treatment was related to IP reservoir, which agrees with results obtained in Walker et al., 2006 trial and problems detected as partitioning, infection, extravasation and rotation[1,13,22]. We must take into account psychological disorders that 3 of our patients presented and derived in treatment stoppage. This fact denotes the need to improve in technical aspects and emotional support related with professional assistance.

Previous results conclude in the importance to count on oncology-trained nurses and with experience in IP chemotherapy administration. Procedures like needle positioning in IP reservoir applying local external anaesthesia beforehand or placing patient in semi-fowler position on bed[5] to improve breathing during treatment, are essential to improve assistant quality.

Establishment of nursing examination room would be essential to provide support to physical and emotional needs from patients and their families. These consultations should deal with key aspects as information about disease, IP reservoir, type of chemotherapy to administer and its possible toxicities. This way, professional monitoring would decrease emotional impact and anxiety.

CONCLUSIONS

Not all patients who suffer from ovarian carcinoma and receive treatment with IP+IV chemotherapy succeed in ending all cycles, mainly because of complications related to IP reservoir and psychological disorders. A trained nursing team is needed in management of technical aspects and able to educate and inform patients and their families to relieve anxiety and to provide full assistance.

Taking into account the reasons described beforehand, oncologic nurses should consider their procedures in this kind of treatments as they need a decrease in the number of patients who do not end IP chemotherapy cycles.

FUTURE EXPECTATIONS

These results can help to develop future standardized procedure diagram as more knowledge about this therapy is given and patients' care would improve.

REFERENCES

1. Lesnock J, Richard S, Zorn K, Krivak T, Beriwal S, Sukumvanich P et al. Completion of intraperitoneal chemotherapy in advanced ovarian cancer and catheter-related complications. Gynecologic Oncology. 2010;116(3):345-350.
2: Sociedad Española de oncología médica. Las cifras del cáncer 2014 [Internet]. 2014 [cited 25 January 2016]. Available from: http://www.seom.org/seomcms/images/stories/recursos/Las_cifras_del_cancer_2014.pdf
3: Sociedad española de oncología médica. Cáncer de ovario [Internet]. 2015 [cited 25 January 2016]. Available from: http://www.seom.org/en/informacion-sobre-el-cancer/info-tipos-cancer/ginecologico/ovario?showall=1

4. Cristea M, Han E, Salmon L, Morgan R. Review: Practical considerations in ovarian cancer chemotherapy. Therapeutic Advances in Medical Oncology. 2010;2(3):175-187.
5. Drake, B. Intraperitoneal chemotherapy: a reemerging approach in the treatment of ovarian cancer.Journal of infusion nursing. 2009 Nov-Dec;32(6):314-22
6. Zeimet AG, Reimer D, Radl AC, Reinthaller A, Schauer C, Petru E et al. Pros and cons of intraperitoneal chemotherapy in the treatment of epithelial ovarian cancer. Anticancer research. 2009 Jul;29(7):2803-8.
7. Gray H, Shah C, Swensen R, Tamimi H, Goff B. Alternative intraperitoneal chemotherapy regimens for optimally debulked ovarian cancer. Gynecologic Oncology. 2010;116(3):340-344.
8. Trimble E, Thompson S, Christian M, Minasian L. Intraperitoneal Chemotherapy for Women with Epithelial Ovarian Cancer. The Oncologist. 2008;13(4):403-409.
9. Armstrong DK, Fujiwara K, Jelovac D. Intraperitoneal treatment in ovarian cancer: the gynecologic oncology group perspective in 2012. Am Soc Clin Oncol Educ Book. 2012:345-8.
10. Wenzel L, Huang H, Armstrong D, Walker J, Cella D. Health-Related Quality of Life During and After Intraperitoneal Versus Intravenous Chemotherapy for Optimally Debulked Ovarian Cancer: A Gynecologic Oncology Group Study. Journal of Clinical Oncology. 2007;25(4):437-443.
11. Bowles E, Wernli K, Gray H, Bogart A, Delate T, O'Keeffe-Rosetti M et al. Diffusion of Intraperitoneal Chemotherapy in Women with Advanced Ovarian Cancer in Community Settings 2003-2008: The Effect of the NCI Clinical Recommendation. Front Oncol. 2014;4.
12. Hess LM, Alberts DS. The role of intraperitoneal therapy in advanced ovarian cancer. Oncology (Williston Park). 2007 Feb;21(2):227-32.
13. Landrum L, Gold M, Moore K, Myers T, McMeekin D, Walker J. Intraperitoneal chemotherapy for patients with advanced epithelial ovarian cancer: A review of complications and completion rates. Gynecologic Oncology. 2008;108(2):342-347.
14. Pepa C, Tonini G, Pisano C, Di Napoli M, Cecere S, Tambaro R et al. Ovarian cancer standard of care: are there real alternatives?. Chin J Cancer. 2015;34(1):17-27.
15. Blinman P, Gainford C, Donoghoe M, Martyn J, Blomfield P, Grant P et al. Feasibility, acceptability and preferences for intraperitoneal chemotherapy with paclitaxel and cisplatin after optimal debulking surgery for ovarian and related cancers: an ANZGOG study. Journal of Gynecologic Oncology. 2013;24(4):359.
16. Elit L, Oliver TK, Covens A, Kwon J, Fung MF, Hirte HW, Oza AM. Intraperitoneal chemotherapy in the first-line treatment of women with stage III epithelial ovarian cancer: a systematic review with metaanalyses. Cancer. 2007 Feb 15;109(4):692-702.
17. Robinson W, Coberly C, Beyer J, Lewis A, Ballard C. Office-Based Intraperitoneal Chemotherapy for Ovarian Cancer. Journal of Oncology Practice. 2008;4(5):225-228.
18. Jim H, Barata A, Wenham R, Jacobsen P. Fatigue, Mood, and Sleep, During Intraperitoneal Chemotherapy: A Pilot Case Control Study. International Journal of Psychological Research. 2013; 6(1): 8-14.
19. Jaka R, Somashekhar S, Zaveri S, Ahmed Z, Ashwin K. Intraperitoneal Chemotherapy for Epithelial Ovarian Cancer – Single Center Experience. Indian J Surg Oncol. 2012;3(3):262-266.
20. Armstrong DK, Fujiwara K, Jelovac D. Intraperitoneal treatment in ovarian cancer: the gynecologic oncology group perspective in 2012. Am Soc Clin Oncol Educ Book. 2012:345-8.
21. Anderson N, Hacker E. Fatigue in Women Receiving Intraperitoneal Chemotherapy for Ovarian Cancer A Review of Contributing Factors. Clinical Journal of Oncology Nursing. 2008;12(3):445-454.

22. Chua T, Chan, Rao, morris D. Intraperitoneal chemotherapy in ovarian cancer: a review of tolerance and efficacy. Cancer Management and Research. 2012;:413.

ISSN 1695-6141