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NEOADJUVANT CHEMOTHERAPY: A NEW CHALLENGE IN TREATMENT OF OVARIAN CANCER

Sadiqul Alam*[1], Abu Saleh Nizam Uddin Siddik[1], Ranadeep Borgohain[2], Priyakshi Chutia[2], Monami Rajiung[3], Md. Ariful Islam[4]

[1*]Department of Pharmacy, Tripura University (A Central University), Suryamaninagar, Agartala, Tripura (W)-799022, India.
[2]Girjananda Chowdhury Institute of Pharmaceutical Science, Azara, Kmamrup (M) -791017, Assam, India.
[3]NEF College of Pharmaceutical Education and Research, Nagaon-782001, Assam, India.
[4]Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh-786004, Assam, India.

ABSTRACT

From literature survey reveals that ovarian carcinoma (Cancer) is the most lethal gynecologic malignancy in females all over the world. Most of the patients who are suffering from ovarian carcinoma clinical complete remissions are obtained through combinations of cyto-reductive surgery and chemotherapy. From this review given us an overview of the origin of ovarian cancer, history of chemotherapeutic regimens and also focused on chemotherapeutic agents which are useful in the treatment of ovarian cancer. For neoadjuvant chemotherapy taxanes are agent which is used widely. This review article adds better advances in medical field may be based on the better understanding and better choice of drugs regimens and better control of cost in routine practice; which opens the new path for neoadjuvant chemotherapy which proves a better option in ovarian cancer treatment in future.

KEYWORDS

Carcinoma, Neoadjuvant chemotherapy, Drugs regimens, Anti-tumor agent and Treatment.

Author for Correspondence:
Sadiqul Alam,
Department of Pharmacy,
Tripura University (A Central University),
Suryamaninagar, Agartala, Tripura, India.

Email: sadiqul2015du@gmail.com

INTRODUCTON

Cancer is a major public health problem in the United States, India and many other parts of the world. Presently one in four deaths in the United States and in India one in five deaths reported due to cancer. Table: Significantly shows the expected number of deaths from ovarian cancer projected for 2011 in the US[1].

An ovarian cancer is the most lethal gynecologic malignancy in the women. Reason and pathogenesis of epithelial ovarian cancer have long been investigated but still not properly understood. Different studies, have shown that epithelial ovarian cancer is not a single disease but is composed of diverse group of tumors that can be classified based on distinctive morphologic and molecular genetics features. Therapy of ovarian cancer is based on the combination treatment of cytoreductive surgery and combination chemotherapy using taxane and platinum[2,3]. Till now primary cytor-eductive surgery followed by platinum and paclitaxel based chemotherapy is currently standard regimen for advanced ovarian cancer management in recent time[4,5].

Cancer in ovary i.e ovaraian carcinoma is one of the most sensitive and solid tumors to anti -neoplastic chemotherapy, and responses are expected in over 80% of women who receive standard platinum and paclitaxel based treatment[6]. The fact is that; the majority of female with advanced ovarian cancer (Carcinoma) will ultimately, relapse and develop drug-resistant disease later on life. Treatment of epithelial ovarian cancer is based on the combination of surgery and chemotherapy[7,8]. From the last few decades surgical tumor debunking followed by platinum-based chemotherapy is the well-recognized treatment for ovarian cancer patient. Although response rates and complete in disease are greater than 80% and 40-60% respectively. After treatment with paclitaxel and carboplatin most patients free survival up to 18 months[9].

While the focus of this article is systemic or regional chemotherapy, selected patients may benefit from secondary cyto-reductive surgery, in any discussion of second-line ovarian cancer therapy. Physicians and patients can benefit from a shared understanding of basic treatment goals for better healthcare[10].

Presently; patients who progress stable disease during first-line treatment of cancer within one month are considered to be, platinum-refractory". Patients who respond to primary treatment and relapse within 6 months are considered to be, platinum-resistant; and "patients who relapse more than six months after completion of therapy are considered to be „platinum-sensitive"[11].

From the literature review it shows that the longer platinum-free Interval (PFI) increases the chances for a benefit by platinum re-challenge.

This has been reported that for Platinum free interval; longer than 12 months and who are relapsing 6-12 months classified as, partially sensitive"[12].

History of chemotherapy regimens

From the last few decades; experts and researcher, scientists groups have explored different combinations of drugs in order to improve the prognosis of ovarian cancer. In 1976, it was report by two Scientists Witshaw and Kroner on the efficacy of Cisplatin in treatment produced the modern era of combination chemotherapy. In the early 1990, a new turning point in the treatment of ovarian cancer was related to discovery of paclitaxel. With comparison cisplatin/paclitaxel with cisplatin/cyclophosphamide, shown extra benefit when cyclo-phosphamide was replaced by paclitaxel. The carboplatin-paclitaxel combination is now considered as universal regimen in treatment of ovarian cancer[13-15].

An Overview of anti-tumor agents for ovarian cancer treatment

Paclitaxel

Paclitaxel has been established as an important initial component of ovarian cancer chemotherapy[7] and should be considered in the management of patients with recurrence. As a result from different data component of initial platinum-based chemotherapy, paclitaxel is presently administered as either a 3-h (175mg/m2) or 24-h (135mg/m2) intravenous infusion. Phase III randomized trials in patients with recurrent disease have evaluated dose intensity (135 versus 175 and 175 versus 250mg/m2) and infusion duration (3 versus 24 h) without a clear advantage to either higher doses or prolonged infusion[16,17].

Docetaxel

Docetaxel has been examined in several clinical trials for management of platinum-resistant ovarian cancer, with an objective response rate of approximately 20% to 35% being documented in this clinical setting[18-20]. The dose of single component docetaxel in these studies has been

100mg/m2, delivered on an every-three-week schedule. It is not known if a lower dose regimen (e.g., 60 or 80mg/m2) might result in a similar response rate with reduced toxicity. From preliminary data gives idea that some patients with paclitaxel resistance may respond to subsequent therapy with Docetaxel[21].

Tamoxifen

Several clinical trials have been documented that tamoxifen is an active antineoplastic agent in platinum-resistant ovarian cancer, with an objective response rate of approximately 15%[22-25]. The main important advantage of tamoxifen in this clinical setting is the highly favorable toxicity profile for the agent, certainly compared to cyto-toxic cancer chemotherapy. As a outcome, tamoxifen may be considered the "treatment of choice" in several specific circumstances in the second-line setting for patients with ovarian cancer and other cancer treatment also.

Gemcitabine

Gemcitabine agent presently approved by the FDA (Food Drug Administration) for treatment of pancreatic cancer, leukemia and other treatment, has been demonstrated to be an active second-line agent in ovarian cancer. Several phase II clinical trials have revealed a 15% to 20% response rate in this clinical setting[26,27] although minimal activity was apparent when evaluated as front-line therapy in poor prognosis patients with advanced disease[28]. Because of the ability of gemcitabine to inhibit DNA repair, combinations with cisplatin and carboplatin are under development[29-31].

Ifosfamide

Multiple clinical trials have studied/demonstrated Ifosfamide to be an active agent in ovarian cancer patients after initial platinum-based therapy (10%-20% objective response rate)[32-34].

S.No	Estimated New Cases			Estimated Deaths	
	Sites	Total deaths	Female	Total deaths	Female
1	Ovarian Cancer	21990	21990	15460	15460

S.No	Origin of Ovarian carcinoma cancer[3]			
	Theories	Serous	Endometrioid/ Clear	Mucinous/ Brenner
1	Traditional	Mesothelium	Mesothelium	Mesothelium
2	Recent	Fimbria	Endometrial tissue	Tubal-mesothelial junction

S.No	Association of Platinum Sensitivity and PFI[3]				
	Platinum Sensitivity	Resistant		Sensitive	
		Refractory	Resistant	Partial Sensitive	Sensitive
1	PFI	During Chemotherapy	<06 months	06-12 months	>12 months

CONCLUSION

Neoadjuvant chemotherapy of ovarian cancer continues to evolve as new agents with diverse mechanism of action. For chronic nature of recurrent ovarian cancer or tumor, the achievement of stable disease with maintenance of performance status is an acceptable goal for many patients. This review covers better advances in medical field may be based on the better understanding of drugs regimen and better control of cost in routine practice which opens the new paths for neoadjuvant chemotherapy/ cancer treatment which proves a better option in ovarian cancer treatment.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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