

ADVANCES IN ONCOLOGY

Current Developments in the Management of Solid Tumor Malignancies

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The Role of Intraperitoneal Chemotherapy in Ovarian Cancer

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H&O What is intraperitoneal chemotherapy?

MM Intraperitoneal (IP) refers to the administration of a drug directly into the abdominal cavity. This route of administration is used with chemotherapy when the malignancy is largely confined to that region of the cavity.

The advantage of this approach is that it brings higher concentrations of the drug in contact with the tumor, in terms of both the peak concentration and the maintenance of high levels for longer periods of time.

IP chemotherapy is simply a route of drug delivery, and can be explored with a variety of agents, some of which will show greater efficacy compared with intravenous (IV) administration and some of which will not. Some drugs will be associated with increased toxicity when given by IP administration.

H&O Has an advantage been found with IP therapy compared with IV therapy in ovarian cancer?

MM Three randomized clinical trials found that IP cisplatin improved survival among patients with ovarian cancer compared with IV cisplatin. These findings were very important in that they confirmed a principal that had previously been only theoretical. Due to the toxicity of cisplatin, it would also be useful to know if IP carboplatin could be given instead. Because IP cisplatin leads to a longer survival than IV carboplatin, it is best to use the former approach. If IP carboplatin is found to be feasible and effective, the systemic toxicity could be reduced; however, there are no data on the use of IP carboplatin.

H&O Has an optimal regimen for the treatment of ovarian cancer been determined?

MM No, we do not yet know what might be the optimal treatment regimen. It may be that a different drug given via the IP route would be more effectively delivered regionally rather than systemically. Perhaps the treatment should be given both regionally and systemically, as was done with paclitaxel in one clinical trial. These questions need to be explored in the clinical trial setting.

H&O What are the challenges in terms of advancing treatment options?

MM As mentioned above, one of the main challenges is the systemic toxicity associated with cisplatin. Also, there is a learning curve for individuals who have not had experience handling catheters. The technical aspects of catheters need to be explored: what is the optimal catheter? What is the best way to insert a catheter, and when should it be inserted? Which catheters are most commonly associated with infection or occlusion? Clinicians are just beginning to ask these questions, and so there are many theories but not much data available right now.

H&O Could you describe how these questions are being studied?

MM Investigators are conducting retrospective analyses of published data. Looking at patients who had problems with catheters, it is possible to determine what might be the most appropriate method for their use. In addition, prospective data are being gathered, although not neces-

sarily in a randomized fashion, regarding the complication rates associated with different types of catheters, and whether patients improve when a different type of catheter is then used. Groups at Memorial Sloan-Kettering Cancer Center and other institutions are able to review their experience with catheters over perhaps two decades in order to determine the optimal approach.

The Gynecologic Oncology Group will be starting a randomized phase II IP study to evaluate several different drugs and therapeutic approaches for the treatment of ovarian cancer, in order to determine if any particular option improves the percentage of patients who are able to continue therapy through more than five treatment cycles.

Although it may take more time to improve the efficacy of treatment, because this requires a randomized trial, an improved toxicity profile could result from modest changes in the selection of drugs used, the dosages, the catheter, and other factors. These aspects do not require a randomized trial, but rather experience and training.

H&O Is therapy administered for six or more cycles advantageous for patients with ovarian cancer?

MM It has not been clearly determined whether it is necessary to administer six cycles of therapy in order to obtain the optimal outcome. In the most recent study, 40% of the patients who were receiving IP therapy were treated for six cycles, versus 80% of the patients receiving standard IV therapy; yet, a survival advantage was observed with the IP treatment arm. There are two ways to look at this finding. On the one hand, perhaps if more patients on the IP treatment arm had received all six cycles, the survival advantage would have been even greater. But on the other hand, patients may not need six cycles in order to achieve the optimal outcome with IP therapy, at least when a platinum agent is used.

It may be that the best way to treat patients with ovarian cancer is to administer one or two cycles of IV therapy followed by three or four cycles of IP therapy. Beginning with IV therapy following surgery may give the patient more time to recover, with less of the discomfort associated with abdominal distension.

H&O Which ovarian cancer patients are candidates for IP chemotherapy?

MM Studies have held varying criteria. In one trial, eligible patients were required to have tumor nodules of no greater than 2 cm. Other studies allowed a maximum tumor nodule of 1 cm. All of these studies showed a survival advantage with IP chemotherapy.

Although there may not be an exact maximum nodule size, the ideal candidate for IP chemotherapy should have small-volume disease; an individual with massive intra-abdominal disease would not be an appropriate candidate for this approach. If the mass is relatively small, there will likely be good local uptake.

However, it may be possible to treat patients with larger volume disease by the combination IV/IP method described above. Using the IV route for the first one or two cycles may lead to tumor shrinkage. Following initial IV therapy with IP therapy will then accentuate the positive effects by bringing higher drug concentrations into the tumor.

We are still learning the optimal way to utilize IP therapy—the best drugs, the best combinations, and the best techniques for delivery.

H&O Is the IP route being explored with novel agents?

MM Yes, there are studies exploring IP administration of biologic agents such as monoclonal antibodies. There is considerable interest in the potential benefit of delivering antiangiogenic agents via the IP route, or giving these agents simultaneously with IP chemotherapy. Antiangiogenic agents work by decreasing interstitial edema in the area surrounding the tumor, thereby allowing increased blood flow. Decreasing interstitial pressure may enable the drug to penetrate more deeply into the tissue locally. This theory has not yet been studied in a clinical setting but is a potentially exciting approach. Combining an antiangiogenic agent with IP platinum or paclitaxel would be a very novel way of using the IP route in order to obtain the optimal benefit of an antiangiogenic agent.

Suggested Reading

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