INTRAPERITONEAL THERAPY FOR BRITISH COLUMBIA

1. BACKGROUND

Multiple studies have shown that regimens including intraperitoneal chemotherapy are superior with regard to progression-free survival and overall survival in women with stage III, residual less than 1 cm epithelial ovarian cancer in the short and medium term compared to the standard 6 cycles of IV chemotherapy (1-7). The long-term disease free survival rate at 8 years is, however, unchanged (2).

Based upon this, it would appear that we should be mandating IP therapy as the standard therapy. However, there are several counter-arguments to this. Essentially these are: (1) the worsened toxicity/quality of life and (2) the unresolved issue of the effect of the increased total dose of chemotherapy in the IP arms. The later paclitaxel containing studies were flawed in that more total dose was given in the IP arms and total dose, unlike dose intensity, may matter in non-curable ovarian cancer (8-14). However, in favour of a direct clinical benefit of the IP route, three of the studies from the pre-paclitaxel era only varied the route of the chemotherapy and not the total dose, with positive results in two of the studies (3-5). As such, until more conclusive data become available IP therapy should be an option, not mandatory.

Given the evidence that IV platinum-taxane regimens are superior to platinum-cyclophosphamide, then we must utilize a taxane containing IP regimen. Thus there is a choice of two: GOG 114 or GOG 172 (1,2). The efficacy is the same: median PFS 28 and 24 months and OS 63 and 67 months respectively. Toxicity is a concern with both of these. Myelosuppression is common to both with grade 4 leukopenia in 28% and 31% respectively (versus 14% in the IV arms). Grade 3 or 4 thrombocytopenia occurred in 49% of women in GOG 114 (secondary to the two initial high dose IV carboplatin cycles) and because of this 18% of women could not receive more than two IP courses. As such, GOG is utilizing the regimen from GOG 172, albeit modified, as their preferred regimen for ongoing use/study. GOG 172 as carried out was significantly toxic. Quality of life was significantly worse during and just after completion of the regimen with resolution by the one year point (1). Due to toxic effects 48% received 3 or fewer cycles of IP therapy. 42% (86/206) switched to IV therapy: 34 secondary to toxicity – 13 GI problems, 8 metabolic and 13 non-characterized and 52 secondary to catheter problems (22 infected ports, 11 blocked catheters, 14 leaking catheters, 5 access problems) (15).

The catheter problems can be addressed by using the correct style and size of catheter (9.5 French silicone single lumen venous access port) correctly implanted

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and tunnelled. The chemotherapy related side effects can be reduced by modifications of the GOG 172 regimen. There is no international consensus as to what to modify but the options essentially involve one or more of the following (1) reduce IP cisplatin to 75 mg/m^2 (2). Substitute carboplatin for cisplatin and (3) drop the day 8 IP paclitaxel.

The BCCA approach is to utilize a modified GOG 172 protocol. This keeps us in line with the international community and more specifically Canadian practice. By comparing the different variants of GOG 172 utilized, a common standard may be identified prior to definitive evidence from well conducted phase III comparisons in which only route, not dose is altered. The first step is to replace the cisplatin with carboplatin. Metabolic and renal toxicity will be significantly less as has been shown with IV regimens (16). There are concerns of potential lesser efficacy. The review by Fujiwara counters these concerns effectively (essentially there was carboplatin under-dosing) and presents evidence for similarly efficacy providing sufficient carboplatin is utilized, AUC ≥ 6 (17). The day 8 IP paclitaxel will be included (to drop the d8 paclitaxel could negate the improved efficacy seen with the total GOG 172 package). If undue peritoneal toxicity still occurs the next step will be to stop the IP paclitaxel. A rate of 30% significant peritoneal toxicity in the first 10 patients will lead to this modification.

2. WHOM

Newly diagnosed women with stage III, less than or equal to 1 cm residual either post primary debulking (6 cycles) or after interval debulking (3 cycles).

Not
- relapsed
- 1 cm residual
- stage I or II or IV

3. CHEMOTHERAPY REGIMEN q3w x6 if upfront debulking; to complete 6 cycles total (IV + IP) if delayed debulking.

		Route	d1	d8
Carboplatin*	AUC = 6	IP	x	
Paclitaxel	175 mg/m^2 x 3h	IV	x	
Paclitaxel	60 mg/m^2	IP		x

* nuclear renogram; paclitaxel before carboplatin

(a) Antiemetics

NB: Systemic levels following ip administration are equivalent to IV. Therefore the same antiemetic regimen is recommended:

Day 1: ondansetron 8 mg po 15-30 mins prior to carboplatin
decadron 4 mg po q12h x 4 doses starting evening of chemo day

Day 8: Prochlorperazine 10 mg po prn

(b) Fluids

- Intraperitoneal Route: Infuse as rapidly as possible.

  Day 1: carboplatin: carbo in 1L dianeal followed by 1L N/S

  Day 8: paclitaxel: paclitaxel in 1L dianeal followed by 1L N/S

- Intravenous Route

  Day 1: paclitaxel: Paclitaxel in 250-500 ml normal saline (non PVC bag) over 3 hours

NB: No pre or post hydration required

(c) Premedications Pre-Paclitaxel (IP or IV)

45 min pre	Dexamethasone 20 mg IV in 50 ml N/S over 15 min
30 min pre	diphenhydramine 50 mg IV and ranitidine 50 mg in 50 ml N/S over 20 mins

(d) Dosage Modification

1. Treatment day Plts < 100 or neutros < 1.5: delay 1 week

2. Nadir

	Carboplat	IP Paclitax	IV Paclitax
Plts < 50 + neutros > 0.5	90%	100%	100%
Plts < 50 + neutros < 0.5	90%	100%	-20 mg/m^2
Plts > 50 + neutros < 0.5 + infection	90%	100%	-20 mg/m^2
Plts > 50 + neutros < 0.5 + no infection	———	100%	———

4. Other

Bacterial peritonitis: remove ip device, switch to IV

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* G3 abdo pain: remove ip device, switch to IV

non-working ip device: remove ip device, switch to IV

* necessitates narcotics or hospital admission.

5. SURGERY AND CATHETER DETAILS

Preoperatively discussion with suspected ovarian cancer should include the possibility of Portacath placement and postoperative IP chemotherapy. All patients with clearly advanced stage disease, ie. Presence of Ascites and upper abdominal disease either clinically or radiologically, and those with pelvic masses suspicious for malignancy, but without definitive preoperative evidence of metastatic disease, should be offered the opportunity for IP therapy, if optimal debulking is achieved (<1cm residual in any one location). Possible Intraperitoneal Portacath Placement should be included on the OR consent form and the OR slate. This discussion clearly, initially, is going to necessitate delivery of chemotherapy by the Vancouver group. This may expand outside VCC, later, once local experience is gained.

The catheter should be ideally placed with the Port over the Right lower rib cage, in the mid clavicular line, for ease of Huber needle placement at subsequent chemotherapy. The catheter itself is tunnelled for 10 cm subcutaneously before penetrating into the peritoneal cavity, where a further 10cm of catheter is placed. Excess catheter is cut off and discarded. If patient body habitus would necessitate an alternative Port placement this may be done, eg Left MCL over lower ribs, or Right or Left lower quadrants (ensure a firm background to aid in postoperative Huber needle insertion).

If a bowel resection is performed Portacath should be placed to avoid having the catheter tip near the anastomotic site, and IV chemotherapy ONLY given for the first cycle. Assuming good postoperative recovery IP chemotherapy may be instituted for second and subsequent cycles.

After completion of chemotherapy, or if complications, as documented above, the Portocath should be removed. This may be done under local anaesthesia.

6. NURSING PROCEDURE FOR IP CHEMOTHERAPY:

Only authorized RNs on identified units who have been successfully accredited to give chemotherapy may administer drugs via this route. (cf BCCA Systemic Program Policies: C252 - chemotherapeutic agents, administration of)

Equipment:

19 gauge Huber Point needle
sterile gloves, 10 ml syringe, 10 ml normal saline
gauze, hypofix and tape
continue flo IV tubing 10 gtts/ml
1000 ml normal saline
chemotherapy
chlorhexidine swab stick

Procedure: DO NOT USE infusion pumps – can cause needle dislocation.

1. Explain the procedure to the patient.
2. Not necessary to warm the ip solutions.
3. Prepare a Luer Lock 10 qtts/ml I.V. administration set with a 500 ml of normal saline using aseptic technique.
4. Cleanse the port area with chlorhexidine and access the indwelling port as per "Venous Implanted Vascular Access Device". Please note once the needle has been inserted into the port, do not aspirate back. Attach Luer Lock tubing to extension tube of Huber point needle. Secure needle in port with gauze and hypofix dressing. Attach Y port.
5. Place patient in semi-fowler's position in preparation for infusion. To verify correct placement of the needle in the port, open the clamp of the administration set and rapidly infuse 200 ml of N/S under gravity while observing for local erythema, edema, leakage of fluid or pain, dyspnea. Stop infusion and notify MD if any of these occur.
6. Once the needle placement has been confirmed, administer chemotherapy according to doctor's orders as rapidly as possible (30 mins to 2 hours is usual range of times).
7. Once the chemotherapy has been infused, flush the catheter with 50 ml of N/S. Clamp chemotherapy tube and infusing remaining N/S as quickly as possible.
8. Position patient in supine position for de-access. Clamp the IV administration set and the extension tubing of the Huber point needle.
9. Obtain a 5 x 5 cm gauze, band aid and sharps container. Put on clean gloves.
10. Disconnect the IV administration set from the extension tube. Remove the dressing to expose the Huber point needle.
11. With your non-dominant hand stabilize the indwelling port by applying a gentle downward pressure around the port. With your dominant hand, remove the Huber point needle using a straight upward motion.
12. Dispose of the needle and extension tube in the sharps container.
13. Place the 5 x 5 cm gauze over the port to absorb any fluid leakage that may have occurred with the removal of the needle.
14. Remove the gauze and apply a band-aid over previous insertion site.

15. Assist the patient to change position every 15 minute in the sequence listed below, for a total of 1 hour.
    a. head up (30^0)
    b. slight trendelenburg
    c. right lateral
    d. left lateral
16. At completion of 1 hour position change, instruct the patient to assume a position of comfort. Laying flat is recommended, however lying with the head slightly elevated may be more comfortable. Out patients will be ambulated and discharged as per doctors orders.
17. Assess the patient's tolerance to the IP chemo; treat and document side effects accordingly.
18. Monitor intake/output and VS as per chemotherapy protocol and document accordingly.
19. Document in appropriate patient records.

Potential Complications:

It is important for the nurse to differentiate between the usual patient responses and the unusual patient reactions that should be reported to the physician.
Common symptoms not requiring a call to the doctor include:

- mild abdominal discomfort
- mild to moderate abdominal distention
- mild diarrhea
- slight shortness of breath
- mild chills (not to the point of shivering)

Symptoms requiring a doctor's attention include:

- symptom of allergic reaction
- moderate to severe abdominal pain
- moderate to severe shortness of breath
- moderate to severe abdominal distention
- fever
- chills to the point of shivering

The doctor should also be notified if a gross discrepancy in intake and output balance occurs and/or if the catheter does not infuse in spite of interventions carried out by the RN.

Nursing interventions for a suspected block catheter included:

Checking the tubing for kinks
Checking proper placement of the needle in the port
Having the patient change position
Injecting 10 ml of N/S via injection site closest to patient – (clamp above the injection site)

SUMMARY OF POTENTIAL COMPLICATION AND INTERVENTIONS OF IP CHEMOTHERAPY

PROBLEM	CAUSED BY	CLINICAL MANIFESTATIONS	INTERVENTIONS/ PREVENTION MANAGEMENT
Abdominal distention or bloating/increase in abdominal pressure. *Most common complaint*	• Large volume of fluid being instilled into the peritoneum (worse in woman of small stature or who have many adhesions)	• Pain during the infusion • Urinary frequency • Usually last 24-48 hrs	• Analgesia as ordered • Offer small, frequent meals • Raise head of bed to 30^0
Abdominal pain	• Loculation of intraperitoneal fluid	• The chemotherapy infusion slows down	• Analgesia as ordered • Encourage patient to change position in bed to help distribute the fluid
Nausea and vomiting	• Shift in fluid and electrolyte balance • Drug side effects	• Nausea and vomiting just after drugs are instilled • Lasts several hours after treatment	• Monitor intake and output • Monitor blood electrolytes and treat as necessary • Offer antiemetics • Frequent small meals • Promote good oral hygiene • Ensure adequate hydration
Respiratory distress	• Sudden rise in intra-abdominal pressure which restricts the diaphragmatic movement	• S.O.B. (severe) • Dyspnea (severe)	• During IP infusion raise the head of bed 30^0 **Severe S.O.B. Develops:** • Stop chemotherapy • Page M.D. STAT • Administer oxygen by mask at 35%, 10 LPM • Raise head of bed to 45^0 • Remain with patient and offer reassurance
Chills	• IP solution is cooler than body temperature	• Uncomfortable cold feeling • Shivering	• Warm IP solution in basin of warm water prior to infusing • Offer extra blankets • Offer hot drinks

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PROBLEM	CAUSED BY	CLINICAL MANIFESTATIONS	INTERVENTIONS/ PREVENTION MANAGEMENT
Catheter Migration	• Improper initial surgical placement of implanted port	• Excruciating pain	• Notify MD immediately • Stop infusion • X-ray to locate catheter • Remain with
Diarrhea	• Increase in abdominal pressure • Drug side effect	• Frequent, loose watery bowel movements • Abdominal cramps • Generalized malaise • Electrolyte imbalance	• Encourage po intake of fluids • Antidiarrheal agents as prescribed • Monitor electrolytes and replace as ordered
Hypomagnesemia	• Severe proximal tubular dysfunction • Side effect of IP cisplatin	• Weakness • Tremor • Muscle twitching • Paresthesias • Ventricular arrhythmias • Refractory hypocalcemia and hypokalemia • Mental status changes	• Monitor electrolytes and replace as necessary • After chemotherapy completed give IV fluids containing magnesium and potassium as ordered.
Unable to infuse properly	• Misplaced huber needle • Kinked catheter • Fibrin sheath		• Check patency of tubing • Check position of huber needle • Change patient position if still problems: contact MD
Peritonitis (will likely occur between treatments)		• Pain/tender • Distention • Rebound • N+V • Chills • Decreased/absent bowel sounds	• Call MD stat

6. Patient Teaching

The patient teaching required for IP chemotherapy administration is similar to what is required for patients receiving IV chemotherapy.

As with IV chemotherapy, the focus of your teaching should be on the drugs that will be used, the side effects of these drugs, and the steps the patient should take to manage these side effects. Since the side effects of the drugs are similar whether they are given IV or IP, you may use the drug information sheets already available for our IV chemotherapy patients.

The other aspect of patient teaching which should be addressed, concerns the side effects associated with giving drugs intraperitoneally. For the most part, these side effects call for interventions, prevention and management on the part of the caregiver (nurse). Many of these side effects are described in this information package and a general overview should be explained to the patient so that she will be aware of what to expect. For example, when the patient is receiving IP chemotherapy the patient will experience a distended abdomen. It is common for patients to experience bloating and a feeling of fullness, etc.

Education upon Discharge

Ensure patients have written information regarding their chemotherapy drug and side effects related to intraperitoneal administration.

The patient should be instructed to notify their doctor or nurse if they develop any of the following symptoms at home following treatment:

- any unusual abdominal pain
- expanding waistline between treatments, chills or fever greater than 38.5^0C or 101^0F
- shortness of breath
- nausea and/or vomiting greater than 3 days
- diarrhea or constipation greater than 3 days

SOME QUESTIONS YOU MAY HAVE REGARDING INTRAPERITONEAL (IP) CHEMOTHERAPY

1. What is intraperitoneal chemotherapy?

Intraperitoneal chemotherapy is the delivery of cancer fighting medication directly into your abdomen through a small tube called an "implanted port".

2. Why am I getting my chemo this way?

This is a way of directly delivering the chemotherapy to the cancer cells in your abdomen. Also, we can give you a higher dose of chemotherapy by this route as compared to intravenously and in some cases, the side effects will be less severe.

3. Who will administer it to me?

Your IP chemotherapy will be given by a specially educated registered nurse.

4. Where do I go to get the treatment?

You may receive your IP chemotherapy in the hospital as an inpatient or as outpatient.

5. How is the treatment given?

The chemotherapy is delivered into your abdominal cavity with a special catheter. The drug will be mixed in about two litres of solution, enough to bathe all the surfaces in your abdomen. It will take several hours for all the fluid to be delivered. You will start to feel full, and you will see your abdomen swell as the fluid is being delivered. The swelling will gradually disappear over a period of several days as your body slowly absorbs the fluid.

You will also have an intravenous in your arm so we can give you other medication such as anti-nausea drugs. You will have to remain in bed during the treatment to prevent dislodging the needle through which the chemo is delivered.

6. What are the possible side effects of IP chemotherapy?

Some of the side effects IP

Potential Side Effects

Abdominal distention

Feeling of Fullness and Bloating

This is a common side effect because of the large volume of fluid being infused into your abdomen. You may feel uncomfortable and have to urinate frequently.

Pain medication will be ordered for you, should you feel this discomfort.

Shortness of Breath

Some patients experience shortness of breath, due to the amount of fluid being delivered. It will help to elevate the head of your bed. If the shortness of breath becomes severe or if you are having difficulty breathing we will stop the infusion immediately.

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	chemotherapy are listed below. You may experience some, but not necessarily all of these side effects. Furthermore, every individual experiences these side effects in different degree, therefore your own experience will be unique to you.	**<u>Decrease Appetite</u>** Some patients experience a decrease in appetite. It may be helpful to eat smaller meals more frequently after treatment when you are waiting for the "swelling" of your abdomen to go down. **8. Other Possible Side Effects?** You should call the clinic or your doctor if you develop any of the following symptoms at home following treatment: • any unusual abdominal pain • expending waistline between treatments, chills, or fever greater than 38.5^0C or 101^0F • shortness of breath • nausea and/or vomiting greater than 3 days • diarrhea or constipation greater than 3 days

IP CHEMOTHERAPY AUTHORIZATION CRITERIA CHECKLIST

NAME: _____ **DATE:** _____

	Satisfactory	Needs Improvement
A. <u>Prepares Equipment & Patient</u> (Describe) • Ensure orders are processed • Explain procedure to patient and provide written material • Prepare appropriate IV administration set with 500 ml of normal saline		
B. <u>Access Implanted Port</u> (Describe& Demonstrate) • Warm chemotherapy for 30 minutes (optional) • Access port using aseptic technique and appropriate needle • Attach administration set to needle access		
C. <u>Prior to Chemotherapy</u> (Describe) • Position patient, elevate HOB 35^0 • Verify correct placement of port needle by rapidly infusing 200 ml • Observe for erythema, edema, pain, and leakage of fluid		
D. <u>Infuse Chemotherapy</u> (Describe) • Check order to drug • Check patients arm band prior to infusing drug • Hang chemotherapy according to hospital policy and procedures • Infuse chemotherapy as ordered		
E. <u>Post Chemotherapy</u> (Describe & Demonstrate) • Flush the implanted port with 50 ml normal saline • Clamp tubing • Wearing clean gloves disconnect the tubing from the extension tube – discard tubing in appropriate chemo waste • Secure port with non-dominant hand and remove needle. Dispose of needle in chemo sharps container • Provide appropriate care to site – (pressure with		

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gauze and then band-aid)		
F. <u>Patient Care – Post Chemotherapy</u> (Describe)		

• Position patient every 15 min x 2 hours using the following sequence:
  • HOB elevated 30^0
  • slight trendlenburg
  • right lateral
  • left later
  • repeat sequence		

G. <u>Common Side Effects and Complications</u>
States a minimum of three common side effects that do <u>not</u> require MD notification
  • mild abdominal discomfort
  • mild to moderate abdominal distention
  • mild diarrhea
  • slight SOB
  • mild chills (not to point of shivering)
 	
States a minimum of three complications <u>requiring</u> MD notification
  • symptoms of an allergic reaction
  • moderate to severe abdominal pain
  • moderate to severe SOB
  • fever
  • chills to the point of shivering		

Authorized by: _____

Date: _____

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