The ROYAL MARSDEN
NHS Foundation Trust

Having surgery for ovarian cancer with Heated (Hyperthermic) Intraperitoneal Chemotherapy (HIPEC)

Gynaecology Unit

Patient Information

NHS

Introduction

This booklet is intended to provide general information only regarding cytoreductive surgery and HIPEC in patients with ovarian cancer. Your Doctor and Specialist Nurse will discuss your specific condition and proposed treatment with you in detail and answer any questions you may have.

Background

In most patients diagnosed with ovarian cancer, the disease is not confined to the ovary but has spread to other organs in the pelvis and abdomen – in particular, to the lining of the abdominal and pelvic cavity – this lining is called the **peritoneum**. The peritoneum is a thin layer that covers most of the organs in the abdomen and pelvis – please see figure 1. Ovarian cancer typically spreads, and attaches to, the peritoneum at many sites. This widespread peritoneal distribution of ovarian cancer is often referred to as advanced stage of cancer.

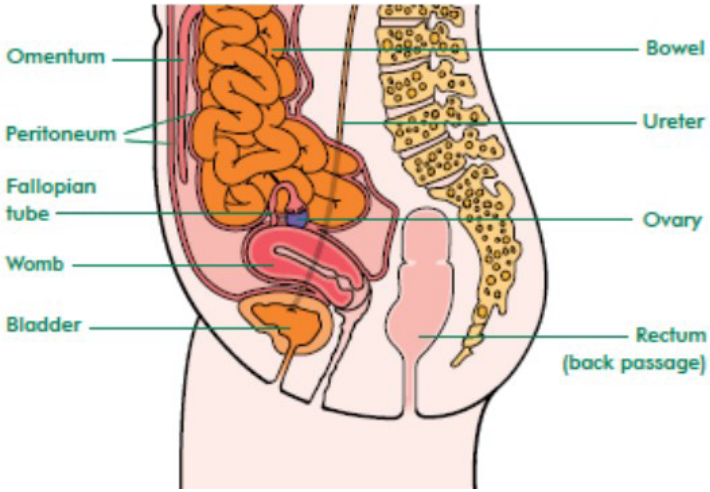

Figure 1 – Peritoneum and surrounding structures

This image was produced by Macmillan Cancer Support and is reused with permission

The standard treatment of ovarian cancer is a combination of chemotherapy and surgery. This combination is often recommended for patients newly diagnosed with ovarian cancer. The chemotherapy is given through a vein, which is called the intravenous route, also known as IV.

Signs and symptoms of disease spread

The spread of ovarian cancer to the peritoneum often causes very few early signs or symptoms and can be difficult to detect on clinical examination. In a few cases, patients may experience an increase in abdominal size or sometimes pain in the abdomen. In about 70% of patients (7 in 10 patients), the cancer is an at advanced stage at the point of diagnosis.

How is disease spread diagnosed?

It may be diagnosed at the time of surgery or by scans, such as a CT scan. Sometimes a biopsy is taken, for example, from the abdomen or pelvis. The biopsy confirms if there is cancer, and if so, the type of cancer. If the biopsy is positive, this indicates that the cancer has spread outside the ovary.

Treatment of ovarian cancer

Cytoreductive surgery

Cytoreductive surgery refers to surgical procedures which are needed to remove cancer deposits that are often distributed in the pelvis and abdomen. In some cases, this may mean that multiple procedures are needed during the one operation to try and remove as much of the cancer as possible.

The goal of surgery is to remove all visible disease. If this is not feasible, then any nodules of disease left behind, referred to as residual disease, should be no bigger than 2.5mm (about an eighth of an inch) in size. Sometimes the surgery can take up to eight hours. This approach, if successful, is associated with maximum benefit to the patient in terms of survival and keeping the disease at bay for longer.

HIPEC

As ovarian cancer is typically contained by the peritoneum, chemotherapy is often delivered into the **peritoneal cavity**. This is known as intraperitoneal or IP chemotherapy, and would be used in addition to the IV route.

Figure 2 – Perfusion device

Research has shown that giving chemotherapy using the IP route, benefits patients with cancers other than ovarian cancer, for example bowel cancer. The IP chemotherapy is given at the end of the operation and is heated to help the chemotherapy penetrate residual cancer nodules. This technique is known as **H**yperthermic (Heated) **i**ntra**p**eriton**e**al **c**hemotherapy (**HIPEC**).

In a recent study, evidence has shown a benefit of HIPEC in patients with advanced ovarian cancer. In this study, all patients were initially treated with IV chemotherapy, then some had surgery with HIPEC, followed by more IV chemotherapy and other patients had surgery alone (no HIPEC) followed by more IV chemotherapy. Those who had received HIPEC were reported to have a longer period of time when the disease was undetected after treatment (called recurrence-free survival) and lived for longer (overall survival).

The addition of HIPEC at the time of cytoreductive surgery is not currently considered standard care in ovarian cancer and continues to be investigated. We are always looking to improve cancer treatments to prolong patients' survival, their experience of care and their quality of life. HIPEC is being further evaluated and the initial study has encouraging results. Just as with new chemotherapy drugs that are tested in clinical trials to determine if they are safe and effective, HIPEC continues to be closely studied in clinical trials. This is also to ensure patient safety. Despite best efforts, all treatments can carry side effects and complications.

The chemotherapy drug used in HIPEC for ovarian cancer is **cisplatin**. This was commonly used to treat ovarian cancer using the IV route and was the first so-called platinum drug for ovarian cancer. Nowadays the usual platinum drug for ovarian cancer given by the IV route is Carboplatin. The dose of cisplatin is calculated based on the patient's body weight. A sterile liquid containing cisplatin is heated to 42°C, and delivered into the abdominal and pelvic cavity using 3 or 4 sterile tubes for 90 minutes using a special apparatus called a perfusion device – please see figures 2 and 3. The fluid containing the chemotherapy is circulated by the perfusion device to the abdomen and pelvis, back to the device and then back to the patient, in a continuous cycle. This machine is supervised by trained personnel, known as perfusionists. The liquid is then washed out of the peritoneal cavity. If there are additional surgical procedures (for example, joining two

ends of bowel) these are now completed and the abdomen is then closed.

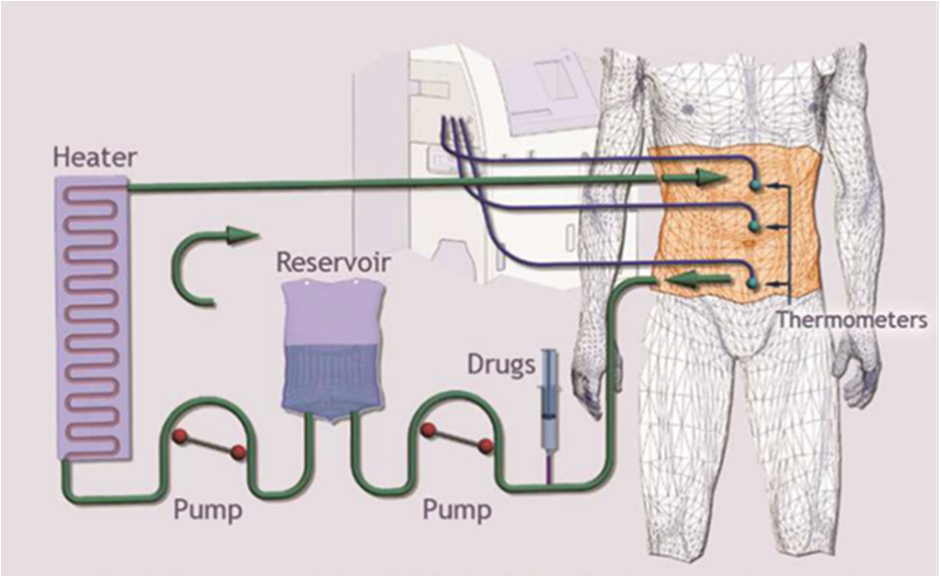

Figure 3 – Hyperthermic intraperitoneal perfusion of chemotherapy (HIPEC)

HIPEC Experience in other cancers

There are many centres throughout the world where HIPEC is a long established and safe technique for the uncommon cancer called pseudomyxoma peritonei (PMP) and the more common colon cancers. In the UK, the HIPEC centres include those in Basingstoke, Manchester, Birmingham, Southampton, and London. The longest established HIPEC centre is in Basingstoke which has delivered more than 3,000 HIPEC treatments. There is extensive experience in delivering HIPEC using different chemotherapy drugs, including cisplatin, and in looking after patients after surgery in intensive care units and on the wards. The safety of both patients and those looking after patients is a priority. The procedure is considered safe and is standard of care in the management of PMP.

HIPEC and The Royal Marsden

To date HIPEC has not been, and is currently not provided routinely at The Royal Marsden. However, we now plan to introduce HIPEC and offer it to eligible patients with ovarian cancer. Ahead of the introduction of HIPEC, our priorities are:

- the safety of patients and staff
- evidence of effectiveness in the treatment of ovarian cancer.

For HIPEC to be offered at The Royal Marsden, it requires collaboration between surgeons, medical oncologists, pharmacists, nurses, as well as teams outside the Trust, for example, perfusionists and the mentors from the HIPEC unit at Basingstoke.

When delivering HIPEC, the surgical team at The Royal Marsden will be supervised by members of a HIPEC team from Basingstoke, which has been an established HIPEC centre in the UK for more than 20 years.

What side effects can I expect?

Surgery

All surgical procedures have some potential risk (see the separate consent form for surgery for ovarian cancer and HIPEC) and these will be discussed with you.

Cisplatin chemotherapy

All chemotherapy drugs have potential side effects. Most of the documented side effects of cisplatin are with the intravenous route (IV). For a full list of these side effects, please see the separate information sheet for IV cisplatin. We do not expect all of these side effects with the intraperitoneal (IP) cisplatin, but it is important for you to be aware of them.

Cisplatin chemotherapy given intraperitoneally may cause the following side effects. These are usually mild but may sometimes be moderate to severe:

- abdominal discomfort or pain
- abdominal distention (swelling)
- diarrhoea
- shortness of breath
- chills (less commonly to the point of shivering)
- fever (above 38°C).

Cisplatin can affect kidney function. To protect kidney function, we use another drug (sodium thiosulphate) with the HIPEC procedure, which is given intravenously.

Sodium thiosulphate

Two infusions are given at the start and end of the HIPEC treatment. This is generally well tolerated with the benefits outweighing the risks, but like all medicines it has some side effects. These include:

- low blood pressure
- headaches
- disorientation
- nausea and vomiting
- prolonged bleeding times
- salty taste in mouth
- warm all-over body sensation.

Are there any other risks associated with the surgery and HIPEC?

The use of HIPEC will increase the whole anaesthetic time by 2–3 hours. This increased period of time under an anaesthetic may increase the likelihood of your staying on the ventilator (breathing machine) after surgery, rather than being woken up from the anaesthetic immediately after the procedure.

The anaesthetist in charge of the case will discuss these issues with you before your operation. Research studies show that the use of HIPEC at the end of surgery not only results in survival benefits for the patient, but also does not increase the serious complication rate associated with major surgery for ovarian cancer.

During the delivery of HIPEC, there is continuous monitoring. Your body temperature is monitored, as is the temperature of the chemotherapy solution being delivered. This is to ensure your core temperature does not rise significantly.

After the procedure you will be transferred to the intensive care unit (known as the Critical Care Unit, CCU) where you are likely to spend one night, sometimes two. This is routine practice for all patients undergoing surgery for ovarian cancer. If you are kept on the ventilator after surgery, in most cases you will be off the ventilator the next day.

When is HIPEC given?

If at the end of surgery there is no visible disease, or any residual disease is no more than 10mm (preferably less than 2.5mm in size) then there is the option to give HIPEC. HIPEC can only be given with your written consent prior to surgery, and on recommendation of the consultant surgeon and consultant anaesthetist. For these reasons, **the decision to administer HIPEC can only be made during surgery.**

If the decision is made to administer HIPEC, the heated cisplatin solution will be delivered to the abdomen and pelvis while you are under anaesthetic, at the end of surgery. The combination of using a chemotherapy drug placed in a heated fluid that is in direct contact with the abdominal and pelvic cavity, helps to destroy and remove cancer cells that could otherwise grow into further tumours. Once the solution is washed away, the surgery is completed, and the abdomen is then closed.

It is very important to note the following:

- For HIPEC to be of benefit to you, the residual disease at the end of the operation must be minimal (microscopic, not visible) or with any single site of residual disease no more than 2.5mm in size.
- We use clinical examination, blood tests (tumour markers), scans, and in some cases keyhole surgery to help in the surgical planning prior to cytoreductive surgery. Although these are beneficial, we cannot always predict in advance of surgery, whether all the disease can be removed, or that any residual disease is no more than 2.5mm. Hence the decision to give HIPEC can only be made during surgery.

If you have any questions, we encourage you to write these down and ask the surgical, anaesthetic or nursing team before your surgery.

What can I expect before and during my hospital stay?

Prior to your surgery you will see the gynaecological oncology surgeon. You will also need to attend the pre-operative assessment clinic where you will be reviewed by an anaesthetist and a nurse to make sure you are fit for surgery. You will have some routine investigations including blood tests and an ECG, a simple test to check your heart's rhythm and electrical activity. If needed, other tests to assess your heart and lung function will be arranged. You will also be advised about Covid-19 precautions.

You will meet one of the clinical nurse specialists (CNS) who will be your Key Worker and you may also meet a stoma therapist. Most patients will be admitted the day of or the day before surgery.

What can I expect after my surgery?

After surgery, you will be routinely transferred to the critical care unit (CCU) or high dependency unit (HDU). You will have a breathing tube inserted during the operation which may be removed after surgery or be left in place until it is considered safe to do so by the CCU and HDU team – this is usually no later than the day after surgery.

A number of drips and drains will be in place and this is entirely normal. This will include a line on the right side of the neck area to allow fluids, medication and sometimes liquid nutrition (parenteral nutrition) to be given. There will a tube inserted through one of your nostrils to drain the stomach contents and a catheter in the bladder to drain urine.

There may also be one or more drains coming out from the abdomen to drain excessive fluid produced after surgery, and drains may have been inserted into the chest on one or both sides to help you breathe better after surgery. These are part of routine practice in patients undergoing surgery for ovarian cancer.

It is expected that you will spend one or more days in CCU before being transferred to the surgical ward. The drips and drains will typically be removed during the week after your operation. You will be reviewed by the specialist nurses, physiotherapists and stoma therapists (if you have a stoma). We will encourage you to mobilise early after the surgery and you can expect to start resuming a normal diet slowly, usually five days after the operation.

The time in hospital varies, but you should expect to be in hospital for about 7 days. After discharge from hospital, you will see the surgical team and the medical oncology team to discuss post-surgery chemotherapy (the usual chemotherapy is a combination of two drugs – Carboplatin and Paclitaxel). You will also discuss other maintenance drugs now routinely used in ovarian cancer, for example Bevacizumab, Olaparib, and Niraparib.

Contact details

Gynaecology specialist nurses	020 7811 8575
Gynaecology surgeons team	020 7808 2623 / 2742

Alternatively, please call:

The Royal Marsden Macmillan Hotline: 020 8915 6899

You can ring the hotline 24 hours a day, 7 days a week.

Call us straight away if you are feeling unwell or are worried about the side effects of cancer treatments.

This service provides specialist advice and support to all Royal Marsden patients, as well as to their carers, and both hospital and community-based doctors and nurses caring for Royal Marsden patients.

Notes and questions

References

This booklet is evidence based wherever the appropriate evidence is available, and represents an accumulation of expert opinion and professional interpretation.

Details of the references used in writing this booklet are available on request from:

The Royal Marsden Help Centre
Telephone: Chelsea 020 7811 8438 / 020 7808 2083
Sutton 020 8661 3759 / 3951
Email: patientcentre@rmh.nhs.uk

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Should you require information in an alternative format, please contact The Royal Marsden Help Centre.

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