Basic Certificate in Palliative Care
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Week-08
Lecture 07: Recent Advances in Nausea and Vomiting

Namaste (Hindi word meaning greetings), this is week number 8, lecture number 6.

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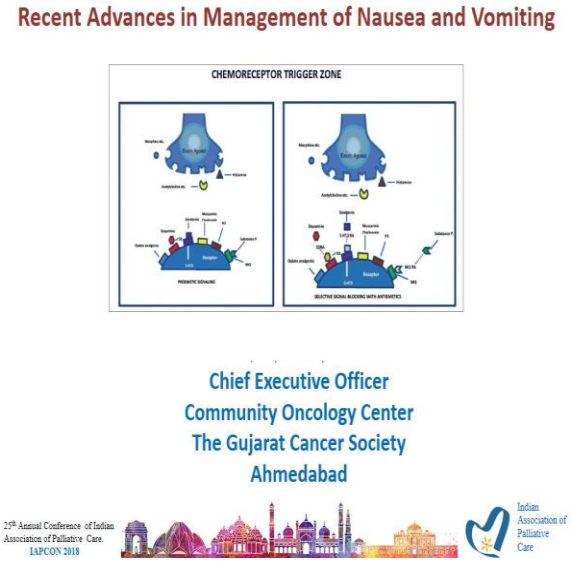

Today, I am to, I am going to speak about Recent Advances in Management of nausea vomiting. We have already studied these symptoms of nausea vomiting under gastrointestinal symptoms, but again I am going to repeat it as this is very important symptom which needs to be managed sometimes by palliative care physician. Almost over 80 percent of our patients are on chemotherapy, either a curative chemotherapy or palliative chemotherapy and they are likely to get nausea and vomiting which is a usual side effect of any chemotherapeutic agent. Even patient on radiotherapy, receiving radiotherapy they are also likely to have nausea vomiting. So, these patient most many a

time they attend chemotherapy and radiotherapy department as well as palliative care department.

So, when they come to us it is our moral duty to do symptom management or sometimes patients are referred to palliative care physician for symptom management and nausea vomiting is the predominant symptoms in group of patients who are attending palliative care OPD and that is why we are revising this subject to some extent and going to have few new drugs studied in this lecture.

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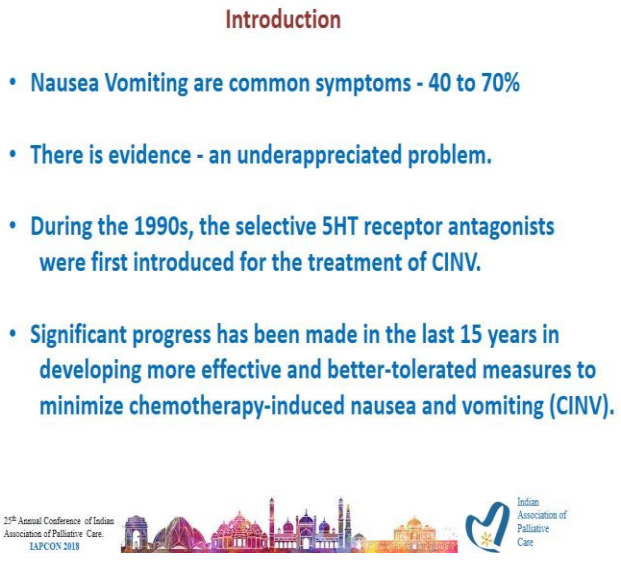

Nausea vomiting is a common symptom in 40 to 70 percent of the patient and there is a evidence that it is highly under appreciated problem or under undermined problem and not attended adequately. So, during 1990 the selective 5 HT receptor antagonists were first introduced for the treatment of chemotherapy induced nausea vomiting, this CINV. And since then significant progress has been made in last 15 years in developing more effective and better tolerated measures to minimize chemotherapy induced nausea vomiting.

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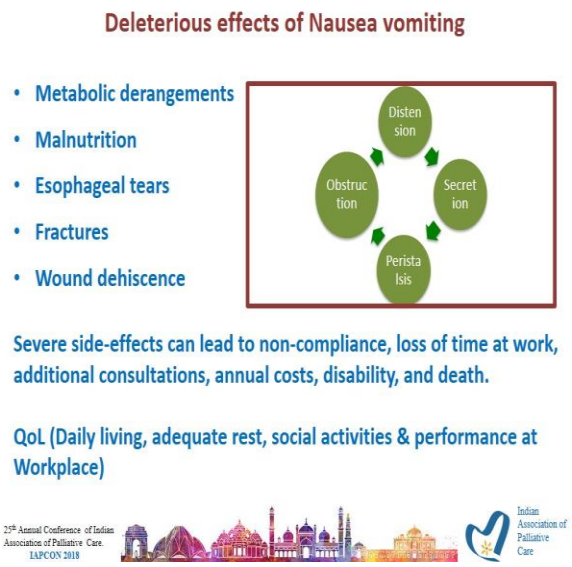

And because of these drugs it has become very easy to administered chemotherapy as patient tolerate chemotherapy well and compliance to the treatment has increased. The nausea vomiting has got a many deleterious effect on the patients body, it will cause metabolic derangements sometimes hypoglycemia, sometimes dehydration, sometimes hyponatremia and which are very frustrating symptoms to attend. Second is malnutrition, esophageal tear, retching very vigorous retching against close glotis can cause tear in the esophagus, fractures and wound dehision, nausea unrelieved nausea vomiting following surgery can cause wound dehiscence the sutures to rupture. So, severe side effect can lead to non compliance patient will refuse the treatment next time mujhe chemotheraphy nahi lenaye hain aur abhi mujhe radiotheraphy ke nahi jaana hain (Hindi word meaning I don't want to take chemotherapy, and right now, I don't want to go for radiotherapy either). These are the common things you will find if the symptoms are not relieved.

Then loss of time at work, additional consultation multiple time they have to attend the hospital to relieve their symptoms that will increase the cost of their treatment disability and death can occur and this all things will lead to poor quality of life in our patients.

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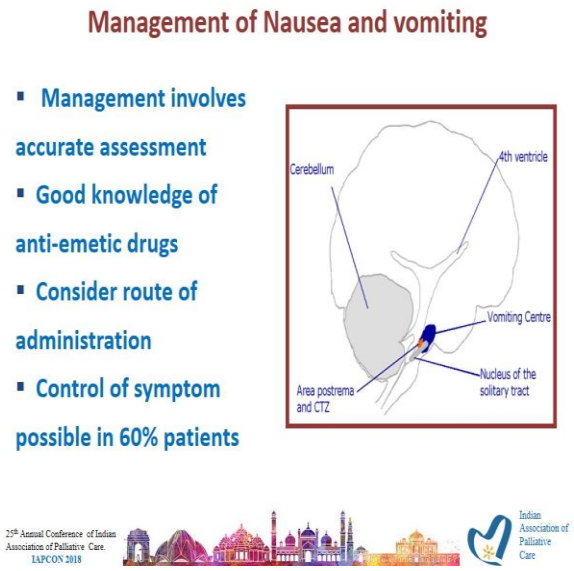

So, management involves accurate assessment. First of all assess the symptoms how since how long patient has, how frequently nausea vomiting has, what is the severity on 0 to 10 vast scale you can judge the severity, then give treatment and again monitor and check the things. So, and one should have a good knowledge of the all aromatic antiemetic drugs which are available in our market. Consider route of administration always not stick to oral route in this patient because they are already vomiting and they will not tolerate extra pills you are going to give to this patient and control of symptoms is possible only in 60 percent of the patient.

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Nausea and Vomiting especially Chemotherapy induced can be....

Types	Description
Acute	Occurring from few minutes to hours and resolving within 24 hours
Delayed	Occurring usually after 24 hours of chemo and will be worst from 48 to 72 hours following chemo and can last 6 to 7 days.
Breakthrough	Occurring despite antiemetic treatment
Refractory	Unmanageable with current antiemetic regime
Anticipatory	Conditioned response prior to chemotherapy

This was already discussed in previous lecture that following chemotherapy patient can have various types of nausea vomiting which can be first of all it can be acute which which occurs within starting of chemotherapy within few minutes of starting of chemotherapy and resolve within 24 hours. Another is delayed which will occur after 24 hours and may last for 3 days, 5 days or 7 days. Breakthrough nausea vomiting though patients nausea vomiting is controlled with one set of drug antiemetic drug, but intermittently she or she may get one or two bouts of nausea vomiting in a day that is called breakthrough nausea vomiting. Refractory this type of nausea vomiting is unmanageable with current antiemetic regime you have and anticipatory sometimes conditioned as soon as patient enters the chemotherapy ward you will get nausea vomiting. So, these are the various types of nausea vomiting found in our patients who are taking chemotherapy.

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The steps in management starts with establish the likely cause, identify the most likely pathway whether it is arising from the stomach or from the labyrinth or from the higher centers, see which receptors are involved, choose the most potent antagonist, choose the most appropriate route of drug administration, review after 24 hours. If it is still not cured or relieved add another drug of for regular rather than PRN doses, always give this medicine regularly means 4 hourly or 6 hourly or 8 hourly rather than PRN dosing means as and when required it is not done like that. Initially it has to be on regular dose schedule, titrate the drug dose accordingly and reassurance of patient and family is very important.

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General principles of Management

- Single anti-emetic may not be adequate
- Multiple causes may require combination
  e.g., for Raised ICP & Uremia
  Dexamethasone, Haloperidol – metoclopramide
- Persistent vomiting – subcutaneous preferable
- Keep in mind side-effects :
  e.g. extra pyramidal, Constipation

Keep in mind one single antiemetic may not work you have to give multiple drugs like multiple cause may require combination like for raised intracranial pressure or uremia. You may need to have give dexamethasone, haloperidol and metoclopramide. Persistent vomiting always secure a cannula in subcutaneous route below the skin and keep in mind the extra pyramidal system whenever you are given using metoclopramide like drug.

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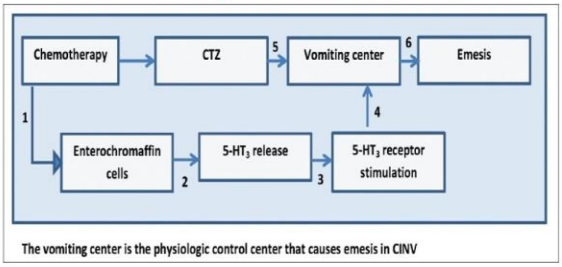
Chemotherapy Induced Nausea Vomiting



The vomiting center is the physiologic control center that causes emesis in CINV

Level 1	Level 2	Level 3	Level 4
(Minimal Risk, <10%)	(Low Risk, 10-30%)	(Moderate Risk, 31-90%)	(High Risk, >90%)
Bleomycin	Cytarabine	Carboplatin	Carmustine
Busulphan	Docetaxel	Cyclophosphamide	Cisplatin
Fludarabine	Etoposide	Daunorubicin	Dacarbazine
Vincristine	Methotrexate	Doxorubicin	Mechlorethamine
Vinblastine	Mitomycin	Ifosphamide	Streptozocin
	Mitoxantrone	Irinotecan	
	Paclitaxel		

So, chemotherapy induced nausea vomiting occurs because of the stimulation of the CTZ that is area in brain and then stimulation of the vomiting center into the brain. Another way is it stimulates the gastric mucosa and releases 5 HT 3 receptors and this receptors are stimulated which in turn will stimulate vomiting center and it will cause nausea vomiting. The nausea vomiting found in chemotherapy patients who are receiving chemotherapy can be of level 1 means only less than 10 percent of the risk, level 2 where the risk of nausea vomiting is 10 to 30 percent, level 3 with the risk of nausea vomiting 30 to 90 percent and very very high risk is level 4 more than 90 percent. So, here they have given the number of drugs which are which will cause this type of vomiting chemotherapy drugs. So whenever, whichever chemotherapy drug is given you can have a anticipation which level of nausea vomiting will occur in this particular patient.

So, patients mostly our patients are on carboplatin or cyclophosphamide they are likely to have moderate risk of having nausea vomiting.

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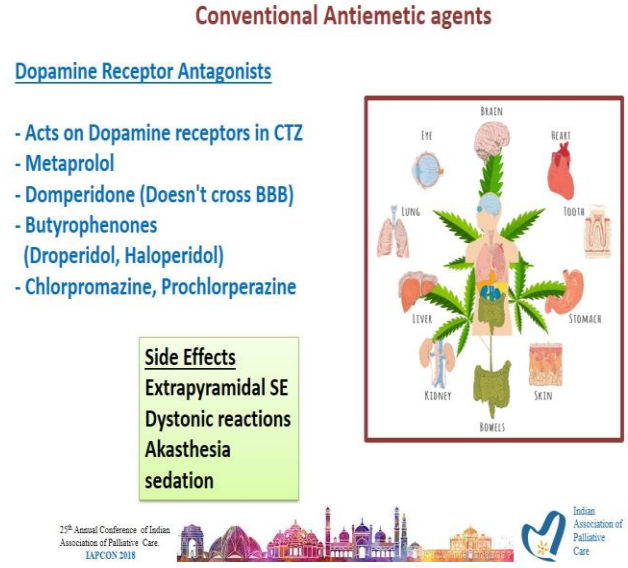

So far available antiemetic drugs which we have are acts on dopamine receptor in CTZ that is metaprolol, domperidone, butyrophenones and chlorpromazine. So, here in this you have to be very careful about extra pyramidal side effect which in terms of maybe seizure, rolling of eyeballs and all like that and dystonic reaction, akasthesia and sedation.

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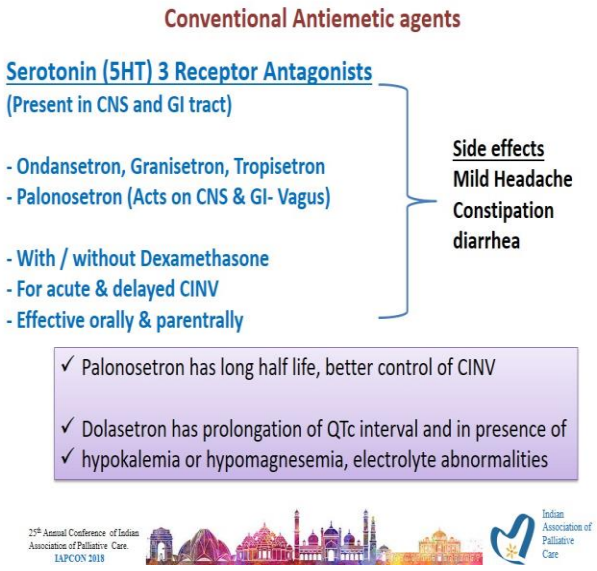

With the new drugs serotonin receptor antagonists 5-HT3 receptor antagonist which are present in CNS central nervous system and GI tract. Here you can give a ondansetron, granisetron, or tropisetron and palanosetron which acts on CNS and GI tract through vagus itself.

One can give this drug with or without dexamethasone for acute and delayed chemotherapy induced nausea vomiting and these drugs are effective orally that is the beauty of it that you need not have venous access or parental infusion for this. The side effects are very mild, mild headache, constipation or diarrhea. Palonosetron has got it is longer acting drug. So, it has got a better control on nausea vomiting and dolasetron you have to be careful with the ECG changes it cause like a prolongation of QT interval.

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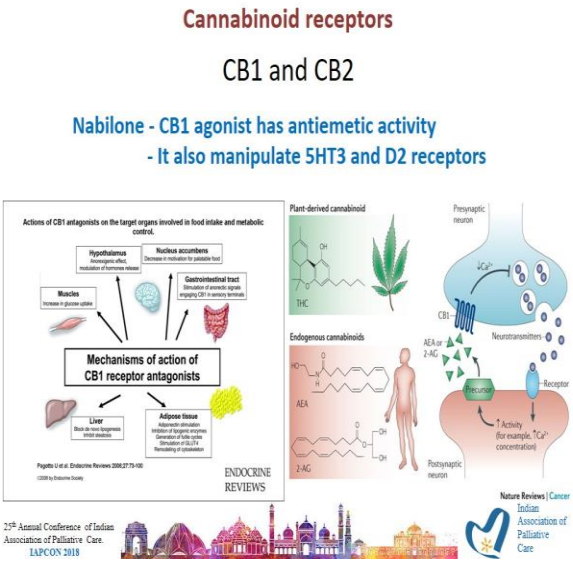

Cannabinoid receptors CB1 and CB2, nebulon agonist has antiemetic activity, but cannabinoid is not easily available and it requires particular license particularly it is sold under AYUSH ministry. So, not available for the, by it is not FDA approved for medical use.

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Newer antiemetic agents like neurokinin 1 receptor antagonists this is substance P and neurokinin 1 receptor in antiemetic pathway. The wonderful drug in this group of

antiemetic is aprepitant it is given orally and it is given over 3 days. First day the dose is 125 milligram and repeat on second and third day 80 milligram. It is given prior to starting chemotherapy. So, it has got a wonderful antiemetic effect and patient can tolerate chemotherapy very well.

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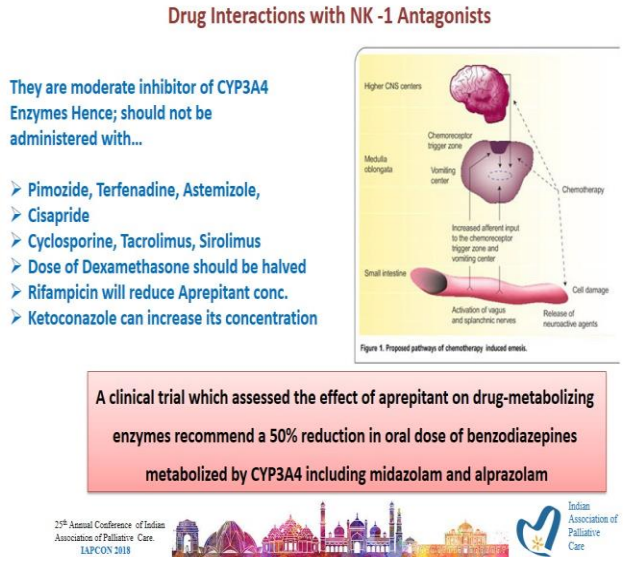

Which are the drug interaction with this drug? They are moderate inhibitor of the CYP3A4 enzymes has should not be administered with the Pimozide, cisapride, cyclosporine and dose of dexamethasone should be half whenever you are using aprepitant and rifampicin will reduce the concentration aprepitant. So, rifampicin should not be you given to the patient on that particular day. A clinical trial which in which assess the effect of a aprepitant on drug metabolizing enzymes recommended a 50 percent reduction in oral dose of benzodiazepines metabolized by CYP3A4 including midazolam and alprazolam. So, whenever you are giving the drug a pepetan you reduce the dose of midazolam or alprazolam if patient is on giving given this drug for insomnia.

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Table 1: Aprepitant/Fosaprepitant dosing regimen for highly emetogenic cancer chemotherapy

Drug	Dose			
	Day 1	Day 2	Day 3	Day 4
Aprepitant	125 mg PO	80 mg PO	80 mg PO	NONE
Dexamethasone	12 mg PO	8 mg PO	8 mg PO	8 mg PO
5-HT3 antagonist	Check prescribing information for appropriate dose	NONE	NONE	NONE

- Fosapreitant may be used on Day 1 only (dose: 115 mg IV)
- Aprepitant should be administered 1 hour prior to chemotherapy
- Dexamethasone should be administered 30 mins prior to chemotherapy on Day 1 and in the morning for Days 2-4

These are the various drug drug and its dosage which is given along with aprepitant like dexona given 12 milligram along with 125 aprepitant on day 1. Day 2 aprepitant 80 milligram dexona 8 milligram, day 3 80 and 8 and day 4 no aprepitant it is given only for 3 days and continue your dexona per oral route.

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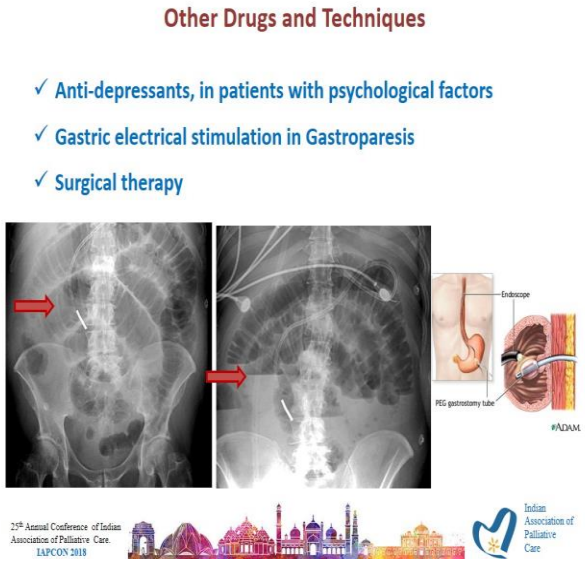

Other drugs and techniques sometimes patient may require anti depression if they are on chemotherapy and having severe nausea vomiting you evaluate the psychosocial aspect

and if you find there is a element of depression you can start anti depression. Then gastric electrical stimulation in gastroparesis and surgical therapy.

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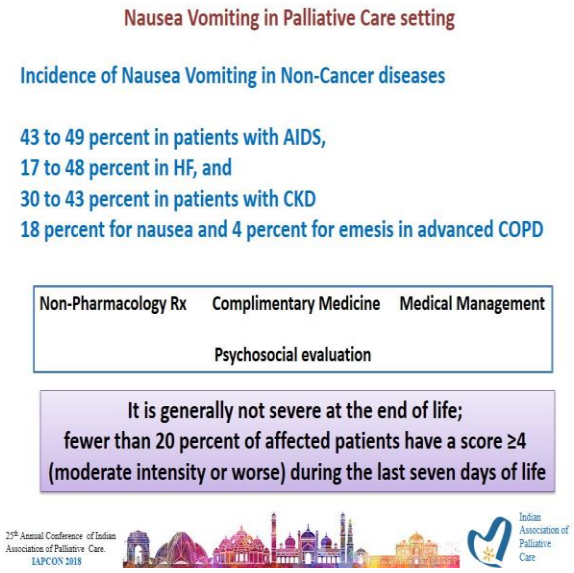

So, what is the incidence of nausea vomiting in in non cancer disease also like it is common in AIDS patient, in chronic kidney disease patient and even in COPD patient and also in heart failure patient.

So, these are the common non cancer disease also where you will find nausea vomiting common symptoms to deal with. Management again like any other palliative care setup it is non pharmacological management, complementary medicine management, medical management and psychosocial evaluation. This the combination of whole and you will be treating the patient as with holistic care then the outcome will be better.

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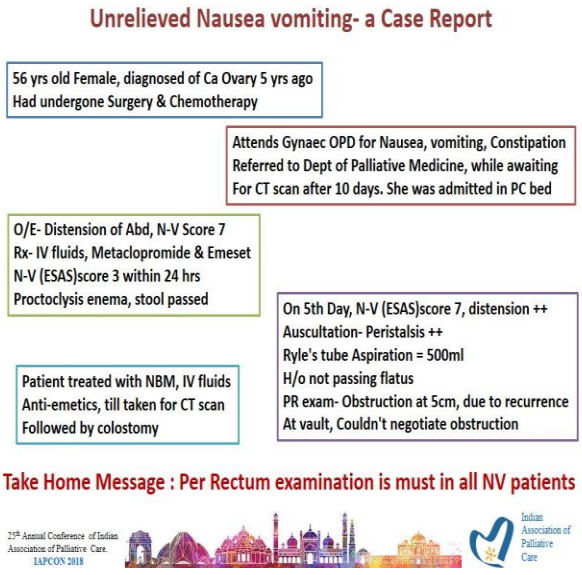

So, here we will discuss one case report a 56 years old female diagnosed with cancer of ovary 5 years ago had undergone surgery and now and chemotherapy. She attends gynaec OPD for nausea, vomiting, constipation and referred to department of palliative medicine while awaiting for CT scan after 10 days.

Her follow up CT scan is planned after 10 days meanwhile he comes to gynaec OPD and then he is referred to palliative care OPD and she was admitted in palliative care bed she was awaiting for the CT scan. On examination it was found that there is a distention of the abdomen the nausea vomiting score was very high 7 means patient had severe nausea vomiting. Initially treated with IV fluid metaclopromide and emeset. ESAS score was 3 so within 24 hour her nausea vomiting came under control and the score came down to 3 within 24 hours. Since she had constipation, keep in mind this, this, these symptoms is usually observed by palliative care team only then proctoclysis enema was given and stool was passed.

On 5th day her again her nausea vomiting worsen. It score went up to 7 again there was distention on auscultation there was peristalsis were present. Patient was underwent ryles tube insertion and it was aspirated that 500 ml of aspirant came up came out came out from the stomach and patient also complained that he does not he is she is not able to pass flatus from below. That means patient is developing malignant bowel obstruction. So, per exam per rectal examination showed obstruction at 5 centimeter due to recurrence

because of the CA ovary there was a recurrence and it was pressing on the rectum and that was obstructing the large bowel and because of that she was not able to pass flatus and she had distention of the abdomen because of that and this obstruction could not be negotiated with the finger or any small spec specula cannula.

So, again patient is treated with nil by mouth. she was kept nil by mouth, put on IV fluid, she was given antiemetic till her we CT scan was hasten up it was taken up as early as possible and on CT scan that recurrent mass pressing on the large bowel was found. So, she was advised to undergo colostomy the obstruction was diverted and colostomy was performed her obstruction was relieved and her nausea vomiting also relieved.

So, you have to keep the whole picture in mind whenever a patient may come with a smallest symptoms like nausea vomiting or only constipation, but you have to keep the whole picture of the patient disease, previous disease and present status of the disease in mind and act accordingly. This way you can relieve the symptoms of the patient, make their life better and improve the quality of life. Thank you very much.