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Empirical Management of Iatrogenic and Non-Iatrogenic Symptoms among Cancer Patients! Clinical Oncologist Perspective

Major Mirza Qaiser Baig[1*] and Mirza Amaan baig[2] **Major Mirza Qaiser Baig[1*] and Mirza Amaan baig[2]**

[1]*Professor, J K Cancer Institute Kanpur, India*

[2]*MBBS student Integral Medical College Lucknow, India*

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Corresponding author: Major Mirza Qaiser Baig, Professor, JK Cancer Institute Kanpur, Uttar Pradesh, India

Abstract

Radiation oncologist may do better job of palliating symptoms and improving quality of life of cancer patients , A part from upfront treatment of cancer patients like surgery , radiotherapy, chemotherapy , immunotherapy , cancer patients do experiences many distressing symptoms during the course of their illness like pain , fatigue , anorexia , weakness , nausea , dry mouth, constipation, dyspnea, vomiting , pain management being very wide and detail topic to discuss in the review article henceforth author will be bit ignorant about the same but however rest all the symptoms shall be discuss in depth regarding the approach towards cancer patients due to iatrogenic and non-iatrogenic causes .

Keywords: Cancer patients; Fatigue; Anorexia; Weakness; Nausea; Dry mouth; Constipation; Vomiting

Introduction

Among the cancer patients some of the symptoms some are because of underline disease but some symptoms are due to iatrogenic reason as many medical intervention having predictable adverse effects such as nausea and vomiting due to ematogenic chemotherapy infusion , constipation with opioids treatment for cancer pain management , post radiotherapy xerostomia dry mouth due to radiation side effects on salivary glands parotid gland , unrelieved sufferings causes demoralization among patients and impair quality of life. Knowing about the principles of symptoms management may help to optimize palliation treatment and improve cancer patients' quality of life. In the patients with advanced cancer the prevalence rate of various symptoms is as given below

- Pain 89%
- Fatigue 69%
- Weakness 66%
- Anorexia 66%
- Nausea 60%
- Xerostomia 57%
- Constipation 52%
- Dyspnea 50%
- Vomiting 30%

Approach towards the symptoms management: while taking history show keen interest in patients symptoms particularly among advance cancer patients , patients believe that suffering is an inevitable part of disease or because of its treatment , asking patients about their symptoms in a positive and detail fashion starting with open ended questions and following up with specific questions , patients may not understand anorexia but loss of appetite can easy explain by them ,as well as Numbness a be explain by patients like loss of sensation and pins and needle sensation in hands and foot as due to toxic effect of chemotherapy induce peripheral neuropathy. Knowing about pathophysiology behind the symptoms: one should understand that in advance cancer patients may have multiple symptoms, but we should prioritize the symptoms according to which one is more bothersome, and treatment should be directed accordingly. When possible, try to choose a drug treatment that targets the likely underline cause like nausea and vomiting may be commonly because of chemotherapy in-

fusion but it may be also due to gastric out let obstruction, hypercalcimia, increased intra cranial pressure due to brain edemas or brain space occupying lesion, opioid use, or due to oesophagitis.

Concepts of drugs dosing, timing and its route of administration: Make it as simple as its not cumbersome and leads to problem of compliance for the patients, it's better to start one medication for most bothersome symptoms if result is good, it will encourage the patient than you can switch on complex list of drugs. Sustained release tablets are often very useful in advance cancer patients' symptoms treatment it's difficult to take 4 hours more than BD dosing. Sometimes one medicine can take care multiple symptoms like Dexamethasone can be helpful for pain, anorexia, low energy level as well as in intractable vomiting. Sometimes there is a problem with breakthrough symptoms that can be tackle with Rescue dosing of drugs or we can use sustained release tablets most of the cases rescue medications are the same medicine used normally like for pain simple tramadol used but for breakthrough pain we can use sustained release tablets. Consideration of general condition of patents along his or her age and fragility: In view of better compliance oral route or transdermal patches preparations are preferred to parental route , if at all parental dosing required we must have open option of subcutaneous route if possible, Discontinue the drug that are unnecessary or in effective and if change of medication required one drug should be change at one time to assess the response in order to understand the change , sometimes same drug should be titrated to its maximum dose before change it suddenly.

Response assessment of medication: A follow up in one week or two is required instruction must be verbal as well as on written to the patient discharged sheet. While during the treatment one must have always plan B management plan as well as other choice medicine, patients as well as his or her attendants must be engaged in discussion about the goal of treatment and procedures palliative care dominates over curative care as cancer stage advances. Although cancer related pain is a dominate symptom found in 89% of advanced cancer symptoms and its management are separate huge topic to discuss henceforth author has skip and consider reviewing it separately. Fatigue, as cancer related symptoms: most of the cancer patients report fatigue as major complain (found in 69% of advance cancer patients) it is not necessarily untreatable symptoms patients report feeling of tiredness unable to carry his or daily activities, fatigue can be physical, emotional or due mental cause it's important to distinguish physical weakness from dyspnea on exertion which commonly reported as fatigue, depression also causes fatigue. Knowing the reversible causes of fatigue given below causes must be ruled out before embarking the treatment of fatigue among cancer patients

- Anemia
- Malnutrition
- Pain
- Depression
- Medical comorbidities like chronic renal disease, chronic cardiac and pulmonary disease
- Hypothyroidism

Non-medical intervention for fatigue: NCCN guidelines suggest energy conservation and patient education are key factor to fatigue treatment, patient should be explained that they have limited pool of energy henceforth they should conserve it and use judicially, study by Schmitz et al found physical activities found to be beneficial so planning for rest and exercise are complimentary to each other as non-medical intervention. Medical intervention for Fatigue, Psychostimulants: includes Methylphenidate (Retalin) 15 to 60mg found to be effective to control in advance cancer related fatigue patients, we can start Methylphenidate 5mg BD and titrated to increase its dose up to 15 mg to 60 mg, benefits is typically observed and noted within 24 to 48 hours but its side effects are anorexia, insomnia, anxiety, tachycardia, above medication should be used with caution in patients with cardiac disease and psychiatric patients. Role of Corticosteroids in fatigue: it may have role in advance cancer patients with fatigue they should be used judicially as their side effects are insomnia, muscle wasting and edema.

Role of Magnesium in Cancer patients' fatigue: Some of the cancer patients are at risk of magnesium deficiency especially those are having prolong illness and certain types of chemotherapy agents like cisplatin, cyclosporine causes magnesium deficiency henceforth magnesium sulphate 2cc injection given along sodium bicarbonate and calcium gluconate injection. Magnesium deficiency may lead to muscle cramps, fatigue and weakness and in severe case even fits or seizures are reported magnesium tablets of 200mg daily used OD basis during chemotherapy for 2 to 3 months particularly in very weak friable cancer patients on chemotherapy. Management of Cancer related Anorexia: Anorexia found in 66% cases of advance cancer related symptoms, appetite loss occurs as Anorexia Cachexia Syndrome as wasting stage seen in chronic advance stage disease including cancer, AIDS, Chronic Renal as well as Chronic Cardiopulmonary disease, on examination weight loss and muscle wasting seen among these patients, anorexia (decrease caloric intake) coupled with hyper metabolic state of malignancy leads to rapid loss of body weight. Reversible causes of Anorexia: reversible causes of anorexia are

- Oral stomatitis (oral mucositis) chemotherapy and radiotherapy induced or oral candidacies due to immune compromised state.
- Constipation
- Severe pain or dyspnea
- Depression
- Gastroparesis

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Treatment of cancer related to Anorexia: a non-pharmacological measure includes nutritional counseling. Increase physical activities advise caloric rich diets, high protein, and high fat diet. Medical treatment intervention includes, Magestral acetate 80mg to 160 mg OD Dose given but studies suggest if we add Olanzapine (Zyprexa) with magestral acetate was associated with significant improvement in appetite among advance cancer patients only side effects magestral acetate is risk of thromboembolism.

Corticosteroids

Dexamethasone 4mg up to 16mg daily show improvement in many symptoms including appetite, one must note that corticosteroids should be discontinue if desired positive effects are not observed within 3 to 5 days if prolong survival expected then wean to the patient lowest effective dose of dexamethasone.

Ryles tube (Nasogastric tube) feeding

this is a temporary measure to not improve survival or comfort in terminally ill patients. On contrary associated with risk of aspiration pneumonia, sepsis, abdominal pain etc., but nevertheless in some patients like patients of esophageal cancer with esophageal fistula, obstruction, or patients those hungry but due severe oral mucositis in this condition Nasogastric feeding works.

Management of Constipation in Cancer patients

Among 52% of advance cancer patients constipation being reported as major symptoms of concern, Constipation is being defined by ROME II criteria for constipation in which at least 2 or more symptoms must be present as given below criteria,

- Straining at least 25% of the time.
- Hard stool at least 25% of the time.
- Sence of incomplete evacuation at least 25% of the time.
- less bowel sounds less than 2 per minute.

Normally bowel sounds are heard on auscultation on the right lower quadrant of lower abdomen at the rate of 3 to 30 bowel sounds per minute. Constipation becomes a major problem among those on opioids treatment for cancer related pain, because opioids work on central nervous system receptor for pain also binds on peripheral receptor including those present in gut as a result opioids interfere with smooth muscle moments of bowel and contractility, increase gut transit time leading to constipation.

Causes of constipation: Factors include

- Low intake of food, especially fibrous diet
- Depression due to Cancer disease
- Intestinal obstruction
- Medical comorbidities like diabetes, hypothyroidism, hypercalcaemia
- Drugs use such as opioids, tricholinergic, antihypertensive, diuretics, iron supplements

Approach to the constipation symptoms treatment: Regular bowel moments are important to slough out bowel endothelium and bacteria are eliminated the goal is to achieved smooth bowel movements constipation treatment must be directed according to the above-mentioned cause of constipation, if opioids are the cause of constipation encourage physical activities and oral fluid intake. We can start with stool softener like Docusate sodium 100 mg Bd and add a laxative agent to enhanced its effect if there are no bowel movements for 48 hours rectal suppositories or enema can be used, Opioids based constipation a μ opioid antagonist is a new agent that blocks the peripheral receptors present in gut produces luxatation within 4 hours in 50% patients since μantagonist of opioid (Methyl Naltrexone , RELISTOR) do not cross blood brain barrier henceforth do not interfere with pain management , dosing of Methyl naltrexone is 8mg or 12 mg subcutaneously given but above drug is contraindicated if the cause of constipation is due to bowel obstruction .

Commonly used drugs for constipation

- Stool softener (docusate sodium) 100mg bd, it increases water penetration in stool.
- Luxative, lactulose works as osmotic action retain water in gut lumen.
- Saline laxative, magnesium hydroxide, magnesium citrate (milk of magnesia) works by osmotic action retaining water in gut lumen.
- Stimulants, Bisacodyl (dulcolex) alter electrolyte transport in intestinal mucosa as well as increase peristaltic movements of gut.
- Opioids Antagonist, methyl naltrexone (Relister) blocks peripheral receptors on gut for Opioids receptors.

Nausea and Vomiting Treatment in Cancer patients: Around 60% patients complain about nausea and 30% cancer patients complaining of vomiting, Nausea, that is sense of vomiting and vomiting defined as forceful expulsion of gastric contents both symptoms diminish quality of life. Potentially reversible causes of nausea and vomiting: Identifying the cause which is sometimes reversible and may help to direct the treatment accordingly. Causes are

- Chemotherapy drugs
- Uremia
- Infection
- Constipation
- Gastric irritation or bowel obstruction

Causes of vomiting can be categorize in chemical cause (drugs

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induced), Metabolic factor for example organ failure like kidney electrolyte imbalance, bowel obstruction. Management of Nausea and Vomiting: Treatment of nausea and vomiting may require multiple anti emetics drugs which may need to be given orally intravenously, choice of drugs for nausea and vomiting depends upon cause of nausea and vomiting

- Nausea due to chemical or metabolic factor Haloperidol (Haldol), Cyclizine used.
- Nausea and vomiting due to sub-acute bowel obstruction requires Metoclopramide, Domperidone.
- Nausea and Vomiting due to Regurgitation, Metaclopramide (Raglan).
- Nausea vomiting due to cranial or ear disease cause requires cyclizine
- Octreoid (somatostatin). Used for vomiting as well as severe Diarrhea 50µ gram TDS Subcutaneously its basically anti vaso active peptide inhibitor which release excess VIP in gut in Vipoma or pancreatic cancer which causes diarrhea.

Metaclopramide if complete bowel obstruction is not suspected oral Metaclopramide tablet which is a dopamine antagonist is our choice of drug its side effects are abdominal pain sedation and diarrhea. Haloperidol is another anti dopamine drug can used for vomiting side effects of haloperidol is prolong QT interval so caution to be taken in Arrhythmias. Olanzapine (Zyprexa) Is also an antipsychotic drug used for nausea vomiting if not controlled by Metaclopramide or do not respond to haloperidol treatment. Ondansetron (Zofar) Is a 5HT3 Receptor antagonist is usually used in chemotherapy induced vomiting or radiotherapy induced vomiting.

Dexamethasone

Those cancer patients having brain mets or brain primary tumor or radiotherapy induced brain oedema respond better with dexamethasone, Acetazolamide (dimox) or mannitol which decreases the intracranial pressure.

Commonly used Antiemitics are

- Metaclopramide (raglan) 10mg BD
- Haloperidol (Haldal) 1mg BD
- Olanzapine 2.5mg BD Sublingually
- Ondansetron 4to 8mg TDS
- Dexamethasone 8mg OD or 4mg BD

Management of Dyspnea in Cancer Patients

Dyspnea found among 50% advance cancer patients although opioids are effective both by oral routes and parental routes both for symptomatic treatment of dyspnea, knowing the fact central control of respiration center present in medulla of brain stem but perception of dyspnea is mediated through sensory cortex area of brain. Opioids are underutilized by physicians other than palliative care specialist because of fear about respiratory depression but approximately titrated dose of opioids do not cause respiratory depression opioids in low dose 2.5mg subcutaneously (dimorpine) was found effective and well tolerated in even in elderly patients with advance pulmonary fibrosis.

Statrs Low and Go Slow

must be strategy with opioids dosing we can start with 5mg morphine tablets or 2mg intravenously every 2 hourly one can evaluate the response and tolerance and further adjust dosing 5mg BD.

Oxygen Therapy

Oxygen therapies of inhalation paradoxically do not improve symptoms of dyspnea. Studies suggest low dose morphine having superior results to oxygen therapy.

Conclusion

Cancer related symptoms are not merely few which have been described by author actually there are plenty of symptoms iatrogenic and non-iatrogenic each symptoms treatment is very specific and precise like chemotherapy induced peripheral neuropathy requires specific treatment, as well as differentiating somatic pain versus neuropathic pain requires altogether different drugs to treat the cause of pain. Although it looks like general management is sufficient for cancer related symptoms but actually it's not true detail understanding of cancer related treatment like radiotherapy, chemotherapy and its side effects as well as in depth understanding of tumor related symptoms and underline causes than to decide line of the treatment of symptoms highly required.

Conflict of interest

None.

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