

A prospective study on the prescription pattern of anti-cancer drugs and adverse drug reaction in a tertiary care hospital

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ABSTRACT

Background: Cancers is a group of disease involving abnormal cell multiplication with the ability to spread to other parts of the body. Common side effects seen with chemotherapy are fatigue, hair loss, easy bruising and bleeding, infection, anemia, nausea and vomiting, appetite changes, constipation etc. The need of this study is to evaluate the prescribing pattern and the adverse drug reaction associated with chemotherapeutic drugs. The study is aimed to analyze the prescribing pattern of anticancer drugs in medical oncology department of a tertiary care hospital, Karnataka.

Methods: An observational study was conducted on 30 patients of either sex admitted for chemotherapy for a period of 6 months in at HCG Cancer Institute, Gulbarga and Basaveshwar Teaching and General Hospital (BTGH), Gulbarga. The data collected is analysed statistically using descriptive statistics and presented as counts and percentages. Results are depicted in the form of tables.

Results: A total of 30 prescriptions were collected with 10 (33.3%) male and 20 (66.6%) female. the maximum number of cases were noted in the age group of 46years to 55 years (10) and least in age group of 15-25 years having a single patient. In our study we found that more number of patients are breast cancer (12 patients) followed by cervical cancer and ovarian cancer (3 patients) and least are Ewing's sarcoma and Non-Hodgkin's lymphoma (1 patient). Most commonly prescribed anti-cancer drug is carboplatin and paclitaxel i.e. for 12 patients out of 30 patients, followed by cyclophosphamide for 10 patients and less commonly prescribed drug being dactinomycin and pemetrexate. Adverse drug reactions seen in maximum patients is hair loss among 20 pts followed by peripheral neuropathy (17) and taste change (16) and the less commonly noted side effects being chest pain and ototoxicity.

Conclusions: The study concluded that the drugs which were used in the treatment of various neoplastic conditions are in adherence and in accordance with the standard treatment guidelines and most of them were prescribed with generic name which leads to reduce in cost of treatment.

Keywords: Breast cancer, Chemotherapy, Mutation, Neoplastic disease

INTRODUCTION

Cancer is a neoplastic disease caused by mutation of the DNA of a cell which may be hereditary or sporadic. The term cancer refers to a group of disease involving abnormal cell growth with the potential to invade or spread to other parts of the body.¹ These are in contrast to benign tumors, which do not spread to other parts of the body. The possible signs and symptoms usually include a lump, abnormal breathing, prolonged cough, unexplained weight

loss, and a change in bowel movements.¹ These symptoms usually indicate cancer, but they may have other causes also. Over 100 type of cancers are said to infect humans.

Tobacco use is associated with the cause of about 22% of cancer deaths. Other 10% are due to obesity, poor diet, lack of physical activity which might be due to professional stress or lifestyle modifications, and excessive drinking of alcohol. Some other factors usually include certain infections, exposure to ionizing radiation and

environmental pollutants and contaminants.² In this developing world about 20% of cancers are due to infections such as hepatitis B, hepatitis C and human papillomavirus infections. These factors act partly by altering the genes of a cell altering their mechanism of function and replication.³ Many genetic changes are required before a normal cell develops into cancerous cell. It is estimated that about 5-10% of cancers are due to the inherited genetic defects from a person's parents. Cancer is usually detected by certain signs and symptoms or screening tests which are helpful in diagnosis of the disease and its extent. It is then typically further investigated by medical imaging and usually confirmed by biopsy and various other techniques.⁴ Many cancers can be easily prevented by not smoking, maintaining a healthy weight, not drinking too much alcohol and frequency of alcohol, eating plenty of fresh vegetables, fruits and whole grains, vaccination against certain infectious diseases, not eating too much processed and red meat, and avoiding too much sunlight exposure.⁵ Early detection through screening is useful in woman for cervical and colorectal cancer.⁶ Cancer is commonly treated with some combination of radiation therapy, surgery, chemotherapy, and targeted therapy, which aimed at reducing the tumor size and decreasing the spread of tumor.⁷ Pain and symptomatic treatment are an important part of care. Palliative care is important in people with advanced stage of cancer. The probability of survival depends on the type of cancer and the extent of disease prior to the start of treatment.⁸ In children under the age of 15 at diagnosis the five-year survival rate in the developed world is on an average of 80%.⁹

According to cancer study in India

- Estimated number of people living with the disease: around 2.5 million.
- Every year, new cancer patients registered: over 7 lakhs
- Cancer-related deaths: 5, 56,400
- Deaths in the age group between 30-69 years
- Total: 3, 95,400 (71% of all cancer related deaths)
- Men: 2, 00,100
- Women: 1, 95,300

The drug utilization studies aim to evaluate factors such as prescribing, dispensing, administering and taking of medication, and its associated events (mostly beneficial).¹⁰ The studies are useful to provide denominators for calculating rates of the reported adverse drug reactions, and to monitor the utilization of drugs from therapeutic categories where particular problems can be anticipated.¹¹ Drug utilization research was defined by WHO in 1977 as the marketing distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences. In a particular setting, it gives an idea about the prescribing practice and characterize the early signals of irrational drug use. With the help of WHO prescribing indicators it is possible to analyze the drug utilization pattern in our setting.¹²

METHODS

The prospective cross-sectional study was conducted for 6 months i.e. from February 2018 to August 2018 at Cancer care unit (BTGH), attached to M.R Medical College, Gulbarga and HCG Cancer Care Hospital, Gulbarga. The patients were recruited after obtaining an informed consent. The study protocol has been approved by the Institutional Ethics Committee of M.R Medical College, Gulbarga. About 30 prescriptions from the newly registered patients were included in the study along with a written performa. The patients were diagnosed with the clinical signs and symptoms of malignancy and later they were documented. In this drug utilization study, demographic characteristics such as age, sex and diagnosis are documented. Once consultation by the physician was over, the prescriptions were copied, and the patients were interviewed as per the WHO guidelines. The following WHO drug use indicators are determined.

Inclusion criteria

- Patients diagnosed with cancer and admitted for chemotherapy
- Individuals of either sex.

Exclusion criteria

- Pregnant and lactating mothers
- Patients with end stage cancer
- Children below 12years.

Core indicators

Prescribing indicators

Average number of drugs per counter was calculated. The percentage of drugs prescribed by the generic name was calculated. The percentage of drugs prescribed from the essential drug list was calculated.

Table 1: WHO prescribing indicators.

| Prescribing indicators | Data |
|--------------------------|--------|
| Average drugs prescribed | 2.06% |
| Generic drugs | 96.84% |
| IV fluids | 100% |
| Injection | 100% |
| On essential drug list | 94% |

Patient care indicators

Average consultation time was calculated. The average dispensing time was calculated. Percentage of drugs which were actually dispensed was calculated.

Facility indicators

Availability of a copy of essential drug list.

Table 2: WHO patient care indicators.

| | |
|----------------------------------|-------|
| Average dispensing time (in sec) | 23.52 |
| Drugs dispensed | 98% |
| Adequate knowledge | 52% |

Complimentary indicators

The percentage of patients who were treated without drugs was calculated by dividing the number of consultations in which no drug is prescribed by the number of consultations surveyed.

Table 3: WHO complimentary indicators.

| | |
|--------------------------|------|
| Complimentary indicators | Data |
| Without drugs | 00% |

RESULTS

A total of 30 prescriptions were collected with 10 (33.3%) male and 2(66.6%) female. The maximum number of cases were noted in the age group of 46years to 55years (10) and least in age group of 15-25years and 26-35years each having a single patient which can be noted down from Table 4.

Table 4: Age wise cancer pattern among adults.

| Age | Count |
|-------|-------|
| 15-25 | 1 |
| 26-35 | 1 |
| 36-45 | 6 |
| 46-55 | 10 |
| 56-65 | 6 |
| 66-75 | 6 |
| Total | 30 |

Table-5: Pattern of cancer distribution among patients.

| Cancer | Count |
|-------------------------|-------|
| Ca. breast | 12 |
| Ca. cervix | 3 |
| Ca. ovary | 3 |
| Ca. pyriform sinus | 2 |
| Ca. buccal mucosa | 2 |
| Ca. lung | 1 |
| Ca. stomach | 1 |
| Ca. colon | 1 |
| Ca. tongue | 1 |
| Ca. hypo pharynx | 1 |
| Ca. submandibular gland | 1 |
| Non-Hodgkin's lymphoma | 1 |
| Ewing's sarcoma | 1 |
| Total | 30 |

Table 6: Drug prescription pattern for various cancers.

| Cancer | Total drugs |
|-------------------------|-------------|
| Ca. breast | 6 |
| Ewing's sarcoma | 6 |
| Ca. ovary | 4 |
| Ca. buccal mucosa | 4 |
| Ca. cervix | 3 |
| Non-Hodgkin's lymphoma | 3 |
| Ca. pyriform sinus | 2 |
| Ca. lung | 2 |
| Ca. tongue | 1 |
| Ca. stomach | 1 |
| Ca. colon | 1 |
| Ca. hypopharynx | 1 |
| Ca. submandibular gland | 1 |

Table 7: Combination of drugs used in various cancers.

| Cancer | Drugs prescribed |
|-------------------------|--|
| Ca. breast | Cyclophosphamide, docetaxel, doxorubicin, epirubicin, paclitaxel, 5-FU |
| Ewing's sarcoma | Cyclophosphamide, doxorubicin, etoposide, vincristine, ifosfoamide, dactinomycin |
| Ca. ovary | Carboplatin, paclitaxel, gemcitabine, oxaliplatin |
| Ca. buccal mucosa | Carboplatin, paclitaxel, cisplatin, 5-FU |
| Ca. cervix | Carboplatin, paclitaxel, etoposide |
| Non-Hodgkin's lymphoma | Cyclophosphamide, doxorubicin, vincristine |
| Ca. pyriform sinus | Carboplatin, 5-FU |
| Ca. lung | Carboplatin, pemetrexate |
| Ca. tongue | Cisplatin |
| Ca. stomach | Oxaliplatin |
| Ca. colon | Oxaliplatin |
| Ca. hypopharynx | Carboplatin |
| Ca. submandibular gland | Carboplatin |

The age wise distribution of the patient showed that there was higher incidence of cancer in this age group. The total incidence of the case constituted 33.3% of the total age group. Aging makes an organism susceptible to cancer due to hormonal disturbance increases in number of loci of chronic proliferation, and the decline in the immune surveillance. Exposure to infectious agents or creation of pro-oncogenic tissue microenvironment with increasing age can promote the development of cancer. In present study authors found that more number of patients are breast cancer (12 patients) followed by cervical cancer and ovarian cancer (3 patients) and least are Ewing's sarcoma and Non-Hodgkin's lymphoma (1 patient), which can be

noted from Table 5. The number of drugs which were prescribed for various cancers is noted in Table 6.

Table 8: Drug prescription pattern.

| Drugs prescribed | Count |
|------------------|-------|
| Carboplatin | 12 |
| Paclitaxel | 12 |
| Cyclophosphamide | 10 |
| Doxorubicin | 6 |
| 5-FU | 6 |
| Epirubicin | 3 |
| Oxaliplatin | 3 |
| Etoposide | 2 |
| Vincristine | 2 |
| Cisplatin | 2 |
| Docetaxel | 1 |
| Gemicitabine | 1 |
| Ifosfamide | 1 |
| Dactinomycin | 1 |
| Pemetrexate | 1 |

Most commonly prescribed anti-cancer drug is carboplatin and paclitaxel i.e. for 12 patients out of 30 patients, followed by cyclophosphamide for 10 patients and less commonly prescribed drug being dactinomycin and pemetrexate, which can be noted in Table 8.

Table 9: Adverse drug reactions among patients.

| ADR | Count |
|------------------------------|-------|
| Hair loss | 20 |
| Peripheral neuropathy | 17 |
| Taste change | 16 |
| Mucositis and Edema | 13 |
| Nausea/Vomiting | 12 |
| Eye and stomach pain | 11 |
| Constipation | 7 |
| Arthralgia and myalgia | 6 |
| Increased urine output | 4 |
| Breathlessness | 4 |
| Pain at site of injection | 4 |
| Diarrhea | 4 |
| Headache | 4 |
| Weight loss | 3 |
| Decreased auditory function | 3 |
| Back ache | 3 |
| Convulsions | 3 |
| Burning sensation in stomach | 2 |
| Dyspepsia | 1 |
| Wt. gain | 1 |
| Chest pain | 1 |
| Ototoxicity | 1 |

Adverse drug reactions seen in maximum patients is hair loss among 20 pts followed by peripheral neuropathy (17) and taste change (16). While the less commonly noted side

effects being chest pain and ototoxicity, which can be noted from Table 9. WHO prescribing indicators showed average number of drugs prescribed is 2.06. The number of drugs prescribed by generic name is 96.84%.

IV fluids were used for all patients and all the drugs were given in injectable form with 94% drugs being on the essential drug list. The WHO patient care indicators demonstrate that the average dispensing time is 23.52s and the percentage of drugs dispensed are 98%. The WHO complimentary indicators illustrate that treatment is not possible without prescription of drugs.

DISCUSSION

Response to drug

In present study mean age was 51.8±5years. Which was in comparison with the study by Jire et al, whose mean age was 52.24±8.66years.¹³ In present study common anticancer drugs prescribed were: carboplatin, paclitaxel and cyclophosphamide. While in the study by Jire et al, cisplatin, paclitaxel, 5-FU were commonly used and cisplatin in study by John et al.¹⁴

ADRs observed in current study are nausea, vomiting, hair loss, peripheral neuropathy, taste change which were in comparison to study by Jire et al, where nausea, vomiting, alopecia, headache were common.¹³

Hair loss has been rated as one of the most distressing side effect of chemotherapy, along with nausea and vomiting by Yeager CE et al.¹⁵

To be of clinical interest a drug shall provide either measurable advantage to patients or to national health services. It shall be more effective than placebo or any other available treatment; if there is no noticeable advantage in terms of efficacy, it should be at least safer, more tolerable, easier to use. The outcome measures used shall be objective, assessing survival or quality of life of the patient.

As for safety is concerned, most drugs have caused the usual signs of cytotoxicity, neutropenia, thrombocytopenia, fever, infections, and gastrointestinal toxicity. In no instance did comparisons between the drugs show a clear-cut advantage, in terms of adverse reactions, over the reference drugs or other analogous agents. The Table 4 gives a brief description of new anticancer drugs approved for cancer chemotherapy in India.

CONCLUSION

The study concluded that, the drugs used in the treatment of various neoplastic conditions are in adherence with the standard treatment guidelines and most of them were prescribed with generic name which leads to reduce in cost of the treatment. Early recognition of the disease leads to a rational approach to case management and good clinical

outcome. Pharmacovigilance should be the part of the patients care in order to reduce the occurrence of adverse

drug reactions and also encourage the practitioners to report the ADR.

Table 10: Features of new anticancer drugs approved for cancer chemotherapy in India.

| Active substance | Indication | Mechanism of action | Safety notes |
|------------------|---|---|---|
| Docetaxel | Breast cancer, non-small cell lung cancer | Increased assembly of microtubule | Mutagenicity positive; Carcinogenicity is not tested |
| Paclitaxel | Soft tissue tumor | Inhibition of microtubule reorganization | Mutagenicity positive; Carcinogenicity is not tested |
| Doxorubicin | Soft tissue tumor, ovarian tumor | DNA intercalation | Mutagenicity positive; Carcinogenicity is positive |
| Cyclophosphamide | Breast cancer; ovarian cancer | DNA intercalation | Mutagenicity positive; Carcinogenicity is positive |
| Docetaxel | Breast cancer, advanced stomach cancer | Microtubule network reorganization inhibition | Mutagenicity positive; Carcinogenicity not tested |
| Epirubicin | breast cancer | DNA intercalation | Mutagenicity positive; Carcinogenicity not tested |
| 5-Fluorouracil | Head and neck cancer; breast cancer | Interferes with DNA replication | Mutagenicity positive; Carcinogenicity negative |
| Etoposide | Ewing's sarcoma; uterine Cancer | prevents re-ligation of the DNA strands | Mutagenicity positive; Carcinogenicity is limited |
| Rituximab | Follicular lymphomas | Bind to CD-20 | Mutagenicity is not tested; Carcinogenicity is not tested |
| Oxaliplatin | Colon cancer; rectal cancer | Interfere with DNA replication | Mutagenicity positive; Carcinogenicity positive |
| Ifosfamide | Ewing's sarcoma, germ cell tumor | Interfere with DNA replication | Mutagenicity positive; Carcinogenicity positive |

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