Practice of Using Plant and Synthetic Derivatives of Anticancer Drugs Among Cancer Patients at NICRH, Bangladesh

A project submitted

by

Najib Hasnat

ID: 12146033

Session: Spring 2012

to

The Department of Pharmacy

in partial fulfillment of the requirements for the degree of

Bachelor of Pharmacy (Hons.)

Dhaka, Bangladesh

July 2017

This work is dedicated to my parents for their love and support.

Certification Statement

This is to certify that this project titled 'Practice of Using Plant and Synthetic Derivatives of Anticancer Drugs Among Cancer Patients at NICRH, Bangladesh' submitted in order to fulfill the partial requirements for the degree of Bachelor of Pharmacy from the Department of Pharmacy, BRAC University under the supervision of Dr. Sharmind Neelotpol, Assistant Professor, Department of Pharmacy, BRAC University and proper referencing have been made where the language, concept or writings of others are used.

Signed,

_____

Countersigned by the supervisor

_____

Acknowledgement

At first, I would like to thank Almighty Allah, to enable me to study in Pharmacy as well as to submit this thesis paper for the degree of Bachelor of Pharmacy, Department of Pharmacy. Foremost, I wish to express my deepest gratitude to my research supervisor Dr. Sharmind Neelotpol, Assistant Professor, Department of Pharmacy, BRAC University. I put forward my most sincere regards and profound gratitude to Dr. Eva Rahman Kabir, Professor and Chairperson (Current Charge), Department of Pharmacy, BRAC University.

Being a student at the Department of Pharmacy, BRAC University is a very special and invaluable experience for me. I have really enjoyed the research technique and atmosphere here. I express my deepest admiration to the Department of Pharmacy for providing me all their support and giving me the honor to perform the research in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

I am grateful to my family for their immense mental support throughout my study/research. Lastly, I offer my regards and blessings to all of those who supported me in any respect during the completion of the project.

Abstract

Myriad lines of therapy are used to treat cancer around the world. The study was conducted on the patients of National Institute of Cancer Research (NICRH) to estimate which type of anticancer drugs are mostly being used to treat selected type of cancer (breast, cervix and throat cancer). The study was based upon two sections- literature review and cross-sectional questionnaire study design. The aim of the study is compare the therapeutic efficacy of plant and synthetic origin of anticancer drugs on the basis of their mode of action. The data taken from the literature review was used to form a list of questions; accordingly a set of variables were developed to use in the questionnaire. As the representatives of the two classes of drugs, cisplatin was selected for the platin based synthetic alkylating agents; paclitaxel was selected for the taxane and vinca alkaloid type of plant derivatives. The platin-based alkylating agents were mostly used in most of these cases while the breast cancer (36%) and cervical cancer (36%) patients were abundant in number. Cisplatin based drugs were used in both cases while antibiotics were used in treating throat cancer. The study did not put up enough evidence for the efficacy of the plant derivatives of anticancer agents (taxanes, vinca alkaloids) however, they do show major improvements in accord to the theoretical data gained from the literature.

Table of Contents

List of Tables

List of figures

Chapter One

Introduction

1. Introduction

Cancer is an uncontrolled growth and differentiation of cells due to loss of homeostasis whereby malfunction of cellular mechanisms lead to events such as occlusion of an essential conduit, formation of mass, ulceration of tissues, perforation of cells, effusion, fistulization, paraneoplastic syndrome, endocrine hyperactivity syndrome and in some cases, genetic predisposition to cancer progeny (Chabner, 2006). However, the cancer process does not begin all on a sudden. A major difference between the normal eukaryotic cells and cancer cells is that the division and growth of normal cells is strictly controlled while the cancer cells do not. The abnormal proportion of growth of the cancer cells in turn proves to be fatal for the organism that it occurs in. The risk of gaining cancer increases incrementally from the age of 40 to 80. Around 80, it reaches a platue level. (Lewin, 2004). From this phenomenon, it can be said that cancer is the result of a random occurrence of a series of stochastic events (approx. 4-10). Another notable fact about the cancer cells is that most of these cells have an increases number of mutations in respect of the normal cells. Hence, the progression of the cancer is directly proportional to the mutations involved. The most prominent types of mutations involved in the genome include- the cluttering of somatic cell mutations and the build-up of gene instability. At each step of development of cancer cells, a cell selection process takes place. The cells capable of growing at an enhanced rate are selected for the rapid spread of cancer to other sites of the body. The selected cell population can move to different part of the body to initiate the growth of cancer. Therefore, in short the cancer growth is initiated by the accumulation of mutation in the cells, which is followed by the selection of rapidly growing cells among dividing cells to speed up the progression of cancer cells. The two major driving genes pushing the cells to cancerous state are mainly- oncogenes and tumor suppressor genes. Oncogenes are capable of triggering tumorigenic state while tumor suppressor genes are the genes that are first to be inactivated, resulting in tumor formation. (Lewin, 2004)

The era of cancer medicine has been rapidly added to the armamentarium to fight against the progressive risk of development of cancer. It has saved time and resources. Moreover, it has lessened the requirement of amputation of limbs infected with cancer that are more obvious

in cases of breast, cervical and colorectal cancer. Added to that, chemotherapy proves to be effective in aggressive cancers such as advanced throat, head, lung and esophageal cancer etc. Cytotoxic antineoplastic agents are used as first-line of therapy for dealing with autoimmune disorders e.g. rheumatoid arthritis, Chron's disease, transplantation of organs, and psoriasis. In spite of all of these merits, these drugs have a very short therapeutic index and severe side-effects. A detailed overview of their pharmacology, therapeutic action, drug interaction, pharmacokinetics and pharmacodynamics, is prerequisite for use of these drugs in a safe and effective manner.

Most of the synthetic and natural chemical agents acting on cancer work on the DNA and its precursors that prevent synthesis of new genetic material. Since the research on drug advancement is going on, new classes of therapies have been innovated. Most of the cytotoxic agents act by inhibiting the S phase of the cell cycle. Hence, their toxicity is very high. The natural drugs, e.g. vinca alkaloids, taxanes block the mitotic spindle formation during the M phase. These agents are potent for rapidly growing tumors. Tumors having incredibly high growth rate- lymphoma, leukemia etc. are highly sensitive to chemotherapeutic drugs. Unfortunately, these neoplasms are similar to normal tissues with accelerated growth and development such as- bone marrow, hair follicles, and intestinal epithelium. Thus, there still remains a high risk of losing a lot of healthy cells in the mode of treatment. Moreover, there is also a risk of development of drug resistance by growing tumors. This new error must be dealt with a combination modality (Chabner, 2006). There is little comparative data available in relation to the efficacy of the available anticancer drugs. Thus, a study needs to be conducted to collect crucial data and information about the antineoplastic drugs in relation to their mode of action.

1.1. Aim

To compare the therapeutic efficacy of plant and synthetic origin of anticancer drugs on the basis of their mode of action.

1.2. Objectives

The objectives of the study are to-

1. review articles regarding the therapeutic efficacy of anticancer drugs on different types of cancer cells.

2. assess the cytotoxic effects of anticancer drugs obtained from plant and synthetic sources.
3. find the most suited therapy that can be used in rapid and slow progressing tumors in terms of pharmacologic activity.

Chapter Two

Methodology

2. METHODOLOGY

2.1.Research Design

A sample questionnaire was developed to collect data from the cancer patients of National Cancer Research Institute (NICRRH) and to get a holistic view of the treatment plans given to the patients. The study topic was selected with the help of reviewing various journal articles including Pubmed, Elsevier, JAMA Network, Oxford Journals, Cambridge Journals, Springer etc. The questionnaire was surveyed among the patients undergoing treatment in the National Institute of Cancer Research Center situated at Mohakhali in Dhaka district. Fixed design is used in this case as it is more theory- oriented. Thus, the variables that need to be controlled and measured aren't omitted in conducting the research design. The flexible research design is discarded here as it emphasizes on innovative techniques and adjustable variables which might lead to faulty analysis. In the field of medical research, the cross-sectional research design is of utmost value. It is used to collect data from a specific set of population over a specific period of time. The design provides more scopes to measure the odds ratio, absolute risk and relative risk ratios from prevalence risk ratios. This data can be used to relate to the prevalence of a disease in a certain population with inferences to the cause and effect of the disease. In the fixed design, the first thing to notice is the planning of the best measures to use the variables taken into account and the statistical tools and methods most suited for the analysis of the results. Finally, the researcher must be sure of the availability of the participants for the study to be conducted and choose an appropriate sample.

As implied by Chris and Diane (2004), data is gathered from a selected population or a subset of the population via a list of questions which is targeted to extract the necessary information the researcher wants to collect in order to determine whether there is a correlation between the measured variables for the conducted research. This is called a cross-sectional research because the study is done by collecting information over a short period of time only. (Olsen & St. George, 2004)In this survey, a questionnaire was prepared and given to a number of patients at random to get an estimate of the credibility of the questionnaire. Then the questionnaire was analyzed by a statistician to test the validity of the list of queries. The tests confirmed that the questionnaire was appropriate to collect the

necessary data related to the survey. The major factor of the questionnaire was that it was understandable to all of the participants and the questions enlisted were close-ended for accurate collection of data regarding the variables. The whole study is of a mixed design of literature review and survey based qualitative research. The literature review was done first to get an accurate idea and build a firm infrastructure for the next part of the study design, the cross-sectional study under the qualitative or fixed research design.

The whole process of literature review was followed according to the Blooms taxonomy of the objectives of educational learning which are- Recollection, comprehension, application, analyzing, evaluation and innovation respectively. In the first step, the relevant books and articles, journals as mentioned above were identified and read. This provides a vast area of information to the researcher which is useful in both sections of the research. Without understanding the data collected, one cannot proceed to assumption and application of the data beforehand. Thus, comprehension of the subject materials is crucial in literature review. After getting a clear concept, the researcher can link the data with the actual project work at hand. This is the step of application in Blooms taxonomy. At the step of analyzing the data, the researcher is able to fit the bits and pieces of the research materials and get them to form a big picture. It is a necessary step to building an outline of the whole project. While evaluating the results the researcher is able to see the loopholes in the project and get a holistic view of the whole study. By precise evaluation, the author is able to find new gaps in the research work as well as draw inferences that ensue to innovative and original insights. A flowchart has to be followed as it is easy to get distracted with the overwhelming amount of books and journals which are quite difficult to keep track of.

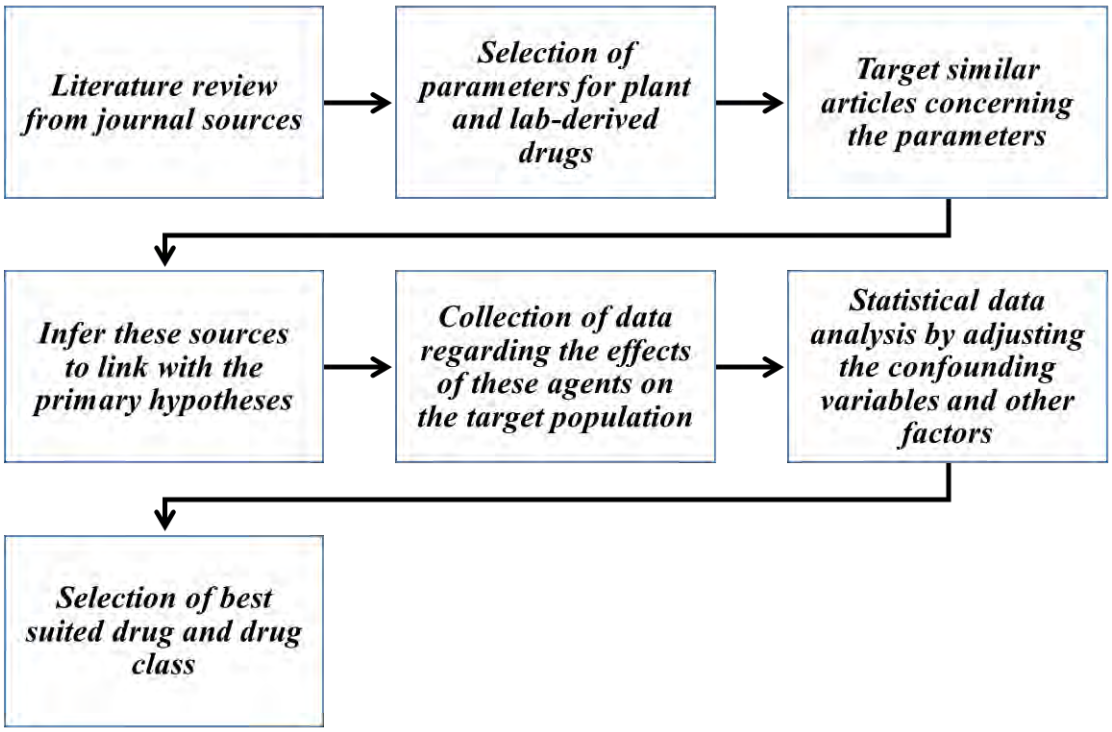

Figure 2.1: A flow chart of the workflow of the study

On the basis of this review, we had to follow these certain steps:

- Ethical permission from NICRH
- Pretesting and validation
- Data Analysis
- Findings

2.2.Ethical Permission

Ethical permission was achieved from the Department of Medical Oncology and the Radiation Oncology, National Institute of Cancer Research Center, Bangladesh. A permission letter was given from the Director of NICRH providing permission of the project with an identification number of NICRH/2017/276/1(6).

2.3.Determination of sample size

For this study the number of study was 30. It is evident that the appropriate sample size should reflect the true picture of the population. According to Johanson and Brooks (2010), participation of 10-30 subjects should be a reasonable number for a pilot study. In the medical field, Julious (2005) reiterated that "a minimum of 12 subjects per group be considered for pilot studies". Therefore, it can be said that, total number of participants of 30 is satisfactory for this pilot study.

2.4.Recruitment of the participants

The participants were recruited from the Medical oncology and Radiation oncology unit of NICRH. Only patient follow-up studies are taken into account from the Gynecology Department for analysis purposes due to time constraint. Data collection was conducted from February 2017-April 2017.

2.5.Development of Questionnaire and data analysis

The questionnaire was developed in such a way that it could collect and extract the information of the participants according to the aim of this study. Before conducting the survey the questionnaire was pre-tested and validated. The questionnaire is divided into 2 sections. The first section involves the general information about the patient such as – age, sex, religion, occupation, workplace/residence etc. The second section of the questions dealt with the issues related to the disease and the treatment plans involved. The name and address of the patients are not going to be disclosed under any conditions. Instead unique serial numbers are placed to identify each patient. The data was analyzed by SPSS software version 23. The sample questionnaire is given at the appendix A section of the thesis.

Chapter Three

Comparative study of synthetic and plant origin: A Review

3. Comparative study of synthetic and plant origin: A Review

The drugs normally used in treating cancer follow identical or similar metabolic systems in the normal cells to destroy the cancer cells. While this line of treatment shows promising therapeutic efficacy in most cases, it is not devoid of the harmful toxic effects. A comparative review of these classes of drugs can help to better clarify the beneficial use of the drugs without causing collateral damage to the healthy cells of the body.

The growth-inhibitory drugs have been tested on complex biological systems. These studies involve- a) enzymatic functions derived from interaction between intracellular substances, b) effects on cellular levels, c) in various species including viruses, vertebrates and invertebrates, d) teratogenic effects of the drug, e) on regenerating cells, f) on organ stems where replication takes place- bone marrow, gastrointestinal tract, and liver, g) on spontaneous and transplanted neoplasm, h) on carcinogenic and mutagenic activity of the drug, i) the pharmacokinetics of the drugs, j) on the mechanism of resistance, k) on the effect on protective and immune responsive chemicals, l) on synergistic effects with radiation or chemotherapy, m) on their route of administration. Moreover, angiogenesis inhibition by the drug on the blood vessels of the tumor, and the immune response of the body is also taken into account.

3.1.Cell cycle

The cell cycle is the most important portion in case of the anticancer drugs. A brief review of the whole cell cycle is given below:

The non-proliferating cells can be targeted by the toxic drugs but the mitotic inhibitors can act at more specific sites created at different phases of the mitotic cycle. The cell cycle observed in higher animal cells can be divided into several phases as the radioisotope labeled DNA precursors appear in different phases of mitosis at distinct time intervals. While the cell is following mitotic division, the cell is assumed to be in the “interphase” level. This phase has been classed into three different intervals in terms of synthesis of DNA required for cell division.

G1 is termed as the post-mitotic phase which takes over half of the total time to DNA synthesis. S is the time for synthesis of DNA that consists of one fourth or one third of the given time. G2 also termed as the pre-mitotic interval is the time required for the ending of DNA synthesis and commencement of mitosis and comprises of the smallest amount of time in the whole cycle (one-fifth). M indicates the mitosis phase and takes an hour to complete.

G1 phase: The chromosomes appear as filaments diffused around the nucleus, the nuclear membrane is visibly intact, and the two parent centrioles are regenerated. In various studies, the fluctuation in inter-mitotic time is due to a variation in G1 in comparison to other phase intervals in the cell cycle. Maximum number of cell growth takes place in this phase. The choice of a cell division depends on this phase whether the cell will fully differentiate or keep replicating. So, G1 in this sense can be a potential target site for the drugs.

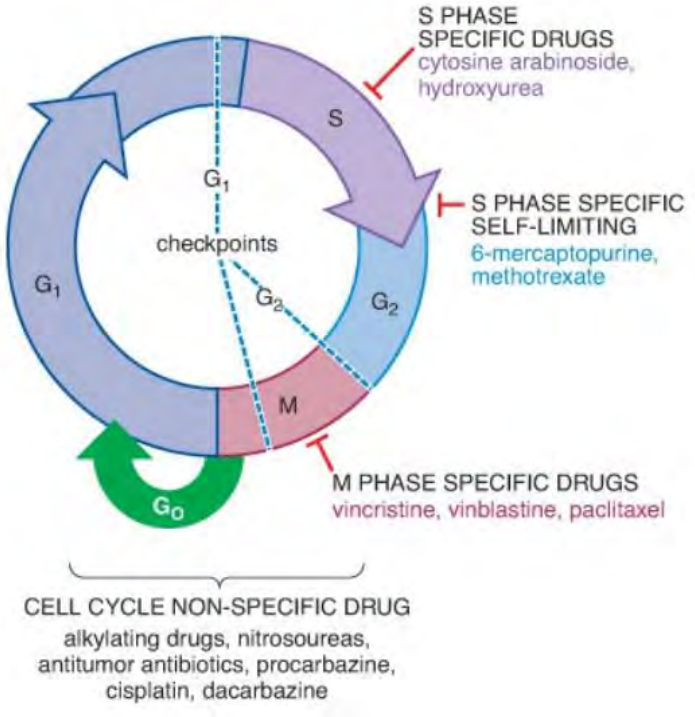

Figure 3.1: Drugs acting on the cell cycle (Source:Chabner, B. A. (2006).

S phase: In this phase, the contents of the DNA are doubled. Mainly DNA replication takes place at this point. Histones are also synthesized to coil around the DNA strands. The polymerization of DNA requires the presence of DNA both as a primer and a template. The creation of this native DNA primer is dependent upon the function of DNAase. So, the

important factors of the S phase include the DNAase and the synthesis of histones and other chromosomal proteins to tie all the DNA molecules.

G2 phase: During this period spindle formation occurs. Moreover, energy reservoirs i.e. mitochondria is formed at this phase. Respiration and oxidative phosphorylation inhibitors can work on this energy stores and stop mitosis. This strategy might be useful if used before chromosomal prophase but can prove to be ineffective after mitosis starts.

M phase: In this phase, the mitotic division occurs. This phase is divided four sub-phases:

a) **Prophase, b) metaphase, c) anaphase, d) telophase.**

a) Prophase: The most noticeable event in this phase is the accumulation of chromosomes that have a thick and tighter coiling along with a short length. Each chromosome comprises of two chromatids that is tied together by a centromere. In the animal cells, the centrioles move to opposing directions as they radiate microtubules. At this stage, they are termed as asters. Nucleoli and the nuclear membrane disappear as the phase progresses further. RNA synthesis stops after a while as the DNA template required for RNA production is compressed into the mitotic chromosomes.

b) Metaphase: The chromosomes align at the equator in the midway region between the two poles. The two sister chromatids attach to two different poles. The three types of fibers- the central spindle that connects the two poles, the spindles around the cell surface radiating from the asters and the spindle linking the kinetochore of the chromosomes to the two poles. The mitotic apparatus is composed of spindles, asters, centrioles and nuclei before they dissolve into proteins the next phases for nuclear division. A handful of proteins comprise most of its mass which usually consists of thiol groups (SH which can be oxidized into disulfer bonds (S-S). When they are amassed, a gel is formed of protein macromolecules via sulfur linkages.

c) Anaphase: This stage progresses rapidly. The centromeres divide into two and go in opposite directions as two forces from the opposing poles pull the chromatids along with their centromeres. The two forces result from- a) the shortening of the chromosomal fibers

connecting the chromatids with the kinetochore and b) the expansion of the central spindle which enhances the gap at the equator region and pushing the chromatids in their ways.

d) Telophase: At this stage, vesicular components originating from endoplasmic reticulum forms two membranes on each chromosome as they aggregate over the surface of each chromosome. As the chromosomes arrive at each pole, their double membranes dissolve and form a seamless nuclear membrane that envelopes the whole set of chromosomes. Subsequently, nucleoli reform and the chromosomes get broken down from their strands and revert back to their interphase form. Telophase can lead directly to cell division stage (cytokinesis).

3.2.Inherited cancer syndrome

The familial cancer syndromes account for only 5-10% of the documented cancer cases. But this holds a major concern due to the fact that cancer being a genetic disease, can be passed on to the progeny who can be at high risk of developing cancer of the same type in the long run.

Genetic predisposition to cancer can develop from two types of gene mutations mainly—one is the inherited type and the other being acquired. Inherited gene mutations are acquired by birth; since the gene is already integrated in the egg or sperm forming the fetus. As all cells are formed from this primary zygote division, the damaged copy of the gene is replicated in all of the cells that are formed over the lifespan of the fetus. This type of cancer gene has a higher risk of being transferred to the next generation. On the contrary, somatic or acquired mutations are more common due to the fact that they are acquired over the lifetime; differing from the inherited type of cancer gene present in the zygote from birth. The inherited cancer type is caused by one damaged gene transfer but the acquired mutation requires two copies of gene alteration to develop cancer. The inherited type of cancer manifests at an early age but the somatic cancer takes time to develop and present with obvious lethal complications. Many family cancer syndromes emerge as a result of inherited mutation of the tumor suppressor genes. These genes regulate cell growth, induce apoptosis, repair DNA errors, and slow down cell division whenever necessary. Tumor suppressor gene is also linked to other growth regulatory genes such as DNA repair genes, apoptosis inducer genes p53, LKB1 gene, CHEK2 variant which can be held responsible for most cases of breast cancer.

These genes are the targets of anticancer agents to root out cancer. Drugs of both plant and synthetic sources targeting these genes will be evaluated in this study and compare the test results derived from various journals.

3.3.Cell function

Though DNA has the major role in controlling cell signaling via informational RNA and other protein synthesis, external and situational factors are also should be taken in account. The environment around the cell, i.e. the substances diffusing through the cell has a major impact on the changes made to the cell. Exactly which factors have a direct effect on cellular mechanism and structures are yet to be identified. But recent experiments may give a clue to some of them. In one experiment done on frog embryos, the nucleoli from frog embryos were transplanted to another to see the growth of cell in the new host. It was seen that the nucleoli obtained before the blastula stage (when the cellular differentiation has not even begun yet) caused normal growth and differentiation in the transplanted enucleated frog eggs while the nucleoli collected after the blastula stage produced imperfect embryos. It can be concluded from this experiment that those cells taken prior to blastula stage had their totipotency intact which lead to the successful growth of the frog eggs. Some distinct features were noticed in these cells under study. DNA triplet formation and replication was not harmonized in the chromosomes and in different parts of the same chromosome. This type of DNA synthesis is similar to that in the chromosomes in Hela cells. It can also be assumed that if this malfunction resists further, the DNA may acquire deformed function and continue to produce faulty cells and enzyme function.

According to J. Carmichael (1994), the pacific yew tree provides a plant alkaloid taxane taxol, which is shown to have potent anticancer action against solid tumors i.e. breast and ovarian cancer. He also explained the role of bryostatin extracted from the marine species, *Bugula neritina***.** Bryostatin is a lactone derivative that alters the action of protein kinase C is important for signal transduction from the plasma membrane to other cellular organelles. But the author pointed out obvious limitation to the fact that those drugs that are only active via immunomodulation and metabolic activation may need a different approach for clinical

use. A difference can be showed between the action of vinca alkaloids and taxanes. The vinca alkaloids prevent the microtubule assembly, whereas the taxanes decrease the resting period and push the equilibrium point set between the tubulin dimers and microtubules to polymerization and stabilization of microtubules ensues. Docetaxel has 1.9 times higher affinity to the binding site than paclitaxel does and shows polymerization of tubules at 2.1 folds lower than the critical concentration of the tubulin. Added to that docetaxel is more potent than paclitaxel in treating tumor xenografts and cytotoxicity. In case of ovarian cancer, a treatment was approved for epithelial ovarian cancer based on the clinical trials of the 24 hour schedule. In the first five trials, 20-48% of women with recurrent disease responded with complete eradication of the disease or a partial response where 50% of the disease was reduced. In total, 32% of women resistant to platinum analogs and 38% of those treated with platinum who relapsed within 6 months after the treatment responded to paclitaxel treatment. Moreover, 1000 of the patients, 22% responded despite their poor condition. Docetaxel has not been used as extensively as paclitaxel but has shown promising results in phase 4 trials. Among 51 patients who were platinum-resistant, 41% of them responded to docetaxel treatment. (Eric, 1997)

Chapter Four

Result and Discussion

4. Results and Discussion

In Table 3.1, the details of the participants on the basis of religion are shown in percentage. As we can see that 76% of the participants were Muslims, 22 % of them were Hindu, and only 2 % were Christians.

Table 4.1: Percentage of participants based on their religion

Variable name	N (%)
Religion	
Muslim	76
Hindu	22
Christian	2
Total	100

From the following figure 3.2, we can get the ratio of male and female participants in the survey. It indicates that maximum percentage of the sample population (74%) were female while the male patients lacked in number (26%).

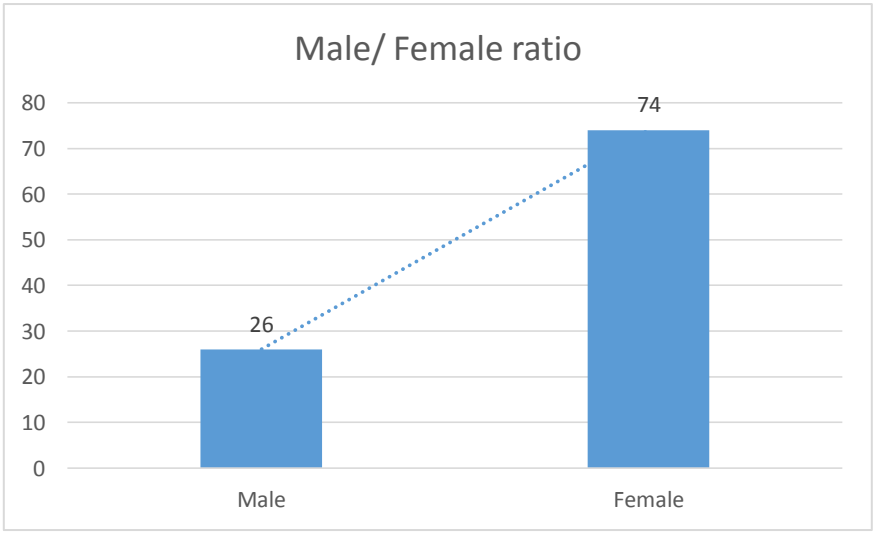

Figure 4.1: The percentage of Male and Female in the participants

Another figure 3.3 shows the percentages at which maximum participants were diagnosed with cancer. As shown in the table, the percentiles are- stage I (18%), stage II (46%), stage III (30%) and stage IV (6%).

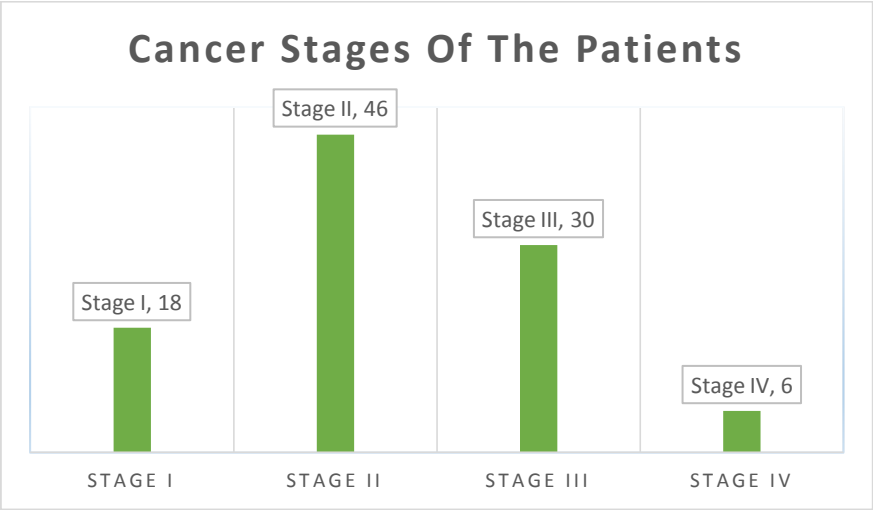

Figure 4.2: Percentage of stages of cancer in the cancer patients

When a frequency table was prepared between two variables- age and type of cancer where age was a scalar variable and type of cancer was a nominal variable. The following table shows the percentage of participants having different types of cancer. The survey was performed on the patients receiving follow-up treatment at the gynecology department and medical oncology department of NICRH. Most of the patients were found to be suffering from breast (36%) and cervical cancer (36%) and a small portion suffered from throat cancer (28%).

Table 4.2: Percentage of types of cancer acquired by the cancer patients under the survey

Type of cancer	N (%)
Breast cancer	36
Cervical cancer	36
Throat cancer	28
Total	100

Correlation was run in SPSS using two variables to find the correlation between stage of cancer and the cycles of chemotherapy required to eradicate the tumor cells. Here, the pearson correlation was used to determine if the results were significant or not. The pearson correlation in this case is measured to be .611 and the significance is at .000 level which is less than 0.05. Hence, it is safe to assume that there is a positive correlation between the stage of cancer patients and the number and cycles of chemotherapy given to the patient overtime.

By running a correlation analysis between the type of cancer patients and the type of chemotherapy they received (neoadjuvant/adjuvant/palliative/concurrent) during their treatment period, it was found that a total of 18 of them were breast cancer patients, 18 were suffering from cervical cancer and 14 of them were being treated for throat cancer. According to the pearson chi-square test of the crosstabs analysis, p value = -.021. So, it points out to a negative correlation between the two variables. As for the table 3.6, it lists the correlation between the type of cancer and type of medicine given to the patients. It can be estimated that the cisplatin-based drugs (17) are more often used to treat the type of cancer patients.

Next in line are the hormone derivatives and the antibiotic or antifungal drugs. In the bar chart (figure 3.6), we can see that a large part of the breast and cervical cancer patients are being treated with cisplatin-based drugs while the patients with throat cancer are mostly treated with antifungals or antibiotics. According to the data stated previously, there is an increasing amount of cancer occurrences in the Muslim (76%) people than others (24%). This may indicate a prevalence of cancer in the population under survey. From the point of view of gender in this study, the females are under massive risk than males. They constitute 74% of the cancer patients in the population. The value coincides with the data suggested by the table 3.2, as most of the patients were female and it is a fact that the women have natural tendency to get affected by breast cancer from birth.

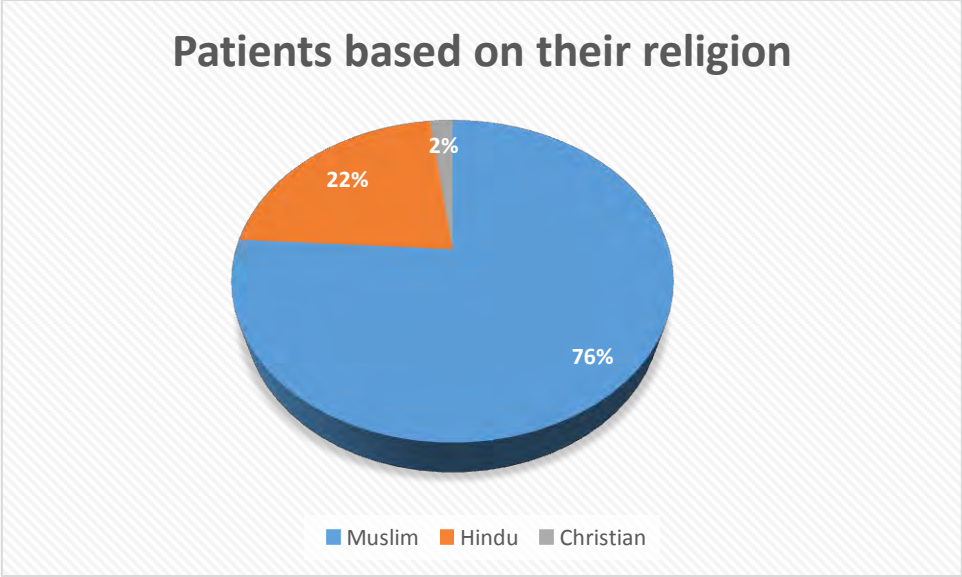

Figure 4.3: Percentage of cancer patients by religion

A similar type of study was conducted on patients detected with Familial adenomatous polyposis which showed that the cumulative prevalence for men and women at the age of 44 years 0.52 and .61 respectively. (Takeo et.al., 1993). The cancer patients are admitted to the hospital or seek intensive care right around the second stage of cancer, as implied by the figure 3.3. It can be clearly seen that the larger portion of the patients are diagnosed with cancer at stage II and stage III due to the apparent nature and growth of the cancer cells. At stage I, the cancer cells are usually non-invasive and the test results are mainly inconclusive. Moreover, at stage IV, there is involvement of metastasis to vital organs and the lymph system which is inoperable in most cases. This could answer the fluctuations in percentages among the data sets. In case of drug of choice, the platin based drugs are used exceptionally in NICRH for solid and progressing cases of tumors. This therapy may be of empirical use due to the bifunctional action of the alkylating agents that are most potent in cases of rapidly progressing and recurring tumors.

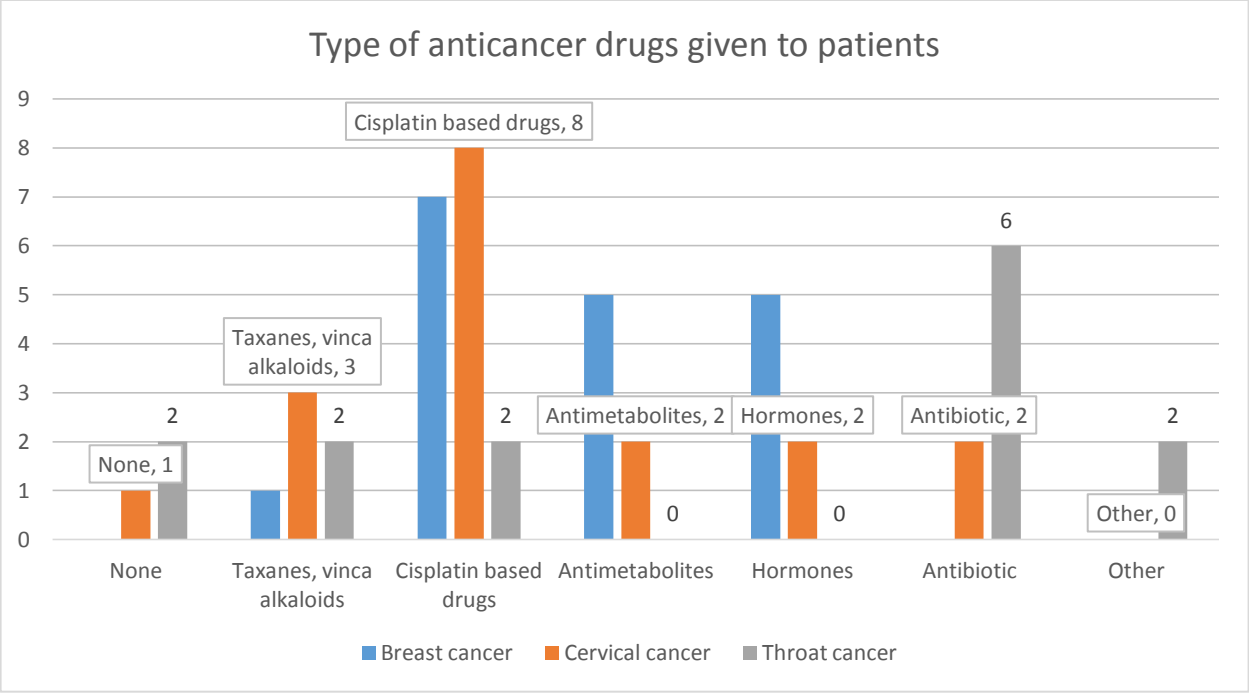

Figure 4.4: Type of anticancer drugs given to patients

Though the taxane alkaloids provided much evidence in accord to the data gathered from literatures, they had not gained that much use in treating patients of NICRH. The minor application of the taxane derivatives can be implied to the unpredictable results of the drugs or slow action. The figure shows that maximum numbers of cervical cancer patients were being treated with concurrent chemotherapy. Added to that, the patients with breast cancer and cervical cancer were larger in number than the ones with throat cancer.

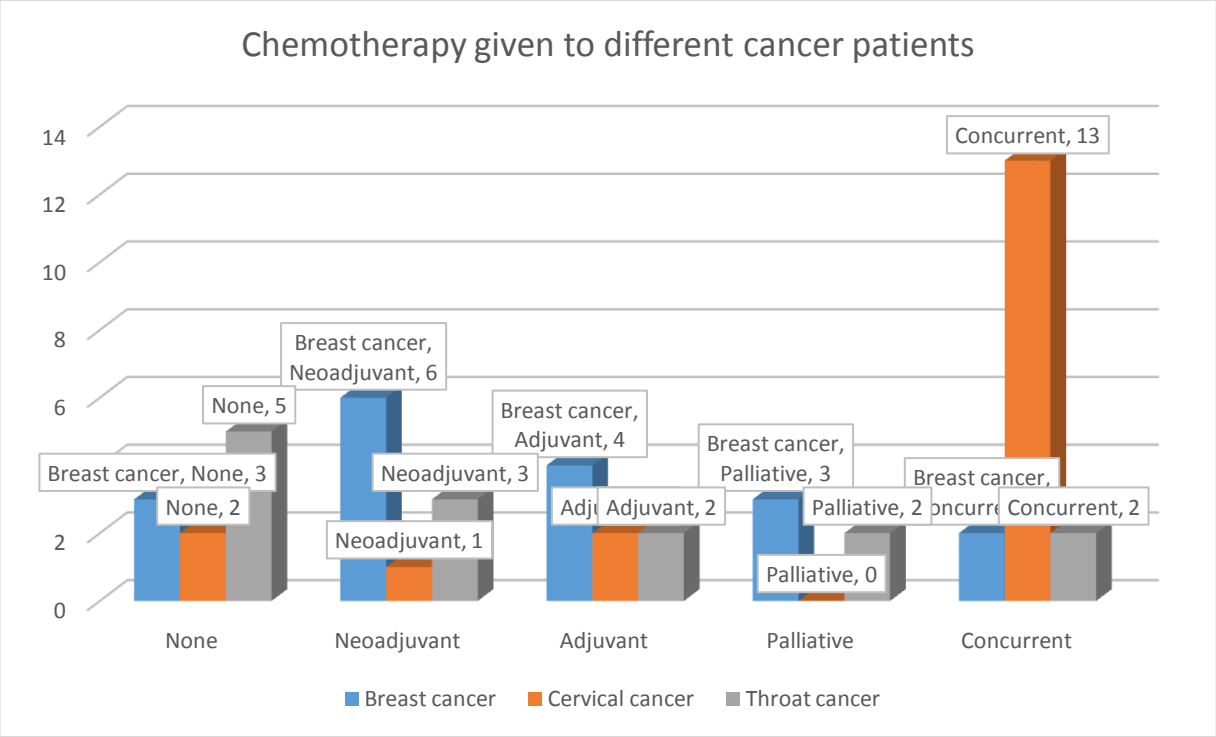

Figure 4.5: Different types of chemotherapy advised to patients

A bar chart is also shown in figure 3.7 which shows the different levels of cancer patients who are receiving distinct types of chemotherapy according to their cancer type. It shows that the cervical cancer patients stand out as the largest portion that are getting the concurrent type of chemotherapy during their treatment in the hospital.

Chapter Five

Conclusion

5. Conclusion

Over the next few years, hopefully a new era of potent anticancer agents will be discovered. Many of them will have different mechanism of action, with different targets in each case. It is tiresome to detect which anticancer agent has the most potential to be used as empirical line of therapy but the agents targeting angiogenesis, signal transduction pathways and tumor invasion and metastasis are gaining higher grounds in comparison to the selective anticancer agents.

The alkylating agents, mainly cisplatin is mainly used in NICRH to treat rapidly growing tumors. But the use of taxane alkaloids (paclitaxel) are also used in these cases. Though the use of alkylating agents are safer due to their well-known efficacy, the plant derivatives should also be taken under consideration to develop better strategies to cope with cancer.

5.1.Limitations

There were some limitations to the study which are stated below:

- Additional lab test results could not be appended due to patient privacy matters
- The Department of Epidemiology of NICRH was not capable of providing information about patient follow-up.

Chapter Six

References

6. References

Backendorf, C., Visser, A. E., Boer, A. G. de, Zimmerman, R., Visser, M., Voskamp, P. Noteborn, M. (2008). Apoptin: Therapeutic Potential of an Early Sensor of Carcinogenic Transformation. Annual Review of Pharmacology and Toxicology, (48), 143–169.

Carmichael, J. (1994). Cancer Chemotherapy: Identifying Novel Anticancer Drugs. British Medical Journal, 308(6939), 1288–1290. Retrieved from http://www.jstor.org/stable/29723544

Chabner, B. A. (2006). General Principles of Cancer Chemotherapy. In L. L. Brunton, B. A. Chabner, & B. C. Knollmann (Eds.), *Goodman & Gilman's The Pharmacological Basis Of therapeutics*: McGraw-Hill Companies, Inc.

Einzig AI,Wiernik P, Sasloff J, et al. 1992. Phase II study and long-term follow up of patients treated with taxol for advanced ovarian adenocarcinoma. J. Clin. Oncol. 10:1748–53

Gibbs, J. B., & Oliff, A. (1997). The Potential Of Farnesyltransferase Inhibitors As Cancer Chemotherapeutics1. Annual Reviews Inc., (37), 143–166.

H P Rang, M. M. D., J M Ritter, R J Flower, Henderson. (2007). *Rang & Dale's Pharmacology, 7th Edition*.

Hong, W. K., Bast, R. C., Hait, W. N., Kufe, D. W., Pollock, R. E., Weichselbaum, R. R., . . . III, E. F. (Eds.). (2010). *Cancer Medicine* (8 ed.). Shelton, Connecticut: People's Medical Publishing House.

Iwama, T., Mishima, Y., & Utsunomiya, J. (1993). The Impact of Familial Adenomatous Polyposis on the Tumorigenesis and Mortality at the Several Organs. ANNALS OF SURGERY, 217(2), 101–108.

Johanson, G. A., & Brooks, G. P. (2010). Initial Scale Development: Sample Size for Pilot Studies. Educational and Psychological Measurement, 70(3), 394–400.

Karnofsky, D. A., & Clarkson, B. D. (1963). Cellular Effects of Anticancer Drugs. Annual Reviews, (3), 357–428.

Kohn EC, Sarosy G, Bicher A, et al. 1994. Dose-intense taxol: high response rate in patients with platinum-resistant recurrent ovarian cancer. J. Natl. Cancer Inst. 86:18–24

Lewin, B. (2004). *GENES VIII* (Vol. VIII). Upper Saddle River, NJ: Pearson Prentice Hall.
Manfredi JJ, Horwitz SB. 1984. Taxol: an antimitotic agent with a new mechanism of action. Pharmacol. Ther. 25:83–125

McGuire WP, Rowinsky EK, RosensheinNB, et al. 1989. Taxol: a unique antineoplastic agent with significant activity in advanced ovarian epithelial neoplasms. Ann. Intern. Med. 111:273–79
Olsen, C., & St. George, D. M. (2004). Cross-Sectional Study Design and Data Analysis. The Young Epidemiology Scholars Program.

Rowinsky EK, Donehower RC. 1995. Drug therapy: paclitaxel (Taxol). N. Engl. J. Med.332:1004–14

Rowinsky, E. K. (1997). The Development and Clinical Utility of the Taxane Class Of Antimicrotubule Chemotherapy Agents. Annual Reviews Inc., (48), 353–374

Sarosy G, Kohn E, Stone DA, et al. 1992.Phase I study of taxol and granulocyte colony-stimulating factor in patients with refractory ovarian cancer. J. Clin. Oncol. 10:1165–70

Thigpen T, Blessing J, Ball H, et al. 1994. Phase II trial of paclitaxel in patients with progressive ovarian carcinoma after platinum-based chemotherapy: a Gynecological Oncology Group study. J. Clin. Oncol.12:1748–53

White, R. J. (1982). Michobiological Models as Screening Tools for Anticancer Agents: Potentials and Limitations. Annual Reviews Inc., (36), 415–33.

Bissery, M., Nohynek, G., Sanderink, G., & Lavelie, F. (1995). Docetaxel (Taxotere®) a review of preclinical and clinical experience. Part I. *Anti-Cancer Drugs, 6*(3), 339-355. doi:10.1097/00001813-199506000-00001

Manfredi, J. J., & Horwitz, S. B. (1984). Taxol: an antimitotic agent with a new mechanism of action. Pharmacology & Therapeutics, 25(1), 83-125. doi:10.1016/0163-7258(84)90025-1

Ringel, I., & Horwitz, S. B. (1991). Studies With RP 56976 (Taxotere): A Semisynthetic Analogue of Taxol. *JNCI Journal of the National Cancer Institute, 83*(4), 288-291. doi:10.1093/jnci/83.4.288

Chen, Y. (2003). Paclitaxel plus gemcitabine may be as active and well tolerated as paclitaxel plus carboplatin for advanced non-small-cell lung cance. *Cancer Treatment Reviews, 29*(1), 69-71. doi:10.1016/s0305-7372(02)00127-5

P. (2013). The Role of Paclitaxel Albumin-Stabilized Nanoparticle Formulation (Nab-Paclitaxel) in the Treatment of Breast Cancer: A Short Review. *Global Journal of Breast Cancer Research*. doi:10.14205/2309-4419.2013.01.01.6

Webster, L., Linsenmeyer, M., Millward, M., Morton, C., Bishop, J., & Woodcock, D. (1993). Measurement of Cremophor EL Following Taxol: Plasma Levels Sufficient to Reverse Drug

Exclusion Mediated by the Multidrug-Resistant Phenotype. *JNCI: Journal of the National Cancer Institute, 85*(20), 1685-1690. doi:10.1093/jnci/85.20.1685

Tsuji, K., Ueno, A., & Ide, T. (1992). Inhibitory Effect of Taxol, a Microtubule Stabilizing Agent, on Induction of DNA Synthesis is Dependent upon Cell Lines and Growth Factors. *Cell Structure and Function, 17*(2), 139-144. doi:10.1247/csf.17.139

Schafer, W., Kim, R., Sterne, R., Thorner, J., Kim, S., & Rine, J. (1989). Genetic and pharmacological suppression of oncogenic mutations in ras genes of yeast and humans. *Science, 245*(4916), 379-385. doi:10.1126/science.2569235

Protein Prenylation PART A. (2011). *The Enzymes*. doi:10.1016/c2009-0-62381-3

Protein Prenylation Part B. (2011). *The Enzymes*. doi:10.1016/c2010-0-66763-0

Armstrong, S. A., Hannah, V. C., Goldstein, J. L., & Brown, M. S. (1995). CAAXGeranylgeranyl Transferase Transfers Farnesyl as Efficiently as Geranylgeranyl to RhoB. *Journal of Biological Chemistry, 270*(14), 7864-7868. doi:10.1074/jbc.270.14.7864

Appendix A

Questionnaire

Practice of Using Plant and Synthetic Derivatives of Anticancer Drugs Among Cancer Patients at NICRH, Bangladesh

- Age-
- Religion- ☐ Muslim ☐ Hindu ☐ Christian
- Sex- ☐ Male ☐ Female
- Weight-
- Occupation- ☐ Service holder ☐ Unoccupied
- Residence- ☐ Rural ☐ Urban ☐ Semi-urban
- Anyone else in the family has cancer- Yes/No, If yes, mention the type and location of the cancer here—
- Location

- Type of Cancer--- ☐ Breast Cancer ☐ Cervical Cancer ☐ Throat Cancer
- Stage of cancer- ☐ St- I ☐ St- II ☐ St.-III ☐ St- IV
- Metastases to other organs- Present /Absent
- Cycles of chemotherapy received—
- Cycles of radiotherapy received—

↳ Type of chemotherapy being administered—

- ☐ Neoadjuvant
- ☐ Adjuvant
- ☐ Palliative
- ☐ Concurrent
- ☐ None

i) Throat cancer

- Other environmental factors than smoking-
- Diagnosis- Mainly focused on X-ray results but biopsy results may be of importance too.
- Treatment—

ii) Breast cancer

- Diagnosis- The results of mammogram, biopsy, or breast exam can detect the breast tumors faster.
- Treatment- In case of endocrine therapy, the presence, or absence of estrogen and progesterone-receptor protein in primary or metastatic tumor tissue is used to predict the use of ablative or additive line of therapy.

iii) Cervical cancer

- Diagnosis- In case of cervical cancers, the Pap test holds most importance. Biopsy results will indicate the stage of the tumor.
- Treatment-

In all cases of treatment, the dose intervals may vary overtime to cope up with the side effects that present with the administration of the drugs over long hours.