

COLORECTAL CANCER AND NOVELTY IN THE TREATMENT**^{1*}Mohit Das, ²Dr. Biswajit Das and ³Dr. Junmoni Kalita**^{1,2,3}Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hatkhowapara, Azara, Guwahati -781017.Article Received on
24 June 2020,Revised on 15 July 2020,
Accepted on 05 Aug 2020,

DOI: 10.20959/wjpr20209-18363

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Pharmaceutics, Girijananda
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Colorectal cancer (CRC), it is the main source of demise in gastrointestinal cancer, additional major source of passing away associated to cancer and worldwide third furthest mutual disease in both men and women. The hazard of colorectal cancer may develop due to the immoral alimentary behaviours, smoking, colonic provocative disease, polyps, hereditaries factors and aging. Inflammation may also associate with the developing cancer which may lead to the severity of the disease, signifying that removing inflammation can epitomize an effective approach for cancer deterrence and therapy. Due to the anti-inflammatory possessions, the nonsteroidal anti-inflammatory drugs (NSAIDs) have been examined for its anticancer belongings in several revisions. This is for the reason that chronic

inflammation for a while related to carcinogenesis. By and of itself, anti-inflammatory drugs are supposed to perform a character in cancer prevention and therapy. Since, monotherapy is usually not a satisfactory treatment of cancer, the collective practice of anti-inflammatory agents and conformist cancer therapy is correspondingly a crucial fact in discussion. This article explores the idea how colorectal cancer start and spread, what are its medication, what are the novelties in treatment and current status of anti-inflammatory agents in cancer treatment.

KEYWORDS: Anti-inflammatory agents, Colorectal cancer, Novelties in treatment, Targeting inflammation.

1. INTRODUCTION

Cancer is a kind of ailment or condition considered by the unrestricted partition and being of anomalous cells. Cells in almost any part of the body can turn out to be cancer, and can

extended to other areas of the body. When this kind of irregular cell evolution arises in the colon or rectum, these are termed as colon cancer or rectal cancer, depending on where they begin. Colon cancer and rectal cancer are habitually convened together for the reason that they have been several attributes in common and it is so-called colorectal cancer.^[1]

The colon and rectum (colorectum), which united are raised to as the large intestine, are the last portion of the gastrointestinal system, which progresses food for energy and liberates the body of solid leftover. After chewing and swallowing, food passes through the oesophagus to the stomach and broken down. From stomach it enters to the small intestine, where maximum of the nutrient is engrossed. In the lower right abdomen, the small intestine joins the large intestine. Colorectal cancer is infrequently mentioned as bowel cancer as because the small and large intestine are now and then called the small and large bowel. Colon is the initial fragment of the large intestine which measures 1.5 meters long and in diameter it is about 5 centimetres.

The colon is separated into 4 segments

- The ascending colon initiates from the cecum and ranges up to the right adjacent of the abdomen. (Cecum is a sack which sustained undigested food after the small intestine)
- The transvers colon proceeds from right to the left side of the abdomen. The ascending and transvers colon are collectively named as the proximal colon.
- The descending colon goes down on the left side.
- The sigmoid colon is referred as the ultimate segment of the colon, which joints rectum. It is “S” shape like structure. The descending and sigmoid colon are mutually denoted as the distal colon.^[2]

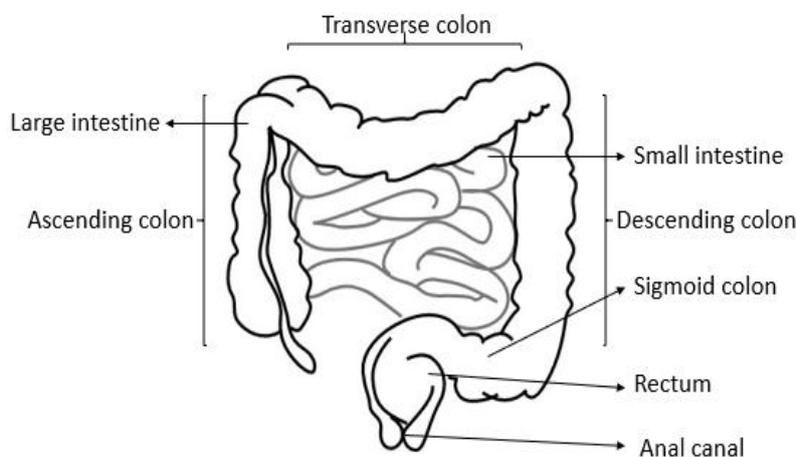


Fig: Anatomy and physiology of colon.

1.1 Stages of colorectal cancer

The 2-utmost familiar cancer staging systems are TNM system and SEER system.

TNM system: it is typically used in clinical settings, in TNM system-

- T denotes the magnitude and degree of the core tumor. The core tumor is generally termed as primary tumor.
- N denotes the amount of neighboring cancerous lymph nodes.
- M denotes whether the cancer has metastasized or not. This indicates that the cancer has extended from core tumor to the further body parts. ^[3]

SEER system: the descriptive as well as statistical analysis of tumour is done by this system.

- In situ: Cancer which haven't yet initiated to entered the barrier of the colon or rectum.
- Local: Cancer that developed into the barrier of the colon or rectum, but haven't prolonged to the barrier to occupy the adjoining tissues.
- Regional: Cancer that have grown to the barrier of the colon or rectum and have attacked adjacent tissues.
- Distant: Cancer that have proliferated to further vital body parts, as for example liver or lung etc. ^[2]

1.2 Types of cancer in the colon and rectum

Adenocarcinomas forms near about 96% of colorectal cancers. These cancerous cells form mucus which lubricate the inner lining of large intestine. Others kinds of tumours may also grow in colon and rectum, too. These are as follows:

- Carcinoid tumours: Carcinoid tumours are developed from special intestinal cells which can make hormones.
- Gastrointestinal stromal tumours (GISTs): GISTs develop from interstitial Cajal cells, the special cells found in the barrier of the colon. These are not usually institute in the colon but anywhere in the digestive tract.
- Lymphomas: These are the cancers of immune system cells. They generally develop in the lymph nodes, but they may also grow in colon, rectum, or further tissues.
- Sarcomas: Sarcomas are normally developed in the blood vessels, muscle layers, or supplementary connective tissues in the barrier of the colon and rectum. ^[1]

1.3 Symptoms of colorectal cancer (CRC)

Initial stages of colorectal cancer are habitually unnoticeable that is why regular screening is important. As the tumour grown up, it may cause bleeding or blocking the intestine. Unusual loss of blood in some cases of cancer can cause Anaemia (less count of RBCs), faintness and sometimes dyspnea in patients. Additional cautionary symptoms of the colorectal cancer are comprising:

- Loosing blood from the rectum
- Having a bowel movement and blood in the faeces
- Unusual colour such as darkish or blackish faeces
- Alteration in bowel behaviour or the form of faeces
- Uneasiness in the lower side of abdomen
- When the bowel is empty an appetite to have a bowel movement
- Constipation or diarrhoea
- Reduced hungriness
- Losing weight ^[2]

1.4 Beginning of Colorectal Cancer

Colorectal cancer usually activates as a polyp. Most of the colorectal cancers initiate as an extension on innermost wall of the colon or rectum. These kinds of progressions are termed as polyps. Furthermost, these polyps can become cancerous.

Two types of polyps are there

- Adenomatous polyps: These polyps from time to time develop into cancer if it is left untreated. These are generally considered as pre-cancerous condition of cancer.
- Hyperplastic polyps and inflammatory polyps: Most commonly found polyps and not having a risk to develop into cancer.

Additional aspects that can turn a polyp into a risk of evolving colorectal cancer in people includes:

- If the size of polyp become bigger than 1 cm
- Presence in excess of two polyps
- After removal of polyp if dysplasia is seen. Dysplasia refers to a part in polyp where the cells appear irregular, that takes part in the development of enlarged tissue or precancerous cells. Dysplasia is another precancerous condition. ^[1]

1.5 Spreading of Colorectal cancer

Initially cancer begins as a polyp, furthermore it can raise over the time into the barricade of the colon or rectum. The wall of the colon and rectum comprises of several layers. Colorectal cancer begins in the inmost layer called mucosa and spread to the layers.

After evolving the cancer cell in the barrier of colon and rectum, they slowly spread into the blood vessels or lymph vessels which transfer leftover fluids. Then they further develop to adjacent or other tissue of the body.

Basically, the phase of a colorectal cancer or degree of spreading of a colorectal cancer be contingent on how intensely it raises the barrier and how much it has affected exterior part of the colon or rectum.^[1]

2. COLORECTAL CANCER RISK FACTORS

The risk of colorectal cancer is accumulating gradually to the unhealthy lifestyle of the people, their diet plan, smoking, consumption of alcohol etc. People who have a well lifestyle, active physically, consumption of limited alcoholic liquor and maintaining healthy diet have lower risk of CRC.

Apart from these, there are some other factors like history of inheritance and medical cases, individual or personal history related to CRC or adenomatous polyps and an individual history of chronic inflammatory bowel disease can also intensification the risk of colorectal cancer.

The reasons associated with CRC risk are briefly discussed below: -

2.1 Heredity and family history

30% CRC patients have affected due to their family history and 5% about them have congenital abnormalities. People having 2 to 4 times risk of CRC those who already have a family history related to the ailment than the people not having any family history, depending on the affected relatives.

Among all the cases of CRCs, 5% are of Characterized hereditary syndromes associated with specific gene mutations. Lynch syndrome, formerly called as hereditary nonpolyposis colorectal cancer or HNPCC is the most commonly hereditary CRC syndrome which is near about two to four percent of all cases. Lynch syndrome in people may develop into a widespread variation of other cancers such as endometrial, ovarian, small intestine, and

stomach. An estimation of 18% men and 19% women of all people those who have Lynch syndrome, will affect CRC by age fifty, and growing over the time to 45% and 54% in men and women respectively, by age 70. ^[2]

The another most common predetermining genetic syndrome is Familial Adenomatous Polyposis (FAP), estimating for lesser than one percent of all CRCs. 100 to 1000 of colorectal polyps develops due to the Familial adenomatous polyposis starting at the age of 10-12 years. The severity of CRC reaches 100% by age forty, if it is left untreated. FAP causing genetic mutation is generally inherited and can also happen normally, thus the peoples those who don't have a family history of the disease they may also be affected by FAP. The typical technique of cancer preclusion is surgery for person affected with FAP. There is increasing attention in refining the identifying approaches for high-risk persons and families as of early detection as well as large potential for CRC prevention. Also, people with genetic tendency for CRC are also at risk for additional cancers. Diagnosing peoples with high risk permits the chance for screening surveillance, which has been helped to lessen CRC and death rate by partial in people having Lynch syndrome. Though, removal of polyp can't reduce all cancers, yet there is growing importance on chemoprevention, for example with nonsteroidal anti-inflammatory drugs such as Aspirin. Though, there are at present no medicines appropriate for CRC deterrence in high-risk patients, yet aspirin rehabilitation noticeably condenses the risk of CRC cancer amid Lynch syndrome patients. ^[2]

2.2 Personal medical history

Individuals having an own history of CRC are further prospective to evolve a consequent cancer in the colon or rectum, particularly when the early analysis was at an early stage. The history of adenomatous polyps especially multiple polyps also rises the risk of CRC. ^[2]

Chronic inflammatory bowel disease

The chances of CRC become double in case of people having chronic inflammatory disease compared to general individuals. Ulcerative colitis and Crohn disease are most commonly observed inflammatory bowel disease. Severity of disease may increase with the extent and duration of time then has lessened over time, probably as a result of regular practice of medication to prevent inflammation and screening surveillance to notice premalignant lacerations. ^[2]

Diabetes

Individuals with type 2 diabetes have higher risk of CRC. Type 2 diabetes and CRC have several mutual aspects like corpulence and an inactive lifestyle and this alliance relies even subsequently considering of physical exercise, body mass index, and middle circumference. Metformin, drug used for lowering blood glucose level also reduces the chances of CRC independently.^[2]

2.3 Behavioural risk factors**Physical activity**

Physical exercise is mainly accompanied only by means of lowered menace of colon cancer, not in rectal cancer. People those who are physically not active have 25% higher the risk of both proximal and distal tumour than physically active people. Moreover, peoples are less likely to die who are physically fit before diagnosis of CRC than not as much of active people. Additionally, most sedentary people have 25% to 50% higher risk of the disease than less sedentary people. Even less sedentary people can reduce the risk of cancer by physically active themselves later on in life.^[2]

Overweight and obesity

CRC increases according to the excess body weight connotation in men than women. Obese men have 50% higher risk of colon cancer whereas in women it is about 20% and in case of rectal cancer men have 20% higher risk while women have about 10% increased risk. Obesity is not dependent upon physical exercise that deliberated the risk of the disease. Abdominal obesity also increases risk when measured by waist circumference, however the practice of body mass index along with waist circumference may be an additional effective sign of severe risk than any measurement alone. Being overweighed in initial maturity versus later in life have more effected on CRC. Moreover, measurement of high body weight in early stage of diagnosis controls the chances of CRC survival. Metabolic health has a negative impact due to the excess body weight and current practices shows that low metabolic fitness may be associated to CRC occurrence and subsistence self-determining of obesity.^[2]

Diet

Diet strongly influenced in the risk of CRC incidence.^[2] Unplanned diet may affect on the health of an individuals by both direct and indirect way. Direct influence includes definite nutritional fundamentals and indirect influences are excessive nutrition and obesity.

The straight character of definite nutrition in cancer incidence is not very easy to estimate for various motives, including

- Problem in outlining and determining diet ingestion, for example problems in the precision of self-reported diet surveys.
- Alterations in the causes of alimentary ingredients and
- The strong association amid nutritional designs and further fitness behaviours.

The summary of the present specific indication for nutrition allied to CRC are as follows

Calcium

Observations shows that calcium consumption from dairy products and supplements diminished the risk of evolving adenomas and CRC. Satisfactory calcium consumption seems to deliberate safety, with partial extra assistance for complex consumption. Furthermore, the connotation may necessitate years to continuation to perceive and be restricted to cancers in the distal colon and rectum.^[2]

Fibre

Even if it is extremely practical that dietetic fibre depresses the hazard of CRC for several causes, for example not as much of interaction to carcinogens for the reason that of more bulk faeces and quicker transfer time, study results, including those from randomized measured trials, keep on indecisive. The American Cancer Society and The World Cancer Research Fund recommends a nutritional plan full of whole grains, fruits, and vegetables for the preclusion of cancer for the reason that of the total health assistances of a fibre-rich diet.^[2]

Folate

Folate including diet or supplements potentially promote the growth of pre-existing tumours but inhibit the development of novel tumours in well tissue that look as if to have a compound affiliation with CRC risk.^[2]

Fruits and vegetables

From several studies specifically evaluating it was found that the interrelation amid fruits and vegetable consumption and CRC risk are varying.^[2]

Red and processed meat

Red and processed meat consumption rises the risk of both colon and rectal cancer. The reason behind it remain uncertain, but may be associated to the components of meat and/or to hazards that occur at the time of high-temperature cooking, curing, and/or smoking.^[2]

Vitamin D

Lower risk of CRC may be associated with the higher blood levels of vitamin but this result is remained questionable. Recently observed that regular consumption of vitamin D did not lessen the danger of adenomas. Upcoming statistics from numerous clinical trials assessing the consequence of vitamin D supplementation on cancer inhibition may aid to elucidate this interrelation.^[2]

Smoking

According to the International Agency for Research on Cancer in November 2009, informed that there is sufficient indication to accomplish that tobacco smoking origins CRC. This interrelation appears to be severe for rectal than for colon cancer and for specific molecular subclasses of CRC.^[2]

Alcohol

Moderate and heavy alcohol consumption may increase the risk of CRC. Individuals who have a lifespan usual of 2-3 drinks per day and more than 3 alcoholic drinks per day have a higher possibility of CRC as compared of non-drinkers and occasional drinkers.^[2] Due to hormone-related differences in men and women this association is vary according to the alcohol metabolism.

3. MEDICATION**Nonsteroidal anti-inflammatory drugs**

There is wide indication that continuing regular habit of Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) reduces the chance of CRC. Individuals having CRC but using Aspirin from long time ago have lesser hostile tumours and improved endurance related to non-Aspirin users. The US Preventive Service Task Force lately skilled an analysis of the indication and acclaims of Aspirin for preclusion of cardiovascular disease and CRC but in low dose for some peoples in their 50s who are at high danger of the cardiovascular disease and less convincing in 60s.^[2]

Hormones

There is inconsistent evidence between the association of postmenopausal hormone use and CRC. Recent studies find that in women lower the risk of CRC with recent use of the hormone, continuing addition data from randomized controlled trials get no expressive suggestion. Alterations in the connotation by cancer subclass and drug preparation partially elucidate these variations. Likewise, even though an earlier suggestion presented that topical oral contraceptive use is correlated with decreased CRC hazard, current analysis do not accept this suggestion.^[2]

Other drugs

Current analysis proposes that oral bisphosphates, which are used in the treatment and inhibition of osteoporosis, may reduce CRC hazard.^[2]

4. NOVELTY IN COLORECTAL CANCER RESEARCH

In the area of colorectal cancer, study is continuously ongoing. In the research, the field of interest for researchers are finding out sources and paths to control colorectal cancer, improved methods of initial diagnosis and ideas to progress medications. Only by means of clinical trial we can achieve these treatments. Some recent researches are illustrated below:^[1]

Reducing colorectal cancer risk

Various ongoing revisions are observing to recognize the sources of colorectal cancer. This might be helpful to identify and control it.

Even researchers are searching to get if particular kinds of diets, dietary additions, or medicines can diminish the hazard of colorectal cancer. From several revisions it has seen that Aspirin and pain killers may help to reduce the chance of colorectal cancer, but then side effects of these drugs may be encountered.^[1]

Early detection

Medics are searching for improved methods to detect colorectal cancer at initial stage via observing novel forms of screening tests and modify the existing methods. Professionals are also concentrating to find out if there is any assessment or screening test that obviously works best. Moreover, anticipating paths to aware the individuals to conduct the periodical screening tests^[1] and recognized to support decrease the numeral demises from this disease.

Diagnosis

Scientists are examining to describe colorectal cancer sub-classes classified on the hereditary alteration in the cancer cells, in what way the cells appear and perform, rate of cell division, and structures of the tumour itself. This might bring about well consideration of disease development and consequences, in addition to further evidently well-defined treatment strategies.

Lab tests to help plan treatment

Laboratory experiments have been established for assistance to guess colorectal cancer reappearance, the cancer reverting later treatment. These trials help to recognise diverse genetic factor in the colorectal cancer cells and being premeditated to observe which treatment strategy is best for one and all. This might as well useful in determining whether further action is required afterwards surgical procedure.

Researchers are trying to know further around the genetic variations in colorectal cancer cells, similarly in search of effective methods to expect consequences and regulate action for the patients.

Surgery

Improvisation in operations are under progress by the surgeons for the colorectal cancer treatment. They are observing at the aids of laparoscopic and robotic surgeries in comparison to open surgeries after larger lacerations are done. Rectal cancer surgery is also being studied which done through the anus, without any cutting.

Sometimes after persisting of colorectal cancer, it extends to the peritoneum and these are habitually tough to treat. But lately specialists have been applying a technique termed as Hyperthermic Intraperitoneal Chemotherapy (HIPEC).

In HIPEC, earliest operation is accomplished to eliminate the cancer from the belly as much as possible. Then, the abdominal cavity is carefully treated in warmth chemotherapy drugs. This helps the chemo for its requisite action to the specific site of cancer cells, and the warmth is supposed to assistance the drugs for the improved action.^[1]

Chemotherapy

Chemotherapy is the most significant step of action for individuals with colorectal cancer, and researches are continuing to accomplish it further active and harmless. For this regard, several strategies are confirmed in clinical trials, counting:

- Trying of novel chemo medicines as well as medicines that previously being utilized in contradiction of additional type of malignancies.
- Searching aimed at best combination of the known drugs that are effective for the colorectal cancer to find out if they effort improved together.
- Searching the greatest conducts to associate chemotherapy along with radiation therapy, targeted therapy, and immunotherapy for improved efficiency.^[1]

Targeted therapy

Targeted therapy drugs acts on specific fragments of cancer cells that varies them dissimilar as of typical cells. They act in another way from usual chemotherapy treatments. Although, numerous targeted therapy drugs are used in the treatment of progressive colorectal cancer, investigators are still searching the right technique to deliver these medicines and finding for different targeted therapy drugs. Researchers are also searching colorectal cancer cells for explicit gene mutations that might be addressed as portion of cancer therapy. Researches are being performed to check in order that the association of intended therapy with chemotherapy in former phase of cancers can aid to decrease the danger of repetition.^[1]

Immunotherapy

Immunotherapy is an interesting field of zone among the researchers.^[1] Immunotherapy is a sort of cancer medications that support your immune system to contest against malignance.

Immune checkpoint inhibitors

A significant portion of the immune response is to identify the standard cells in the body and others it detects as “external”. This helps the immune response to target only the external cells at the same time parting the standard cells individual. For this regard, on certain immune cells it uses “checkpoint” proteins. These proteins act as switches, and to start an immune response it needs to be turned on or off. Cancer cells are condemned by the immune response through these checkpoints.

Cancer vaccines

Specialists are searching to treat colorectal cancer by using numerous vaccines or keep it away from recurrence after treatment. These vaccines are different from other vaccines that prohibit the disease, these vaccines help to better find and fight colorectal cancer cells by boost up the immune system of an individual.

Several kinds of vaccines are being examined. Such as, some vaccines are made from dendritic cells. Dendritic cells are own immune system cells of an individual which is removed from the tumour and treat them with an element that help them to identify and target the cancer cells, and then placing them return into the individual's inside.

Targeting inflammation for Cancer Therapy

Although numerous tumour properties are there, swelling has turned out to be a goal for cancer anticipation and cure. There are so many kinds of targets, for instance cytokine receptors, chemokine receptor and vascular endothelial growth factor have also been studied but cyclooxygenase 2 (COX-2) is often estimated anticancer anti-inflammatory target.^[4-7] It was already demonstrated that non-steroidal anti-inflammatory drugs (NSAIDs) have colon cancer preventive properties.^[8-9] According to the other clinical trials, longstanding routine of aspirin or other non-steroidal anti-inflammatory drugs helps to reduce the rate of colorectal cancer as well as other cancers such as oesophageal, breast, lung and bladder cancers.^[10] Initially research concentrated on several wide range non-steroidal anti-inflammatory drugs which generally prevent both COX-1 and COX-2 later on researches have analysed celecoxib, a COX-2 specific agents.^[11] But the practice of those drugs remains at issue the use of such agents remains controversial due to the given gastrointestinal harmfulness, irresolute action of NSAIDs^[12] and the cardio activity of COX-2 specific inhibitors.

However, specified that their harmful activity is moderate as related to other chemotherapeutic drugs, several anti-inflammatory drugs are still being examined for cancer treatment and inhibition. Number of anti-inflammatory drugs, like NSAIDs, massive promise against cancer as they can modify the tumours themselves or the tumour microenvironment, potentially reducing migration, growing apoptosis, and cumulative sensitivity to other treatments.^[13-15]

5. CURRENT STATUS OF ANTI-INFLAMMATORY AGENTS FOR CANCER THERAPY

There are several FDA-approved anti-inflammatory drugs are there for preventing inflammation which serves a key role in chronic ailment, counting cardiovascular disease, diabetes, psoriasis, arthritis and cancer.^[16] These drugs also express additional significant for example anti-thrombotic, anti-emetic, anti-angiogenic, pro-apoptotic activities and antiproliferative,^[17-19] enhancing them effective for cancer treatment and inhibition though they were intended to reduce or avoid inflammation.

NSAIDs

According to the epidemiological data, it suggests that incidence of lung cancer, breast cancer and colorectal cancer is contrariwise associated to the habit of taking aspirin and other nonsteroidal anti-inflammatory drugs.^[20] Additionally, colorectal cancer individuals who were long-standing NSAID consumers had lesser death risk than non-NSAID users.^[21] Randomized studies have established that aspirin can decrease the hazard of colon adenomas and lung cancer in individuals with a former record of adenomas and non-smokers or former smokers respectively.^[22-23] However, in individuals having breast cancer it did not express any lessening in cancer hazard for individuals having aspirin up to 10 years of continuation.^[24] An investigation of figure from research revealed that with prolonged use of aspirin as 300mg per day for less than or equal to 5 years can decrease the chance of colon adenomas after a 10year potential phase.^[20]

Moreover, Sulindac also reduce the polyp count in familial adenomatous polyposis (FAP) individuals and help in prevention from reappearance^[25] and initiate the deterioration of remaining adenomas. Additional NSAIDs, like piroxicam and ibuprofen have also been expressed to reduce the hazard of evolving malignancies in individuals.^[26-28] Thus, there seems to be an important relationship among NSAID practice and reduced rate of main and frequent cancers and diminished death rate, even though the outcomes may differ by the period of follow-up, duration of exposure, dose, and cancer type. FDA approved all these drugs for several signs, and might be included for the treatment of cancer.

Specific COX-2 inhibitors

Beside NSAIDs, novel drugs were intended to prevent COX-2 in an attempt to make extra effective composites with diminished gastro intestinal harmfulness. Commencing clinical studies showed that celecoxib, a specific COX-2 inhibitor, in individuals with FAP induced

substantial deterioration of prevailing adenomas.^[26] Researches have also specified that celecoxib may have activity against ovarian cancer, as well.^[29] Various clinical studies demonstrating that the complexes do not possess substantial useful properties for individuals, so the use of celecoxib and other non-steroidal anti-inflammatory drugs for cancer prevention and therapy remains controversial. Also, due to the partial gastro intestinal harmfulness to cardiotoxicity of NSAIDs agents, less interest for their usage, particularly for cancer preclusion. Due to the consequence of their harmful effects, many COX-2 specific drugs have been remote from the market.

In spite of the removal of Valdecoxib and Rofecoxib, Celecoxib still have a great level of curiosity equally in clinic and in pre-clinical studies. Celecoxib is the only FDA approved nonsteroidal anti-inflammatory drug for individual having familial adenomatous polyposis (FAP).^[30] Currently it is analysed in series of phase II and III clinical trials for both single and in combination with other usual chemotherapeutic agents. Despite of their harmful effects and the disagreement about their cancer prevention and curative action, it is improbable that COX-2 inhibitors will perform a key role in cancer preclusion, though they may characterize fruitful actions when applied as adjuncts with other methods.

Corticosteroids

The corticosteroids, are well known to control the reactions of radiation and chemotherapy, they have as well exposed anti-cancer action either used single or in combination with other usual chemotherapeutic agents. An experimental result shown that the glucocorticoid dexamethasone to A/J mice led to a more than 60% reduce in lung tumour rate.^[31] Analysis have exposed that preliminary treatment with dexamethasone can boost up the activities of traditional treatments counter to animal models of glioma, lung, breast as well as colon cancers. In actual fact, coadministration of dexamethasone led to a 2-4-times intensification in the effectiveness of gemcitabine and carboplatin.^[32-33] A current observation in xenograft model and in cell lines established that dexamethasone therapy consequences in substantial progress reserve of renal cell carcinoma.^[34] Prevention of the growth factor of oestrogen dependent breast cancer can also be inhibited by the dexamethasone by antagonizing oestrogen sulfotransferase.^[35] Moreover, other glucocorticoids, such as prednisone and hydrocortisone, have similarly been demonstrated to inhibit the progress of cancer cells and to reduce the development of in vivo xenograft tumours.^[36,37]

Therefore, anti-inflammatory drugs expected to express promising effect for the therapy of several human cancers. These drugs, mainly the nonsteroidal anti-inflammatory drugs, have been recognized to extend apoptosis,^[14,39] prevent migration,^[13] and decrease angiogenesis^[41,42] of tumours. These epidemiological indication and effects of reduced cancer occurrence and proliferation, driven the several researches about the capability of anti-inflammatory drugs for cancer preclusion and treatment. Although, the outcomes until now have been unsatisfying, these agents may characterize fresh, harmless, drugs for cancer therapy. Though, maximum of the drugs presently used, the anti-inflammatory agents will probably need to apply as portion of a combination regime to attain positive abolition of recognized tumours.

6. CONCLUSION

Besides heredity and family history of the disease, personal medical history and behavioural risk factor also perform a key part in the beginning, development and prediction of cancer. Evolving of inflammation along with the cancer may lead to the severity of the disease. The utilize of anti-inflammatory drugs may help in reductions the occurrence and repetition of many cancers, and can recover the diagnosis for patients. Moreover, the usage of anti-inflammatory drugs in association with standard anti-cancer treatments are beneficial field, and is probable to get various new therapeutic methods for the treatment of cancer in near future. However, the techniques behind these activities are not well-known, a great field of research is still needed to completely illuminate which kind of cells are responsive to cancer preclusion or therapy along with anti-inflammatory drugs. Thus, more study in this field is promised for served the following generation of care for both inflammatory ailments and malignancies.

7. ACKNOWLEDGEMENT

The authors thank the Department of Pharmaceutics of Girijananda Chowdhury Institute of Pharmaceutical Science for all the support.

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