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ORIGINAL RESEARCH ARTICLE

Toxicities Profile of Bevacizumab in Cancer Patients Treated in a Tertiary Care Cancer Institute

Gaurang Gupta[1], Adadi Srinivasa Naidu[2*], Piyush Kumar[3]

ABSTRACT

Introduction: Bevacizumab, a recombinant humanized monoclonal antibody against vascular endothelial growth factor (VEGF), inhibits tumor growth by blocking angiogenesis. Bevacizumab was approved in common solid tumors with high therapeutic need. Overall, bevacizumab is generally well tolerated. Some side effects can be fatal, its critical to determine risk factors, toxicity profile and set up treatment plans to reduce treatment related morbidity and death. The present study aims to assess side effects of bevacizumab mainly hypertension,proteinuria and hepatotoxicity.

Material and Methods: About 25 patients treated with bevacizumab for a time period of 3 months from January 25th to March 25th in the year 2025 were recruited between age group of 18 to 60 years. People unwilling to sign the informed consent form and people who are not showing up on time for therapy or evaluation were excluded in this study. Urine sample were collected for the evaluation of proteinuria, blood sample for checking transaminitis and regular mesearement of blood pressure for hypertension evaluation. All the toxicity were assessed according to CTCAE.

Results: The study shows that bevacizumab is associated with a significantly increased risk of proteinuria and hypertension in patients who received treatment for metastatic cancers of the lung, hepatocellular, gastroesophageal, colorectal, and ovarian. Over 40% of patients show hypertension either as a new onset (20%) or exacerbation of previous hypertension (80%). About 28% of patients had mild or moderate proteinuria, high grade proteinuria was found in only 4% of patients and none of our patient had advanced to nephrotic syndrome. No liver toxicity as all the alanine aminotransferase and aspartate aminotransferase levels were within normal range.

Conclusion: The administration of bevacizumab requires disclosure of the risks and the benefits and alternative therapies to patients in an informed consent-like process. With evolving precision oncology the role of bevacizumab continuous to grow and care givers should be aware of the toxicities of the drug.

Keywords: Bevacizumab, VEGF targeted therapy, Anti-angiogenesis.

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Undergraduate (MBBS)[1]; Assistant Professor[2], Professor[3],

[2]Department of Medical Oncology, [3]Department of Radiation Oncology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

***Corresponding Author:** Adadi Srinivasa Naidu, Assistant Professor, Department of Medical Oncology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India. e-mail: adadivas45@gmail.com

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INTRODUCTION

Bevacizumab, a recombinant humanized monoclonal antibody against vascular endothelial growth factor (VEGF), inhibits tumor growth by blocking angiogenesis. The immediate mechanism of action of bevacizumab is to bind and inactivate VEGF, thereby inhibiting endothelial, and possibly tumor cell activation and proliferation.[1] VEGF inhibition has also been shown to induce so-called vascular normalization, a restoration of normal structure, function, and flow to the disorganized, leaky vessels characteristic of malignant tumors, which improves the delivery of oxygen, nutrients, and cytotoxic chemotherapy to the tumor.[2,3]

Bevacizumab was approved in common solid tumors with high therapeutic need; namely, colon, prostate, lung, breast cancers metastatic non-small cell lung cancer (mNSCLC) metastatic colorectal cancer (mCRC) and metastatic renal cell carcinoma (mRCC) and glioblastoma multiforme.[4-7]

Overall, bevacizumab is generally well tolerated. Its toxicities are usually nonoverlapping with those of cytotoxic chemotherapy but may add to the AEs commonly seen with chemotherapy and, again, its vascular normalization properties are postulated to improve the efficacy of cytotoxic drugs. The novel mechanism of action of bevacizumab is accordingly associated with a unique adverse event profile. The majority of adverse events are mild in severity and manageable, but some do result in significant morbidity and even mortality. In addition, some toxicities – such as bowel perforation in ovarian and mCRC, and pulmonary hemorrhage in squamous NSCLC – are seemingly disease site-dependent. Others – such as mucosal bleeding, hypertension, and proteinuria – are more nonspecific.

The primary objective of this study isto assess side effects of bevacizumab namely hypertension, proteinuria, and hepatotoxicity in cancer patients.

MATERIAL AND METHOD

Study Setting

Tertiary cancer care center in central Uttar Pradesh.

Type of Study

Prospective observational cross-sectional study.

Participants

All the cancer patients being treated with bevacizumab targeted therapy.

Inclusion Criteria

- All the people. being treated with targeted therapy.
- Age between 18 – 60 years.

Exclusion Criteria

- People unwilling to sign the informed consent form.
- People who are not showing up on time for therapy or evaluation.

Sample Size

All the patients who are treated with bevacizumab in the study setting for a period 3 month from January 25 to March 25 in the year 2025.

Sample Collection

- Urine collected in universal container labeled with name and age of patient for evaluation of proteinuria.
- Blood collected in yellow top vial with name and age of patient for evaluation of asperate amino transferase (AST), alkaline phosphatase (ALP), alanine amino transferase (ALT), albumin and bilirubin.

Clinical Methods

Regular measurement of blood pressure of the patient every time the patient comes for infusion of medicine as well as on the symptomatic basis for evaluation and grading of hypertension.

Laboratory Method

Evaluation and grading of proteinuria every time the patient comes for infusion of medicine as well as on symptomatic basis evaluation and grading of AST, ALP, ALT.

Instruments

Sphygmomanometer, stethoscope, universal container, yellow blood collection vial.

RESULTS

In this study total of 25 patients were included during the study period of 3 months.

Demographics

A total of 25 patients 10 male (40%) and 15 (60%) were receiving bevacizumab. The age of the patient varies from 44 to 59 years. Majority of patient were falling under the age of 45 to 50. male:female ratio 2:3

Amongst the incidence of various cancersmajority were of ovarian cancer (36%, n = 9) patients followed by colon cancer (20%, n = 5), lungadenocarcinoma (20%, n = 5), glioblastoma multiforme (8%, n=2), cervix cancer (8%,n=2), gastroesophageal junction cancer (4%, n=1) and hepatocellular carcinoma (4%, n=1).

Toxicities

Hypertension

Our recent study vividly illustrates that from 40% who developed hypertension, 20% of patients developed new-onset hypertension after starting treatment. Even more strikingly, a significant 80% of patients who already had a history of high blood pressure experienced an exacerbation of their existing hypertension, highlighting a substantial challenge in managing cardiovascular health in this patient population.

Proteinuria

Proteinuria, or the presence of protein in the urine, is a prevalent and expected side effect of bevacizumab administration, impacting up to 28% of treated patients. In the present study, while most cases experienced mild to moderate proteinuria, a notable 4% presented high grade proteinuria (grade 3 or 4), underscoring the importance of diligent monitoring of renal function throughout bevacizumab therapy.

Liver toxicity (Serum Transaminitis)

However, increased hepatic toxicity was also noted with the addition of bevacizumab. In present study we did not find any liver toxicity as all the alanine aminotransferase and aspartate aminotransferase levels were within normal range.

DISCUSSION

Our study shows that bevacizumab is associated with a significantly increased risk of proteinuria and hypertension in patients who received treatment for metastatic cancers of the lung, hepatocellular, gastroesophageal, colorectal, and ovarian. With the increasing use of angiogenesis inhibitors like bevacizumab in patients with several metastatic cancers because of the associated survival benefit, oncologists, internists, and nephrologists must monitor and manage these side effects appropriately to ensure that patients.

Hypertension, both new onset and the worsening of pre-existing high blood pressure, stands out as the

most frequently reported adverse event associated with bevacizumab therapy.

In previous studies Economopoulou P. *et al*,[8] conducted a review for the evaluation of cardiovascular events linked with administration of bevacizumab in patients of colorectal cancer (CRC), non-small-cell lung cancer (NSCLC), breast cancer, glioblastoma, renal cell cancer (RCC). HTN is a common adverse event occurring in patients treated with bevacizumab, with an overall incidence of 4 to 35% reported in clinical trials. The median interval from the initiation of bevacizumab to the development of hypertension (HTN) is approximately 4.6–6 months. HTN was statistically significant more frequently in the bevacizumab-treated arm. In present study, 40% of patients show hypertension either as a new onset (20%) or exacerbation of previous hypertension (80%). These results were in accordance with the previous studies. The present study recorded reading from the arm bevacizumab in which was administered.

Typically, this treatment-related proteinuria is of mild severity and does not necessitate a reduction in drug dosage. However, in rare instances, it can escalate to nephrotic syndrome, a more severe condition characterized by substantial protein loss, fluid retention, and other metabolic disturbances.[9,10]

In studies by Wu *et al*,[11] performed a systematic review and meta-analysis on bevacizumab therapy for the incidence of proteinuria and renal damage analyzed data from 16 studies comprising 12,268 patients with a variety of tumors it concluded that the incidence of high-grade (grade 3 or 4) proteinuria with bevacizumab was 2.2% (95% confidence interval [CI] 1.2 to 4.3%). Higher dosages of bevacizumab are associated with increased risk for proteinuria. We found in present study that 28% of patients had mild or moderate proteinuria, high grade proteinuria was found in only 4% of patients none of our patient had advanced to nephrotic syndrome.[12,13]

In studies conducted by D.G Power *et al*,[14] conducted a clinical trial study on 205 patients on hepatic arterial infusion (HAI) with floxuridine + dexamethasone and oxaliplatin + irinotecan was given with bevacizumab which is an active agent that was added to these HAI regimens to increase efficacy (disease-free survival) in colorectal cancer liver metastases and primary liver. It concluded that in univariate analyses, no clinicopathologic variable was significantly associated with increased risk of hepatic toxicity. Usual bevacizumab toxicity (e.g., increased clotting and hypertension) was seen as expected. However, increased hepatic toxicity was also noted with the addition of bevacizumab. In present study we did not find any liver toxicity as all the alanine aminotransferase and aspartate aminotransferase levels were within normal range.

In summary, bevacizumab is the first biologic therapy targeted at tumor pathophysiology to show significant activity in ovarian cancer, colon cancer, lung adenocarcinomas, hepatocellular carcinomas and other cancers with acceptable added toxicity. The adverse events associated with bevacizumab, however, are specific to its biologic effects and are potentially serious, even fatal which is not seen in present study.

CONCLUSION

Bevacizumab is currently listed as an active treatment for recurrent ovarian and primary peritoneal cancers by the National Comprehensive Cancer Network, and is also FDA-approved for these indications. The administration of bevacizumab requires disclosure of the risks and the benefits and alternative therapies to patients in an informed consent-like process. With evolving precision oncology the role of bevacizumab continuous to grow and care givers should be aware of the toxicities of the drug.

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