Impact of Steroid in Cancer Patients

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ABSTRACT

Introduction: A study was conducted to determine the interaction and interrelationship of BMI and steroids on blood glucose levels in 110 cancer patients on chemotherapy. Patients with cancer are often treated with glucocorticoids as part of therapy, which may cause hyperglycemia. During the study we have seen that prediabetic patients and patients with higher Body Mass Index are more susceptible to develop diabetes mellitus which could be secondary to steroids. Study aimed to correlate that patients with higher BMI and prediabetes are prone to develop diabetes mellitus.

Material and Methods: 110 cases undergoing chemotherapy were selected randomly and studied. Their pre, concurrent and post-chemo blood sugar levels were recorded. Their pre, concurrent and post-chemo blood sugar levels were recorded at 1st 2nd, 3rd, 5th, 7th, 9th, 11th and 14th day.

Results: During the study 110 cases undergoing chemotherapy were selected randomly and studied; 86 patients (78.18%) were having Normoglycemia during the chemotherapy and post chemotherapy. It was found out that only 24 patients (21.81%) developed mild elevation of glycemic levels and in which 17 patients glycemic levels revert to normal with diet modification and life style modification only, remaining 8 patients (7.27%) developed diabetes, predominantly there was postprandial hyperglycemia. Only one case having normal BMI went in to complications and developed DKA in our study.

Conclusion: Cancer patients, radiation patient or bone marrow transplantation patient do receive glucocorticoids as a part of treatment and Hyperglycemia is a common adverse effect. Further studies and investigate are needed to prove the clear link between hyperglycemia and patient or cancer outcomes. We recommend that all cancer patients who are receiving glucocorticoids as a part of treatment should be screened for hyperglycemia with atleast random glucose test prior and 4–6 hours after the most recent glucocorticoids dose.

Keywords: Steroid, Cancer

INTRODUCTION

Hyperglycemia, or high blood glucose, is a defined as excessive glucose amount which circulates in the blood which develops due to little insulin or when body cannot utilise insulin properly. A number of medical conditions can cause hyperglycemia, including diabetes mellitus (DM), obesity, pancreatitis, chronic stress, Drugs like Corticosteroids and cancer. Glucocorticosteroids (steroids) plays an important role and have significant effects on Glucose metabolism, especially on postprandial hyperglycemia. Glucocorticosteroids can lead to gluconeogenesis Stimulation, especially in the liver and also lead to Amino acids Mobilization from extrahepatic tissues and Glucose uptake Inhibition in muscle and adipose tissue. Cancer patients usually receive steroids as a part of chemotherapy for the treatment or prevent of nausea, or it is also used as an adjuvant therapy.

Incidences of hyperglycemia during chemotherapy are known but no adequate measures are taken to control the glycemic levels properly. Good literatures on this subject are not easily available in India. Hence this study was conducted to create awareness of the incidence and strictly estimating the glycemic levels in chemotherapy patients. It is real importance to record before, during and after the cancer therapy in established diabetic patients and more so in Non-Diabetic and Pre-diabetic patients. Very rare complication like DKA can develop if proper care and management is not done.

In 1885 Hyperglycemia was first reported in cancer patients, it was first suggested by Warburg et al in the year 1920 that the tumour tissues were found to have sustain elevated glucose utilization levels than compared to normal tissues.[1] There is significant clinical evidence which indicates a positive association between abnormal metabolism of glucose and neoplasia. Moreover, several groups had described that there is a specific cellular mechanisms associated with glucose uptake in malignant tissues. Most tissues of malignant have increased uptake of fludeoxyglucose (18F) (18F-FDG) and it is associated with an increased glycolysis rate and transportation of glucose.[2] Study aimed to correlate that patients with higher BMI and prediabetes are prone to develop diabetes mellitus.

MATERIAL AND METHODS

This study was done in Indo-American Cancer Hospital and Informed consent was taken, 110 cases undergoing chemotherapy were selected randomly and studied. Their pre, concurrent and post-chemo blood sugar levels were recorded at 1st, 2nd, 3rd, 5th, 7th, 9th, 11th and 14th day.

The Age, Sex, and BMI of the patients were noted along with diagnosis and the chemotherapy being given. The patients having fasting blood sugar level of 100-125mg/dl were identified. Patients with pre-existing diseases like Accelerated Hypertension, CAD, and complication of diabetes (acute or chronic) were excluded from the study.

Complete Medical History and examination was done, and baseline investigations like HBA1C, serum creatinine, microalbuminuria, lipids, retinal examination, chest X-ray and ECG were done.

Majority of the chemotherapeutic agents are given with dexamethasone in a dose of 8 – 16 mg and in cases of multiple myeloma the dexamethasone is given as high as 40 mg. Most of the times dexamethasone causes derangement of blood sugar levels.

STATISTICAL ANALYSIS

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Descriptive statistics like mean and percentages were used to calculate the results. Microsoft office 2007 was used to make tables and graphs.

RESULTS

Among the 110 patients studied, 86 (78.18%) cases remained at normal glycemic levels throughout chemotherapy and 24 (21.81%) developed a derangement of their blood sugar levels (Figure-1).

During the study it was noted that there was significant increase in BMI in 17 patients, and these patient had elevated glycemic levels.

During the study we also found out that only 24 patients developed mild elevation of glycemic levels in which 17 patients' glycemic levels (FBS 94 ± 10.77, PPBS 138 ± 40.25) revert to normal with diet modification and life style modification only, remaining 8 patients (7.27%) developed diabetes (FBS 130 ± 28.19, PPBS 215 ± 79.41), predominantly there was postprandial hyperglycemia. Only one case having normal BMI went in to complications and developed DKA in our study. The patient was a case of acute lymphocytic leukemia, which was given L-Asparginase and High dose steroid. The majority of patients who developed diabetes had BMI which was higher than normal and had various maladies like Carcinoma Breast, Non-Hodgkin's Lymphoma, and Multiple Myeloma for treatment with chemotherapy. We had also seen in this study that 15.45% of study group patient had BMI more than normal.

DISCUSSION

Prediabetes is the state in which some of the diagnostic criteria are meet but not all criteria of diagnostic for diabetes are meet. Prediabetes is also termed as impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or borderline diabetes.[3]

Impaired fasting glucose (IFG) is referred as elevation of fasting blood glucose above normal level but it is not so high enough to be termed as diabetes mellitus. It is also known as pre-diabetic state and patient in prediabetic states may be associated with increased cardiovascular pathology and insulin resistance. Many studies have cited that Patients with known IFG can progresses to type 2 diabetes mellitus. It is been suggested by some groups that there is a risk of 50% risk over the next 10 years for the progression of IFG to overt diabetes.[3]

- **IFG Criteria by WHO**: FBG 6.1 mmol/l – 6.9 mmol/l or 110mg/dl to 125mg/dl.
- **IFG Criteria by ADA**: FBG 5.6 mmol/l – 6.9 mmol/l or 100mg/dl to 125mg/dl.

The possible mechanism which was attributed to hyperglycaemia and DKA and HONK are as follows:[4]

1) Steroid induced diabetic ketoacidosis
2) Cancer Chemotherapeutic drugs along with steroid, hand in hand may lead diabetes mellitus which if uncontrolled or in septicaemia may leading to ketoacidosis
3) Glucose intolerance induced by steroids with superadded to ketoacidosis which could be flare up by Starvation.

Patients with BMI in between 25 to 30 are of greater importance superadded if these patients are having Co-existing risk factors like Hypertension, Dyslipidemia, and features of metabolic syndrome, these patients are surely the candidates for therapeutic treatment.

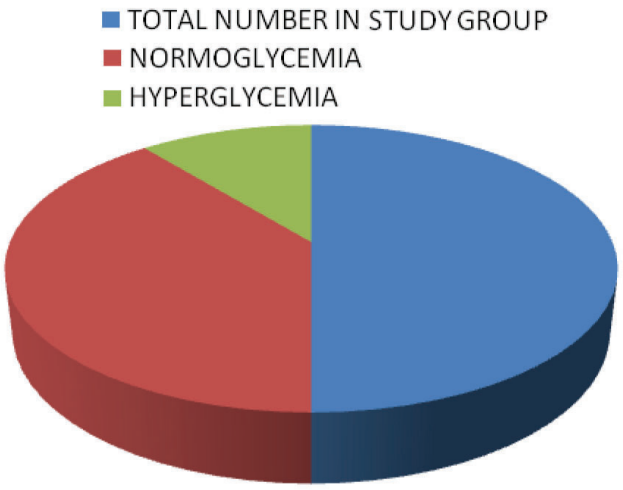

Figure-1: Pie diagram shows the Illustration of total number of patients who had received chemotherapy, out of which only 21.8% developed Diabetes and remaining 78.2% were normoglycemic

Osinsky SP et.al. 1990 had observed in animal and human tumours that hyperglycemia produces some microphysiological changes which enhances the antitumor effects of some cytostatic drugs.[5]

Feng j p et.al. had shown that 422 patients who received 5 fluorouracil chemotherapy for colorectal cancer 11.6% patients developed Diabetes due to chemotherapy which required anti-diabetic treatment.[6]

Lalaine Audrey G Matitu- Untalan et.al. reported Secondary Diabetes Mellitus (DM) has been associated in about 1-14% of patients with hematologic malignancy treated with L-asparaginase.[7]

Multiple studies and reports are there in relation to drug induced insulin dependent diabetes mellitus., predominantly it has been seen with following agenets like L- Asparginase, Streptozocin and Cytokine interferon – alpha.[8-14]

Brunello A1 et.al.2011 had found that, In NHL patients, hyperglycemia correlates with non-haematological toxicity (NHemT). Further studies are to be done to confirm regarding the improvement and outcomes which could be better in patient with Normoglycemia on chemotherapy.[15-16]

Zeng L et.al 2010, had suggested that the prognosis is affected adversely in breast cancer, if there is co- existing Diabetes, obesity, or metabolic syndrome. Hyperglycaemia conferred resistance on malignant cells, but not on non-malignant cells, to chemotherapy-induced cell death.[17]

Other chemotherapy drugs like Doxorubicin causing severe hyperglycaemia and insulin resistance.

D Harris et.al 2013 recommends that all patients who were diagnosed with cancer and are on steroids should be screened for Hyperglycemia at least 4 to 6 hrs after administration of Glucocorticoids.[18]

Redaniel et. al. 2012 shown that there was a weak evidence of diabetes associated with a increased risk of breast cancer but there was small increase in the incidence of the patient which could not be clearly explained.[19]

Lansang MC et.al 2011 found that Glucocorticoids used commonly to treat multiple inflammatory processes can lead to complication like hyperglycemia, Cushing syndrome, adrenal suppression during the study.[20]

Brunello et al 2011, In NHL patient's hyperglycemia correlated with NHemT, and less clear pattern was seen in PC patients. Study concluded that Prospective studies are required to assess whether a good glycemic control during the chemotherapy can improve toxicity and outcomes.[21]

We are continuing our study to establish the interrelation of diabetes and cancer chemotherapy agent.

CONCLUSION

Emphasis is to given to early diagnose patients with obese prediabetes and treat according in the initial stages to prevent them from developing complications. Patients with BMI in between 25 to 30 are of greater importance superadded if these patients are having Co-existing risk factors like Hypertension, Dyslipidemia, and features of metabolic syndrome, these patients are surely the candidates for therapeutic treatment. The present study was done to highlight strict glycemic control,(FBS< 110 and PLBS< 140-160 mg/dL) to prevent the complication of diabetes apart from progression of tumour cells in view of hyperglycemia.

Cancer patients, radiation patient or bone marrow transplantation patient do receive glucocorticoids as a part of treatment and Hyperglycemia is a common adverse effect. Further studies and investigate are needed to prove the clear link between hyperglycemia and patient or cancer outcomes. We recommend that all cancer patients who are receiving glucocorticoids as a part of treatment should be screened for hyperglycemia with atleast random glucose test prior and 4–6 hours after the most recent glucocorticoids dose.

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