Annals of Diabetes Research

Research Article
Published: 27 Mar, 2019

Acute Dysglycaemia in Patients Hospitalised with Cancer

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Abstract

Aims: In patients with cancer, diabetes is associated with worse outcomes and prognosis. We undertook a retrospective audit for inpatients with both cancer and diabetes to identify the prevalence of dysglycaemia and patient characteristics.

Methods: We identified all inpatient admissions with cancer and diabetes between October 2014 and October 2015 at a tertiary hospital. A subgroup of patients with dysglycaemia, as defined by the presence of hyperglycaemia and or hypoglycaemia, was further identified.

Results: A total of 4583 admissions occurred with a diagnosis of cancer and 536 (11.6%) admissions had both cancer and diabetes. We identified 105 admissions for cancer and dysglycaemia; 96 of these were available for review. In this subgroup, the median age was 69 years (range 43 to 89). Most individuals had Type 2 Diabetes Mellitus (96%) and 54% were insulin requiring. Bedside blood glucose was well documented (96%) but only 20% of patients had an HbA1c performed. The diabetes team were consulted in 22% cases. Eighteen (19%) patients died during the admission and infection was a cause of death in 10 cases (55.6%).

Conclusion: This audit describes a group of inpatients with cancer and acute dysglycaemia. A standardised approach to managing diabetes for these patients may improve glycaemia and related adverse events.

Keywords: Cancer; Diabetes; Hyperglycaemia; Acute Dysglycaemia; Inpatient Diabetes

Introduction

Diabetes has a prevalence of up to 20% in the cancer population [1]. Observational studies and meta-analyses suggests diabetes is associated with the development of liver, pancreas, endometrium, colon, breast and bladder cancers, likely relating to both direct and indirect metabolic effects of hyperglycaemia, insulin resistance, hyperinsulinemia and elevated insulin-like growth factor [1-4].

In patients with cancer, diabetes is associated with increased morbidity and mortality. Studies have shown worse prognosis and outcomes in patients with pre-existing Type 2 Diabetes Mellitus (T2DM) and colorectal cancer, breast cancer, renal cell carcinoma, hepatocellular carcinoma, pancreatic cancer and glioma [5-11]. In haematological malignancies, hyperglycaemia is associated with increased risk of infection, organ dysfunction and mortality [12].

In hospitalised patients, hyperglycaemia is associated with increased mortality, hospital-acquired infections and acute myocardial infarction [13-16]. The mechanisms for this include neutrophil and endothelial dysfunction, oxidative stress, platelet activation and osmotic diuresis leading to acute kidney injury [15,16]. In patients with acute illness, hyperglycaemia may progress to the acute hyperglycaemic syndromes of diabetic ketoacidosis and hyperosmolar hyperglycaemia state. These complications are associated with greater difficulty tolerating chemotherapy regimens, increased hospital length of stay, shorter remission periods, shorter median survival and higher mortality rates [1,13,16]. In the palliative setting, symptoms of hyperglycaemia can lead to reduced quality of life [17]. Likewise, hypoglycaemia is associated with increased mortality and longer length of stay through neuroglycopaenia, adrenergic and counter-regulatory responses leading to falls, seizures and arrhythmias [16].

Multiple factors contribute to the complexity of glycaemic management in patients with cancer, including high dose glucocorticoids and chemotherapy agents, poor oral intake, use of total parental nutrition and severe illness such as infection and multisystem organ failure. The effect of glucocorticoids on glycaemic control has been well described in other patient populations. Glucocorticoids exacerbate post-prandial hyperglycaemia through increased insulin resistance, increased gluconeogenesis and decreased insulin production and secretion [1,18,19]. Generally,

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Received Date: *11 Feb 2019*
Accepted Date: *25 Mar 2019*
Published Date: *27 Mar 2019*

Citation:
Qian SY, Parlapiano C, Marley KA, Kyi M, Fourlanos S, Rosenthal M, et al. Acute Dysglycaemia in Patients Hospitalised with Cancer. Ann Diabetes Res. 2019; 3(1): 1010.

insulin is required to achieve post-prandial glycaemic targets [18-20].

Patients with cancer receiving palliative treatment or who are in the terminal phase of their illness are a unique subpopulation. The use of glucocorticoids for symptom management can lead to hyperglycaemia, and reduced oral intake due to nausea, vomiting and fluctuating conscious state is a risk factor for hypoglycaemia [1]. Attention to glycaemic control with the aim to avoid symptomatic hyperglycaemia and hypoglycaemia is an important consideration in maintaining patient comfort and dignity [17,21].

Currently, there is a lack of data on the prevalence of hyperglycaemia and hypoglycaemia in cancer patients. Furthermore, there are no guidelines for appropriate glycaemic targets, monitoring and management. We undertook a retrospective audit of a group of inpatients with cancer and acute dysglycaemia to assess patient demographics, routine investigations and complications to better understand the characteristics of this population.

Materials and Methods

This audit was conducted at the Royal Melbourne Hospital, a major tertiary centre in Australia with a large oncology and haematology service. A retrospective review of the hospital medical records was conducted over a 13-month period between October 2014 and October 2015 (inclusive).

Admissions were identified by ICD-10 discharge diagnosis codes, which were assigned by the hospital's health information services staff based on documentation by the treating medical team in progress notes and discharge summaries. These codes provide information that is used for both administrative and funding purposes in the provision of health services.

Firstly, the total number of inpatient admissions with concurrent diagnosis of cancer (C00-D48) and diabetes with dysglycaemia (E10.64, E10.65, E11.64, E11.65, E14.64, E14.65, E11.0, E11.1, E10.1) was identified. All haematological and oncological cancers were included. Day stay admissions were excluded. Next, a subgroup of inpatients with concurrent diagnoses of cancer and dysglycaemia were identified for more detailed analysis. Dysglycaemia included codes for 'hyperglycaemia, 'hypoglycaemia', 'unstable diabetes' and 'diabetes related emergencies'. Hyperglycaemia was defined as blood glucose measurements >10 mmol/L and hypoglycaemia was defined as blood glucose readings less than 4 mmol/L. Unstable diabetes was defined as the presence of hyperglycaemia, hypoglycaemia or both. The specific codes identified in the study population are listed in appendix 1.

Histories and pathology results were reviewed and basic demographics, diabetes and oncology history, monitoring of glycaemia, investigations, referral to specialist diabetes services, acute diabetes-related complications and inpatient mortality was recorded. Palliative management was defined as treatment of cancer with non-curative intent. The terminal phase of illness was defined where death was thought likely in a matter of days, with no further acute medical intervention planned.

Results

During the 13-month audit period, a total of 4583 admissions occurred with a diagnosis of cancer and 536 (11.6%) admissions had concurrent diagnoses of cancer and diabetes. There were 105 admissions identified with both cancer and dysglycaemia. This represented 19.6% of all admissions with cancer and diabetes and 2.3% of all admissions with cancer. Of the 105 discrete admissions, medical records were accessible for 96. The median age of patients was 69 years (range 43 to 89), and 55% were male (n=53).

Table 1: Patient Demographics and Cancer History.

Total Admissions	N=96
Gender	
Male	53 (55%)
Female	43 (45%)
Age (years)	
Median	69
Range	43-89
Cancer Type	
Solid Tumours	68 (71%)
Colorectal	18 (26%)
Upper GIT†	18 (26%)
CNS‡	10 (15%)
Lung	6 (9%)
Other	16 (24%)
Haematological	28 (29%)
Leukaemia	13 (46%)
Lymphoma	12 (43%)
Multiple Myeloma	3 (11%)
Intent of cancer treatment	
Curative	52 (54%)
Palliative	28 (29%)
Terminal Care	16 (17%)
Cancer Related Treatment	
Glucocorticoids	44 (43%)
Chemotherapy	19 (20%)
Surgery	35 (37%)
Radiotherapy	1 (1%)

†GIT: Gastrointestinal; ‡CNS: Central Nervous System

Table 1 details the demographics and cancer history of the group. The majority of patients had solid organ malignancies (71%, n=68), with colorectal and upper GI cancers accounting for the majority (53%, n=36). During the admissions, 19 (20%) patients underwent chemotherapy and 35 (37%) underwent surgical procedures. Patients received steroids in 44% of admissions with dexamethasone being the most common glucocorticoid used (n=33, 79%). Of the total episodes of care assessed, 29% received palliative treatment with non-curative intent (n=28). Of these patients, 12 were in the terminal phases of their illness and were receiving end of life care.

Table 2 describes the diabetes history of the group. All patients had known diabetes prior to admission. Diabetes type and treatment prior to admission was documented in progress notes in most cases. The majority of patients had T2DM (96%, n=92), and were on insulin treatment (52%, n=50) prior to admission. Duration of diabetes was not documented in 59% (n=57) of cases. Of the patients in whom duration of diabetes was available, 33% (n=13) had diabetes for over 20 years and the majority (79%, n=31) had diabetes for over 5 years. Nineteen (20%) patients were documented to be under the care of an

Table 2: Diabetes History.

Type of Diabetes (n,%)	
Type 1	4 (4%)
Type 2	92 (96%)
Duration of Diabetes (n,%)	
<5 years	8 (21%)
5 to 10 years	9 (23%)
10 to 20 years	9 (23%)
>20 years	13 (33%)
Treatment (n,%) where known	
Diet Controlled	7 (7%)
OHA†	39 (41%)
Insulin Only	27 (24%)
OHA and Insulin	23 (24%)
Major inpatient complications	(n= 4)
Hyperosmolar Hyperglycaemic State	
Lactic Acidosis in setting of metformin use and acute kidney injury	
Hyperglycaemia and diabetic foot ulcer requiring admission	
Hypoglycaemia in the setting of poor oral intake requiring admission	

†OHA: Oral Hypoglycaemic Agents

endocrinologist prior to admission.

The median duration of hospitalisation was 9 days (range 1 to 80 days). Glycaemic emergencies were identified as the reason for admission in three cases - one case with a hyperosmolar hyperglycaemic state, one with severe hyperglycaemia in the setting of non-adherence with insulin and one due to severe hypoglycaemia. Most admissions (n=93, 97%) were not related to a glycaemic emergency; 42% were for cancer specific treatment (n=39), 34% for symptomatic management (n=32) and 24% for diagnostic workup (n=22).Of note, 6 of these patients had localised infection or sepsis as a secondary issue at admission (6%).

Most patients (96%, n=92) had capillary blood glucose measurements, and 57% (n=55) had laboratory plasma glucose measurements recorded in their files. An HbA1c was performed in 20% (n=19) of patients during their admission. Of patients in whom HbA1c was available, the mean was 7.6% (60 mmol/mol), the median 7.3% (56 mmol/mol); range 5.4% to 13.6% (36 mmol/mol to 125 mmol/mol). The management of diabetes was predominantly performed by the admitting unit, with the diabetes team consulting in 22% (n=21) of cases. Of the 19 patients who were under the care of an endocrinologist prior to admission, only 16% (n=3) were discussed with or reviewed by the diabetes team during their admission.

In this group of patients with dysglycaemia, 64 patients (67%) had hyperglycaemia only, 8 patients (8%) had hypoglycaemia only and 24 patients (25%) had a combination of both. In admissions with hyperglycaemia, significant contributing factors included glucocorticoid use (44%, n=42) and infection (28%, n=27).

Eighteen patients (19%) died during the admission and 12 of these deaths occurred in those in the terminal phase of their illness. No patient died as a result of a severe glycaemic complication. Infection was a factor in 10 deaths (56%), with chest infection being the most prevalent 60% (n=6). Of the 28 patients who were treated with palliative intent, 27 (96%) had bedside capillary blood glucose monitoring. Of the 12 patients in the terminal phase of their illness, 11 received ongoing bedside blood glucose monitoring.

Discussion

Dysglycaemia in the cancer population is associated with increased morbidity and mortality [1]. This retrospective audit describes the characteristics of cancer patients with dysglycaemia in a real world setting. At our centre, 12% of all cancer patients with multiday admissions had a concurrent diagnosis of diabetes, and of these 20% were identified as having dysglycaemia. We believe the true prevalence of diabetes is probably higher, given the significant limitations in data collection through hospital coding. Diabetes coding can underestimate the true prevalence in the hospital setting by up to 40% and it is likely that this audit has only discovered the 'tip of the iceberg' [15,22]. With new technologies, including networked point of care glucose monitoring in hospital, the true prevalence of dysglycaemia will become evident.

The overall rate of complications relating to acute severe glycaemic events was low, with only 3% of admissions directly related to glycaemic emergencies, and none that lead directly to death. However, dysglycaemia is associated with other conditions. Hyperglycaemia causes immune dysfunction and impaired leukocyte function through reduced phagocytosis, impaired bacterial killing and chemotaxis, leading to an increased risk in infection as well as reduced wound healing [14,15]. In this cohort, infection was present in 6% (n=6) of patients at admission, 28% (n=27) during admission and implicated in 56% (n=10) of patient deaths.

This audit identified inconsistencies in the documentation of diabetes history and basic screening investigations. Clear documentation of the diabetes history including duration, management and specialist care is important to provide context and guide treatment. Similarly, HbA1c gives an indication of background glycaemic control, although care must be taken in the interpretation given common co-existing factors such as anaemia or recent blood transfusions [23].

There were relatively few patients with dysglycaemia that had consultations by diabetes specialists. The management of inpatient diabetes does not always require specialist review, but the involvement of a specialty team in this complex patient group may improve glycaemic control and potentially decrease adverse outcomes as demonstrated in other studies [24-26]. Guidelines to prompt referral to inpatient diabetes teams may be beneficial to improve glycaemic control and safety.

A significant proportion of patients were treated with palliative intent (28%). A modified approach focusing on symptom management is needed in patients receiving end of life care and for those in the terminal phase of their illness [17]. In this setting, glycaemic management should be rationalised, however, it is very important to avoid symptomatic hyperglycaemia, which is associated with polyuria, dehydration and altered conscious state. Likewise, symptomatic hypoglycaemia is unpleasant and associated with increased morbidity and mortality.

Conclusion

Cancer patients with diabetes are at risk of marked hyperglycaemia and hypoglycaemia, which in turn is associated with poor outcomes. Of patients admitted to hospital with cancer and diabetes, one in five had acute hyperglycaemia or hypoglycaemia and this is likely to be an

underestimation of dysglycaemia. Although glycaemic emergencies were uncommon, infections, which can be related to hyperglycaemia, affected one in four patients with diabetes.

This audit supports the need for standardised management in patients with diabetes and cancer. Multifaceted interventions including education, improved care guidelines and early identification and management of diabetes in these patients may reduce the incidence of dysglycaemia and improve clinical outcomes.

Contributors

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