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ELECTROLYTE DISORDERS IN CANCER PATIENTS

Biochemistry

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ABSTRACT

Background : Cancer patients frequently suffer electrolyte abnormalities that complicate the management of their primary pathology. The most commonly occurring derangement is hyponatremia, while hypochloremia, hypernatremia, hyperkalemia and hypokalemia, are also encountered. The etiology of these abnormalities is often identifiable, and early diagnosis and management can prevent delays in necessary anti-cancer therapies. This study aimed at determining the pattern of electrolyte abnormalities in hospitalized cancer patients.

Methods : Electrolyte data were collected from the laboratory database during 1 October 2019 and 30 march 2020. Hospitalized Patients with the diagnosis of cancer were selected from mahavir cancer sansthan, patna. comorbidities, and clinical data, including survival, and length of stay, were extracted from the medical records of the patients.

Results : Among 8482 electrolyte tests performed during the study period, 2711 diagnosed admitted adult cancer patients with electrolyte data were found. 1,150 cases had at least one electrolyte abnormity. Hypokalemia (27.8%) was the most common electrolyte disorder, hypochloremia (23.5%) and hyponatremia (28.5%), hyperkalemia (14%) others 6%. renal dysfunction, receiving surgery/chemotherapy, anemia and hypoalbuminemia were screened out as the major risk factors. In-hospital mortality of these patients were 12% as compared to those with normal electrolytes (3%). The risk of death significantly increased among patients with severe electrolyte imbalance. Similarly, the length of stay and hospital cost also increased as the number and severity of electrolyte imbalance increased.

Conclusion : Electrolyte disorder is commonly encountered in cancer patients and associated with very bad prognosis. Patients with comorbidities, renal/liver dysfunction, and anti-tumor therapy are at a higher risk. Regular monitoring of electrolytes, intravenous infusion, modifiable factors and appropriate management for the same should not be neglected during anti-tumor treatment.

KEYWORDS

Na, K, Cancer

INTRODUCTION

Cancer is rapidly emerging as an important cause of mortality and morbidity globally in recent years. In 2016, there were 17.2 million cancer cases worldwide and 8.9 million deaths. The global cancer cases increased by 28% over the past decade[1]. As one of the largest developing countries, new diagnosed cancer cases in India in 2015 reached 4.2 million with an incidence of 258 per 100,000 .

Electrolyte disorders shows the disequilibrium of the human body, involving mechanisms of malnutrition, organ decompensate, endocrine dyscrasia, etc. It makes electrolyte disorder ubiquitous in patients diagnosed with cancer. Previous studies reported the incidence of hyponatremia and hypokalemia in cancer patients was up to 47–64%[4,5] and 41–48%[6,7] respectively. The occurrence of various electrolyte disorder is concomitant and can trigger a series of symptoms such as delirium, fatigue, constipation, nausea, vomiting, and even the in-hospital death. In most cases, electrolyte disorder is associated with the etiology seen in general inpatients and not specifically allied to the underlying cancer. While in others, it is caused by anti-tumor treatment or due to the existence of paraneoplastic syndromes[10]. It is estimated that the direct cost of treating hyponatremia in the United States reached $1.6~$3.6 billion annually[11], let alone treating other types of electrolyte disorder with far more significant consequences.

Early detection and prompt correction of electrolyte disorder can improve patients' short-term outcome and quality of life[12]. However, the epidemiology of electrolyte disorder in cancer patients and its relationship with clinical outcomes remains to be studied. Objective of our study is to delineate the incidence of electrolyte disorder in patients with different malignancies, to identify the factors that could increase the risks of electrolyte disorder, then to assess the impact of electrolyte disorder on patients' in-hospital mortality.

MATERIAL AND METHODS

Study design and population

This study is retrospective cohort study based on the medical records and data in Mahavir Cancer Sansthan, Patna, India. Patients who were diagnosed with cancer and admitted into the hospital between 1 October 2019 and 30 March 2020 were recruited. The exclusion criteria is the following: (1) patients with a stay of admission less than 24 hours; (2) patients under 14 years old, (4) patients with renal transplantation and (5) patients without electrolyte tests.

Data collection

Demographic information, comorbidities, clinical records, as well as electrolyte were taken from the hospital medical records and clinical biochemistry data. Renal function was measured by the estimating serum creatinine and blood urea. Liver function was measured by aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Other biochemical indicators contained albumin, hemoglobin, and leukocyte count. In-hospital mortality was regarded as the primary clinical outcome.

Definition of electrolyte disorders

Electrolytes for study include serum sodium, potassium, and chloride. The reference value range is 135–145 mmol/L in sodium, 3.5–5.5 mmol/L in potassium, 99–110mmol/L in chloride respectively. A value less than the lower range of each electrolyte is considered as hypo-electrolytemia, and a value greater than the upper range is considered as hyper-electrolytemia. patient suffered from at least one kind of electrolyte disorders during the hospitalization.

Statistical analysis

Continuous variables are described as mean±standard deviation or median with interquartile range, whereas categorical variables are presented as numbers and percentages. After adjusting the demographic factors, the adjusted odds ratio (aOR) and its 95% confidence interval (CI) of associated factors with AKI are estimated, including present comorbidity, treatment, renal/liver function, and biochemical test. All data analysis was run using SpsS v9software.

RESULTS

Out of 8,482 Electrolyte tests performed in the study period,

2,711admitted patients with medical records were selected in the study, excluding the outdoor patients and pediatric group. Average age of the patient was 55 +/- 10 c years. All of the eligible participants had received sodium, potassium and chloride tests. Of them, 1,150 patients (42.0%) were recognized with at least one category of electrolyte abnormalities.

Risk factors for electrolyte disorder incidence in-hospital AKI was observed as the major risk factors contributing to electrolyte disorder (aOR = 2.93). Preexisting hypertension and diabetes were also associated with a higher electrolyte disorder incidence (aOR = 1.14/1.14). Patients with high creatinine and blood urea and severe hyperuricemia (≥550 mmol/mL) showed a higher probability of electrolyte disorder (aOR = 1.37/2.21). Compared with untreated/ palliative care, patients receiving surgery (aOR: 5.58), chemotherapy (aOR = 1.35) and interventional therapy (aOR = 1.09) were more predisposed to electrolyte disorder. Another positive association with electrolyte disorder incidence was observed in abnormal biochemical test. The aORs of patients with lower albumin and hemoglobin level were estimated as 2.64 and 1.67, respectively. Assuming the renal/liver function and biochemical results are remediable in advance, these features are regarded as modifiable factors for the progression of electrolyte disorder. The risk of electrolyte disorder among patients with modifiable factors significantly increased in different treatment settings with an aOR ranged from 1.67 to 3.00. It implied that correcting these modifiable factors on the initial anti-tumor treatment could decrease the likelihood of electrolyte disorder remarkably.

In-hospital mortality and Length of stay among electrolyte disorder patients

In cancer patients with electrolyte disorder, the in-hospital mortality rate was 2.1%, which was significantly higher than those with normal electrolytes (0.3%,). The top electrolyte disorder associated with high mortality were as follows: hyperkalemia (17.2%), and hypernatremia (6.9%). Similarly, patients with severe electrolyte disorder had a higher risk of in-hospital mortality than patients without electrolyte disorder.

DISCUSSION

In this study, the incidence of electrolyte disorder was estimated as 42.0% in cancer patients, which was remarkably higher than reported populations, including patients referred to the emergency department (13.7%)[9] and the elderly (22.0%)[10]. It suggests that electrolyte disorder in cancer patients should be paid as much attention as other medical conditions, especially in those receiving surgery and chemotherapy. Another study in fifty-four patients with acute leukemia also reported that 75.9% had at least one electrolyte disorder disorders[11]. Leukemia-related electrolyte disorders are mainly considered to be associated with the leukemic process, organ infiltration, cell death and/or therapeutic interventions. Related to obstinate vomiting with increased upper gastrointestinal losses induced by chemotherapy, resulting in hypovolemia and hypokalemia[12]. Worsening of the condition also relates to the presence of renal failure[13].

It was observed that 28.5% and 27% of cancer patients suffered from hyponatremia and hypokalemia respectively in this study. Volume depletion is the main reason for hyponatremia, which usually occurred in hemorrhage, diarrhea, vomiting, drainage of ascites or pleural effusion, peritonitis, or ileus. Besides, syndrome of inappropriate antidiuretic hormone (SIADH) is considered as another common cause of hyponatremia in cancer condition. Sorensen et al. reviewed that SIADH occurs in 3% of patients with electrolyte disorder and neck cancer, in 0.7% of patients with non-small cell lung cancer, and in 15% of patients with small cell lung cancer[14]. In terms of the hypokalemia mechanism, poor nutrition, anorexia and volume depletion can induce inadequate potassium intake. Vomiting generates the loss of potassium. Alkalemia also causes a shift of potassium into cells, thus producing hypokalemia. Furthermore, in patients with leukemia, the increased production of blast cells can cause hypokalemia[15]. Besides, The occurrence of hypocalcemia may be resulted from malnutrition, hypoalbuminemia, sepsis or tumor lysis syndrome (TLS).The release of phosphorus from damaged cells and cellular shift from intracellular to extracellular can give rise to hyperphosphatemia, in situations including rhabdomyolysis, respiratory alkalosis and lactic and ketoacidosis. Additionally, many of the fluids used for hydration and resuscitation contains high concentrations of chloride, and it also may induce or exacerbate hyperchloremia and MAC[16].

In our study, patients with chronic diseases and renal/liver dysfunction were more predisposed to electrolyte disorder. Previous studies also reported that a higher electrolyte disorder incidence in patients with hypertension[17], heart failure and renal insufficiency. Diabetes is described as an independent risk factor for hyponatremia. For every 5mmol/l rise in serum glucose level, there is a decline in serum sodium by 1.6–2.4mmol/l, as glucose acts together with sodium in maintaining osmolality. It suggests that electrolyte disorder might be prevented by early correction of renal/liver dysfunction and other biochemical features at admission.

Anti-tumor chemotherapy, including cytotoxic drug, antibiotics and contrast agents, represent the well-established causes of electrolyte disorder in cancer patients. In this study, we found that patients receiving chemotherapy and interventional therapy had a higher risk of electrolyte disorder (aOR = 1.55/1.18). Cyclophosphamide, vincristine, and polymyxin B have been proved to impair renal excretion of water. Cyclophosphamide can potentiate the renal effect of anti-diuretic hormone or directly affect the tubular function, resulting in hyponatremia. Polymyxin B-induced nephrotoxicity is associated with hyponatremia, hypocalcemia, and hypokalemia. The synergistic effect of anti-neoplastic drugs and electrolyte disorders may even result in fatal arrhythmias[13]. For these reasons, oncologist and nephrologist should be vigilant for the use of anti-tumor agent as well as correction of these modifiable factors of electrolyte disorder before the initiation of chemotherapy as well as during treatment.

In one meta-analysis also reveals that hyponatremia patients had a higher risk of re-admission after the first hospitalization[18]. Hence, regular monitoring of electrolytes can improve the clinical outcomes in cancer patients, especially those with advanced age, underlying diseases or patients receiving surgical/chemotherapy.

We retrospectively described the electrolyte disorders in various clinical settings and evaluated their impacts on patients' in-hospital mortality and healthcare utilization. However, the study was limited on certain aspects. Firstly, this was a single center-based study, so the extrapolation of research finding was restricted. Secondly, we did not collect the detailed medication history and it would obscure the relations between chemotherapy and electrolyte disorder. Thirdly, we did not listed the incidence of other electrolytes like calcium, magnesium, phosphate and acid base disorders in specific cancer categories due to the limited sample size. In the future, a multi-center investigation with inclusion of acid base abnormality is intended to be conducted to achieve a larger sample size and assess the long-term impacts of electrolyte and acid base disorder.

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