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Letter To Editor

Electrolyte Abnormalities in Cisplatin Based Chemotherapy

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Sir,

Cisplatin is one of the most important chemotherapeutic agents, which has a central role in cancer chemotherapy, despite its toxicity. Chemically it is a co-ordinate metal complex containing platinum (1). It is being used in treatment of head and neck, lung, ovary, gastric and testicular malignancies (2). The main adverse effects are nephrotoxicity (3) and electrolyte imbalances. The most common electrolyte abnormality associated with cisplatin is hypomagnesemia (4) due to renal magnesium wasting. Others include hyponatremia (5), hypokalemia, hypocalcemia and hypophosphatemia.

We conducted a study among the patients registered in the Department during the period of January to March 2014. Patients having a histological diagnosis of cancer aged 18 years and older and receiving cisplatin based chemotherapy as single agent; or combination with not more than two drugs in the combination regime including cisplatin. Patients having altered renal, liver function or electrolytes as baseline value, with documented cardiac and any neurological ailments, or already on any nephrotoxic drugs and who did not complete at least three cycles of the chemotherapy either due to death or drop out, were excluded.

Baseline investigations including complete blood count (CBC), renal function tests (blood urea and serum creatinine), liver function tests, serum electrolytes including sodium, potassium, calcium and magnesium were routinely done for all patients prior to the chemotherapy.

Cisplatin was administered at varying doses based on the schedules for each individual malignancy which ranged from 70 to 120 mg. The inter-cycle interval varied from weekly cycle to every 3 weekly cycle as per the protocol. Cumulative dose of cisplatin was recorded each cycle along with the values of basic lab investigation and serum electrolytes. The electrolyte abnormalities were graded as per the Common Toxicity Criteria (CTC) version 3 of WHO. The incidence and the grade of electrolyte abnormalities in terms of CTC toxicity criteria was expressed as percentages. The median dose and the number of cycle at which each of the electrolyte abnormality first occurred, was analyzed using the Kaplan Meir survival analysis.

There was a total of 85 patients whose age ranged from 21 to 89 years and the male to female ratio wsa 3:1. There was no significant variation in hematological parameters between cycles of chemotherapy.

Among all cycles of chemotherapies taken, the most common individual abnormality was of magnesium which was seen in 91.8% of patients, followed by hyponatremia of 88.2%. Hypocalcemia incidence was 70.6% and hypokalemia was further rare at 27.1%.

All the electrolyte values remained normal only in 1 patient (1.2%). All abnormalities occurred in 20% of patients, whereas the most common constellation of abnormalities were that of sodium, calcium and magnesium together (38.8%). It may also be noted that the incidence of potassium abnormality is lowest as individual or in combination with other electrolytes.

The critical dose at which half of the patients had hyponatremia (median dose) was 195 mg (SE 16.46, 95% CI 162.73–227.27). This occurred in cycle 2 (SE 0.23, 95% CI 1.55–2.45). The median critical dose of potassium was 560 mg (SE 101.56, 95% CI 360.95–759.05) and occurred in cycle 7 (SE 0.82, 95% CI 5.39–8.61). Similarly median critical dose and cycle of calcium and magnesium are 240 mg

(SE 8.14, 95% CI 224.05–255.96) at cycle 3 (SE 0.323, 95% CI 2.37–3.63) and 160 mg (SE 2.79, 95% CI 154.53–165.47) at cycle 2 (SE 0.14, 95% CI 1.73– 2.27) respectively.

The significant portion of all the abnormalities detected were grade 1 in general for all four electrolytes. Grade 4 abnormality was seen only with sodium (2.4%). Grade 3 hyponatremia was maximum in the third cycle, seen in 13 patients (15.3%). The grade 3 abnormalities of calcium and potassium was only a meagre 3 to 5%. It is noteworthy that although magnesium was the most common individual or combination abnormality, there was no grade 3 or 4 hypomagnesaemia.

Cisplatin chemotherapy causes hypomagnesaemia in a highly significant percentage of patients. Incidence increases with increase in the cumulative dose of cisplatin. Frank clinical manifestations associated with this abnormality is rare. This may be due to the low grade of hypomagnesaemia which may be asymptomatic or only subtle changes. Since clinicians fail to monitor it, it is commonly underestimated. Due to the high incidence and also being a correctable cause, it must be always kept in mind and monitored regularly. This become significant when associated with other electrolyte abnormalities as well.

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