Glucose Intolerance During Adjuvant Chemotherapy for Breast Cancer

The recent news story by Hede (1) highlighted research exploring the relationship between diabetes and breast cancer, the context being that up to 16% of breast cancer patients worldwide have diabetes and that diabetic individuals tend to have poorer outcomes following treatment for breast cancer (2). A related issue that has not been studied is the possibility that breast cancer treatment influences glucose metabolism. During chemotherapy, the glucocorticoid dexamethasone is widely used to prevent side effects (3). However, glucocorticoid administration is associated with impairment of insulin sensitivity, elevations in peripheral glucose levels, and the suppression of the hypothalamic–pituitary–adrenal axis for up to 3 weeks (4). We measured changes in blood glucose levels with each cycle of chemotherapy in 39 nondiabetic women (mean age [SD] = 58.6 years [12.8]; mean body mass index [SD] = 27.2 kg/m^2 [4.9]) who were recently diagnosed with breast cancer. This study was approved by the local ethics committee, and all patients gave written informed consent.

The women received either six cycles of fluorouracil, epirubicin, cyclophosphamide (FEC) (18 women) or three cycles of FEC, followed by three cycles of docetaxel (21 women). Before each cycle of FEC chemotherapy, each woman received 8 mg of dexamethasone (by oral administration). The women who were treated with docetaxel received 8 mg of dexamethasone (by oral administration) 24 hours, 12 hours, and immediately before receiving docetaxel (per the product specification). For each cycle of chemotherapy, the nonfasting blood glucose level was measured before the treatment cycle began, immediately after the prechemotherapy dexamethasone was administered but before the administration of chemotherapy, immediately after chemotherapy, and 10 days after each chemotherapy cycle.

We found that there was a statistically significant increase in blood glucose levels with later cycles among women who received the higher dose of dexamethasone in combination with docetaxel (cycle 5: $P < .001$; cycle 6: $P = .002$ [paired t tests]) (Table 1). Before the first cycle of chemotherapy, none of the women had blood glucose levels in either the impaired glucose tolerance range (ie, 7.8–11.1 mmol/L) or the diabetic range (ie, >11.1 mmol/L). However, as the cycles progressed, an increasing number of women developed degrees of glucose intolerance: six women had blood glucose levels in the impaired tolerance range and eight women had levels within the diabetic range following the fifth chemotherapy cycle. Because these women were not diabetic before chemotherapy, it is likely that their hyperglycemia was associated with transient hyperinsulinemia.

Breast cancer cells express high levels of the insulin receptor, and activation of the insulin and the insulinlike growth factor pathways and regulation of endogenous sex hormones have been implicated in the etiology of breast cancer (2,5). Goodwin et al. (6) also found a direct association between insulin concentrations in fasting blood samples and cancer recurrence and death in a cohort of nondiabetic women with early-stage breast cancer. Transient hyperglycemia may also influence the anticancer efficacy of chemotherapy through perturbations of the tumor microenvironment (7). The implications of the impact of transient chemotherapy-associated hyperglycemia on the clinical efficacy of chemotherapeutic agents used in breast cancer treatment are unclear but warrant further investigation.

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Table 1. Mean blood glucose level (SD) before the treatment cycle, after prechemotherapy dexamethasone but before chemotherapy, immediately after chemotherapy, and 10 days after chemotherapy*

Cycle	Before treatment cycle	Immediately after dexamethasone but before chemotherapy	After dexamethasone and chemotherapy	10 d after chemotherapy
1	5.8 (1.1)	4.8 (0.7)	5.7 (2.0)	5.7 (0.7)
2	5.5 (0.9)	5.6 (1.0)	5.5 (0.8)	5.5 (1.0)
3	5.3 (0.9)	5.5 (1.3)	5.9 (1.5)	5.8 (1.4)
4	5.6 (0.9)	6.0 (1.6)	6.4 (1.8)	5.6 (0.8)
5	5.3 (1.0)	7.7 (3.0)	7.8 (2.7)	6.0 (2.0)
6	5.5 (0.8)	8.0 (2.7)	8.1 (3.1)	6.0 (1.2)

* Glucose levels are expressed as mmol/L.

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Notes

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