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The Role of Prostaglandins in the Excessive Nausea and Vomiting after Intravascular *cis*-Platinum Therapy

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Ten patients had serial evaluations of plasma prostaglandin E_2, prostaglandin $F_{2\alpha}$, and 6-keto-$PGF_{1\alpha}$ during administration of *cis*-platinum chemotherapy. No significant changes were noted in $PGF_{2\alpha}$ and 6-keto-$PGF_{1\alpha}$ whereas PGE_2 showed a decrease. This would indicate that the nausea and vomiting of platinum therapy is not a result of tumor release of prostaglandins. All patients had known residual cancer and all had elevated levels of PGE_2 and 6-keto-$PGF_{1\alpha}$.

INTRODUCTION

Recently several published reports have demonstrated significant elevations in plasma prostaglandins in patients with known malignancies [1,2]. Side effects of exogenously administered prostaglandins include severe gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Since *cis*-platinum therapy has similar gastrointestinal side effects it has been postulated that the nausea and vomiting during such therapy may be a result of increased prostaglandin release [3]. To test this hypothesis we measured plasma prostaglandin PGE_2, PGF, and the prostacyclin breakdown product 6-keto-$F_{1\alpha}$ during *cis*-platinum chemotherapy.

MATERIALS AND METHODS

Ten patients with known residual gynecologic cancer being treated with intravenous *cis*-platinum at a dose of 50 mg/m^2 had plasma drawn before a course of therapy and immediately after the onset of severe vomiting. All patients received intramuscular Compazine as their only antiemetic drug and all experienced moderate to severe nausea and vomiting. The plasma prostaglandin levels were measured by previously published techniques [4,5]. Table 1 indicates the normal levels for this laboratory.

RESULTS

Table 2 shows the plasma levels of prostaglandins in relation to side effects of *cis*-platinum therapy. The first samples were always drawn prior to the in-

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TABLE 1
NORMAL LEVELS OF PROSTAGLANDINS

	pg/ml
PGE_2	<200
$PGF_{2\alpha}$	<125
6-keto-$F_{1\alpha}$	<250

stitution of therapy and thus act as a baseline. It is noted that all patients had elevated PGE_2 and markedly elevated levels of 6-keto-$F_{1\alpha}$. No changes are noted between the baseline and post-therapy levels in PGF and 6-keto-$PGF_{1\alpha}$, however, PGE_2 was significantly decreased (P value < 0.25) when compared to the baseline level.

DISCUSSION

cis-Platinum shows some promise in the treatment of gynecologic malignancies, but the gastrointestinal effects are quite severe [6,7]. These side effects are similar to those seen with exogenously administered prostaglandins. Since steroids have been shown to alleviate nausea and vomiting during chemotherapy possibly by inhibiting prostaglandin synthesis [3] it was postulated that these gastrointestinal symptoms were due to increased prostaglandin release. Our study fails to reveal any significant elevation of prostaglandin levels during *cis*-platinum-induced nausea and vomiting. This indicates that prostaglandins are not responsible for these gastrointestinal side effects observed in *cis*-platinum-treated patients.

TABLE 2
PROSTAGLANDIN LEVELS (pg/ml) IN PATIENTS RECEIVING *cis*-PLATINUM CHEMOTHERAPY

	Before Rx			During GI toxicity		
Patient	E_2	$F_{2\alpha}$	6K	E	$F_{2\alpha}$	6K
1	1188	114	11,654	306	28	1498
2	920	232	2,606	639	109	3992
3	1140	414	15,132	561	65	1689
4	559	292	5,188	483	28	3766
5	268	76	1,675	284	56	1076
6	516	109	1,949	253	52	992
7	437	65	2,699	489	26	2420
8	313	23	968	247	27	980
9	973	253	4,173	904	284	4496
10	712	53	1,170	529	51	1191

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