Brief Reports

Comparison of Dexamethasone and Metoclopramide as Anti-emetics in Children Receiving Cancer Chemotherapy

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Nausea and emesis following chemotherapy are often reported by patients. The commonly used standard antiemetic drugs such as metoclopramide(l), prochloperazine(2) and dexamethasone(3) have been demonstrated to be only moderately effective in controlling these symptoms. Recently newer 5-HT_3 receptor antagonists like ondansetron(4) and granisetron(5) have been used in controlling emesis.

The aim of present study was to compare the efficacy and safety of dexamethasone versus metoclopramide in prevention of nausea and emesis in children receiving cyclophosphamide based chemotherapy as outpatients.

Subjects and Methods

From December 1993 to February 1994, we enrolled children (<15 years) with malignancies receiving cyclophosphamide based chemotherapy as outpatient at Tata Memorial Hospital, Bombay. We used a randomized, single blind, cross-over trial in which every patient would be control of his own. During two consecutive courses of same chemotherapeutic drugs, each patient received either dexamethasone (8 mg/m^2 IV slowly 15 minutes prior to chemotherapy) or metoclopramide (1.5 mg/kg IV 15 minutes prior to chemotherapy). During the next cycle, patients received the alternate treatment protocol. In order to assess response, patients were called next day and asked about nausea, emesis or any other side effects. Nausea was graded as: complete response (no nausea or looking not at all sick), moderate (tolerable, interference with activity or looking more sick) and severe (intolerable, bed ridden for over 2 hours or looking very much sick)(6,7). Emesis was graded according to number of emetic episodes: complete response (none), major response (1-2 episodes), minor response (3-4 episodes) and failure (> 5 episodes)(6,7). Possible side-effects of drugs like dystonia, insomnia, elated mood, depression, lack of appetite, abdominal discomfort and head-ache were also noted. The first author (M.B.) assessed the response for nausea and emesis.

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Received for publication: June 17,1994; Accepted: May 29,1995

Results

Twenty seven children receiving a total of 53 chemotherapeutic cycles were entered in this study. Of twenty seven, 26 children were in Group A receiving dexamethasone and 27 were in Group B receiving metoclopramide. One patient from Group B could not complete the cross-over trial. Clinical characteristics of patients are shown in *Table I.* All patients received intravenous cyclophosphamide in dose of 600 mg/m^2 or more along with other drugs like doxorubicin, vincristine and prednisolone.

Complete response for emesis in Group

A was significantly greater than Group B (16 *vs* 8, p <0.02), while for nausea complete response in Group A was 15 while in Group B it was 7 (p<0.02). Major, minor responses or failure for emesis (3 *vs* 6, 3 *vs 7,* 4 *vs* 5) and for nausea were (4 *vs* 5, 4 *vs* 4,3 *vs* 10) in Group A and B respectively. Side-effects were minimum. Dystonia (one case in Group B), insomnia (one case in Group A), depression (one case in Group A, 3 in Group B), lack of appetite (one in Group A, 4 in Group B), abdominal discomfort (one in Group A, 2 in Group B) and headache (one case in Group B) were seen.

Discussion

Antiemetics previously used to control nausea and emesis induced by chemotherapy include high dose metoclopramide(l) and prochlorperazine(2). They have limitations like sedation and extraphyramidal reactions. Methylprednisolone was first used as an antiemetic in 1980(8). This was followed by the use of dexamethasone in various studies in various doses as an antiemetic(3,7,9).

TABLE I-*Patient Characteristics*

No. of patients	
Randomized	27
Evaluable	26
No. *of chemotherapeutic cycles*	53
Age (years)	
Range	3-14
Median	7
Boys: Girls	21: 6
Type of cancer	
Ewing's sarcoma	8
Non Hodgkin's lymphoma	8
Hodgkin's disease	6
Rhabdomyosarcoma	3
Retinoblastoma	1
Acute lymphoblastic leukemia	1

This randomized, single blind, crossover design eliminated a number of inherent drawbacks in comparing one drug with another. Since each patient received the same chemotherapeutic agents in same doses for both cycles of chemotherapy, both dexamethasone and metoclopramide were tested against the same emetic stimuli.

Our results demonstrate the better efficacy of dexamethasone and its superiority over metoclopramide in alleviating the nausea and emesis when used before administrating cyclophosphamide based chemotherapy. Dexamethasone administration caused no major side effects and was tolerated quite well. Addition of dexamethasone to 5-HT_3 receptor antagonists has been shown to increase antiemetic efficacy as compared to when used alone(l0). Although, the exact mechanism of action of dexamethasone as an antiemetic is not known, few hypotheses have been put forward. Corticosteroids may act on the activated prostaglandin pathway(8). They may act on the chemoreceptor trigger zone either by modifying capillary permeability(11) or by stabilizing the membrane or intracellular components and may have a role in endorphin release(12).

Thus we conclude that dexamethasone is effective in preventing nausea and emesis following cyclophosphamide based chemotherapy. Its antiemetic activity appears to be superior to metoclopramide. Further studies are needed to determine the optimal dosage schedule of dexamethasone either alone or in combination with others.

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