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Clinical Evaluation of CHLORPROMAZINE HYDROCHLORIDE**
in Acute Nausea and Vomiting

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The following report on the study of Chlorpromazine Hydrochloride was an unbiased effort to gain knowledge of its applicability and success in treating the following conditions: post-operative nausea and vomiting, hyperemesis gravidarum, and nausea, vomiting and intractable pain in terminal carcinomatosis.

Chlorpromazine Hydrochloride was termed S. K. F.—2601-A in earlier reports, and chemically is 10-(3-dimethyl-aminoprophyl)-2 Chlorphinothiazine Hydrochloride. It was originally synthesized by the Rhone-Poulenc Research Laboratories in France, and is known as "largactil" in Canada, England, France and Italy; as "Megaphin" in Germany; as "Ampliactil" in Argentia; as "Amplictil" in Brazil and "Hibirnal" in Sweden.

MATERIAL.

Twenty-four patients were picked at random, and various doses were given according to the severity of the symptoms. All four cases of malignancy were suffering from adenocarcinoma of the ovaries with generalized metastasis. The patients were subjected to the following gynecological procedures: vaginal hysterectomy with cystocele-rectocele repair, eight patients; dilatation and curettage of uterus, six patients; bartholin cyst removal, one patient; acute mesenteric adenitis, one patient. All cases, except the mesenteric adenitis and hyperemesis, were acute with severe nausea and vomiting following operations under general anesthesia. Almost 100 per cent of the patients received ether as the general anesthetic though induced with sodium seconal intravenously. All of them received morphine sulfate gr. 1/6 and scopolamine gr. 1/150 I.M. preoperatively with the usual preoperative nothing by mouth from midnight. All patients were to receive regular diet as tolerated post-operatively. The hyperemesis and mesenteric adenitis patients were on nothing by mouth, and thus received intravenous supportive therapy.

RESULTS.

The results are best explained by comparative charting, and are, shown in Table 1. The side effects were noted, with desired effects as well, and the dosage used.

Table 2 summarizes the per cent of good results of nausea and vomiting controlled in relation to the side effects.

The commonest side effect was drowsiness which occurred in approximately 20 per cent. Other side effects were dry mouth—10 per cent faintness, tachycardia, pyrosis, conjunctivitis and hypotension of approximately one to two per cent. There was no jaundice noted in any patient.

DISCUSSION.

"Thorazine" is related chemically to antihistamine in that it is a Phenothiazine derivative. However, its antihistaminic, antispasmodic and adrenolytic effects are of such a low order that it accounts for practically none of the actions of the drug. It is a central nervous system and autonomic depressent by modifying or interfering with synaptic transfer of excessive psychomotor excitement between cortical areas and the

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**THORAZINE, Smith, Kline and French Labs., Philadelphia, Pa.

diencephalon so that conscious perceptions are altered. It also acts to a lesser extent on ganglia and the peripheral autonomic system. It definitely potentiates, in-

Diagnosis	Pt. No.	Side Effects	Results	Initial Dosage
Terminal	1	drowsiness faintness	stopped vomiting	25mgm. IM a. c.
carcinomatosis	2	drowsiness faintness	poor results	25mgm. IM a. c. h. s.
	3	none	reduced demoral to 1/3	25mgm. IM a. c. h. s.
	4	none	no change	25mgm. IM a. c. h. s.
Vaginal hysterectomy	5	none	good	25mgm. IM a. c. h. s.
Cystocele and	6	none	fair	25mgm. IM a. c. h. s.
rectocele repair	7	acute pyrosis	poor	25mgm. IM a. c. h. s.
	8	none	good	25mgm. IM a. c. h. s.
	9	none	good	25mgm. IM B. d.
	10	none	good	25mgm. IM a. c. h. s.
	11	none	good	25mgm. IM b. d.
	12	none	good	25mgm. IM b. d.
Dilatation and	13	none	good	25mgm. IM a.c.
curettage	14	none	good	25mgm. IM q. 6h.
	15	none	fair	No medicine
	16	acute drowsiness	good	25mgm. IM a. c.
	17	none	good	25mgm. IM b. d.
	18	none	good	25mgm. IM q. 6h.
Hypertension	19	none	poor	25mgm. IM q. 6h.
Post-radiation	20	none	good	25mgm. orally q. 6h.
Hyperemesis	21	acute drowsiness	poor	25mgm. IM a.c.
gravidarum	22	none	fair	25mgm. IM b. d.
Bartholin cyst excision	23	none	poor	25mgm. IM a. c. h. s.
Mesenteric adenitis	24	conjunctivitis, acute drowsiness	no benefit	25mgm. IM a. c. h. s. varied c no benefit

Table 1. Diagnosis, side effects, results and dosage.

No. Cases	Disease	% Good Response	% Side Reactions
4	Terminal carcinomatosis	50%	50%
8	Vaginal hysterectomy, cystocele-rectocele repair	88%	12%
6	Dilatation and curettage	100%	12%
1	Hypertension	100%	0%
2	Hyperemesis gravidarum	100%	50%
1	Bartholin cyst excision	0-poor	0%
1	Mesenteric adenitis	very poor	100%
1	Post radiation reaction	100%	0%

Table 2. diagram illustrates the percent of side effects in relation to the percent of good, fair or poor response.

tensifies and prolongs the action of various drugs—notably narcotics,[7,5] hypnotics, sedatives,[6] anesthetics,[6,11] alcohol and muscle relaxants. The important anti-emetic effect is believed to result from blocking emetic impulses at the chemoreceptor trigger zones and reticular mechanism in the medulla. It is a relatively non-toxic drug with no clinical evidence to date of any damage to tissues, organs and body fluids from prolonged use, as well as free from addiction production.

Its apparent site of detoxification is the liver and shows little effect on renal function with only slightly increased sodium excretion observed. Friend and Cummins,[3] showed it to be very effective against nausea and vomiting of uremia.

Its delightful effects were producing, as Howell, Harth and Dietrick,[9] described, a curtain between the patient and his pain. Sadove, Levin, Rose, Schwartz and Witt,[7] noted their patients spoke of their pain as an objective phenomenon.

It is essential to bear in mind that the dosage of "Thorazine" must be highly individualized, varying widely from indication to indication; from patient to patient and according to the severity of the condition and the degree of response in each patient. Caution must be used and frequent blood pressure recordings must be ordered on the charts of all patients to detect early hypotention and possible shock, especially until tolerated maintenance dosages are established.

Although juandice occurs in very few cases, it has not been proven to date that "Thorazine" is hepatotoxic, although the liver function tests are similar to those in obstructive juandice, i. e. elevation of serum bilirubin, elevated alkaline phosphatase, increased serum cholesterol concentration and detection of bile in the urine.

In the above cases oral administration was used when possible. However, almost all were given initial doses I. M. to be followed by oral use as soon as tolerated. The results, overall, were gratifying with the average percent of side effects in the same range as those recorded by numerous other investigators.

SUMMARY

1. The many methods of administration of "Thorazine" makes it easily selectable to fit the individual.

2. The diversity of its pharmacologic action and the necessity of variation in dosage emphasizes the importance of determining the optimal dosage regime for the condition and for the individual.

3. The primary acute nausea and vomiting was well controlled in the majority of patients in spite of the rather high incidence of side effects noted. However, most patients preferred the side effects rather than the more distressing initial complaints.

4. Caution, and frequent blood pressure recordings, should be ordered on all patients receiving "Thorazine" until the maintenance dose is ascertained.

5. The severity of the side effects of the drug varied according to the size dose given, and many of these side effects are easily controlled by other drugs.

6. It is important to note that our evaluation was limited to a relatively small number of patients. We found that for certain specific complaints, the drug produced encouraging results. This may lead one to use the drug empirically to treat acute nausea and vomiting which is certainly wrong, in that the cause of nausea and vomiting should always be established before "Thorazine" is administered, so that the diagnosis will not be obscured.

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