B. GASTROINTESTINAL USE

(1) HALDOL - 1.0 mg

1. Leslie, R.E., M.D. (10) - Study No. 1
A double-blind evaluation of the antiemetic properties of HALDOL in nonhospitalized patients with nausea and vomiting as a result of gastrointestinal disorders.

Fifty-four patients who required antiemetic treatment for moderate to severe vomiting with nausea were entered into the study. Ten patients were excluded because vomiting was due to conditions other than gastrointestinal disturbances (e.g. vascular headache, and digitalis toxicity, etc.).

The characteristics of the remaining 44 patients are shown in Table XLIV. Either HALDOL 1.0 mg or placebo was administered intramuscularly as a single dose following the development of vomiting.

Table XLIV
Patient Characteristics

Drug Group	Age		Sex		Weight		Total Cases
	Mean	Range	Male	Female	Mean	Range	
HALDOL	54.0	23-84	5	18	158.6	102-301	23
Placebo	58.6	17-85	4	17	147.2	91-253	21

Patients were evaluated for 12 hours post-drug administration. The episodes of vomiting were recorded initially and every two hours for the first four hours and every four hours for the next eight hours (up to 12 hours). These data are presented in Table XLV.

Table XLV
Episodes of Vomiting

Time of Observation	Drug Group	Frequency						Total Patients
		0	1	2	3	4	>5	
Initially (Pre-Study Drug)	HALDOL	0	0	9	9	2	3	23
	Placebo	0	0	2	10	7	2	21
During First Two-Hour Post-Study Drug	HALDOL*	15	6	2	0	0	0	23
	Placebo	6	10	4	1	0	0	21
During Two-Hour to Four-Hour Period	HALDOL*	21	2	0	0	0	0	23
	Placebo	12	6	2	0	0	0	20
During Four-Hour to Eight-Hour Period	HALDOL	23	0	0	0	0	0	23
	Placebo	18	1	1	0	0	0	20
During Eight-Hour to 12-Hour Period	HALDOL	22	1	0	0	0	0	23
	Placebo	20	0	0	0	0	0	20

*Statistically significantly fewer episodes of vomiting during this particular period ($P \leq .05$, Rank "t" Test)

A review of Table XLV reveals that there were fewer episodes of vomiting in the HALDOL-treated group than in the placebo group. The difference between the two treatments in the episodes of vomiting was significant ($P<.05$) favoring HALDOL at the 2-hour and during the 2-hour to 4-hour evaluation points. The data are presented graphically in Figure 7.

The incidence of vomiting in the HALDOL drug group was significantly ($P<.01$) less than in the placebo group over the 12-hour evaluation period. Similarly, the incidence of vomiting in the HALDOL group during the 4 to 8-hour period and during the 8 to 12-hour period was also significantly ($P<.01$) less than in the placebo group during these periods. This continued difference between test groups indicates prolonged effectiveness of HALDOL.

During the 12-hour observation period, 15 (66%) of the 23 HALDOL patients but only 5 (24%) of the 21 placebo patients were free of vomiting. This difference between the two treatments is statistically significant ($P<.01$) in favor of HALDOL.

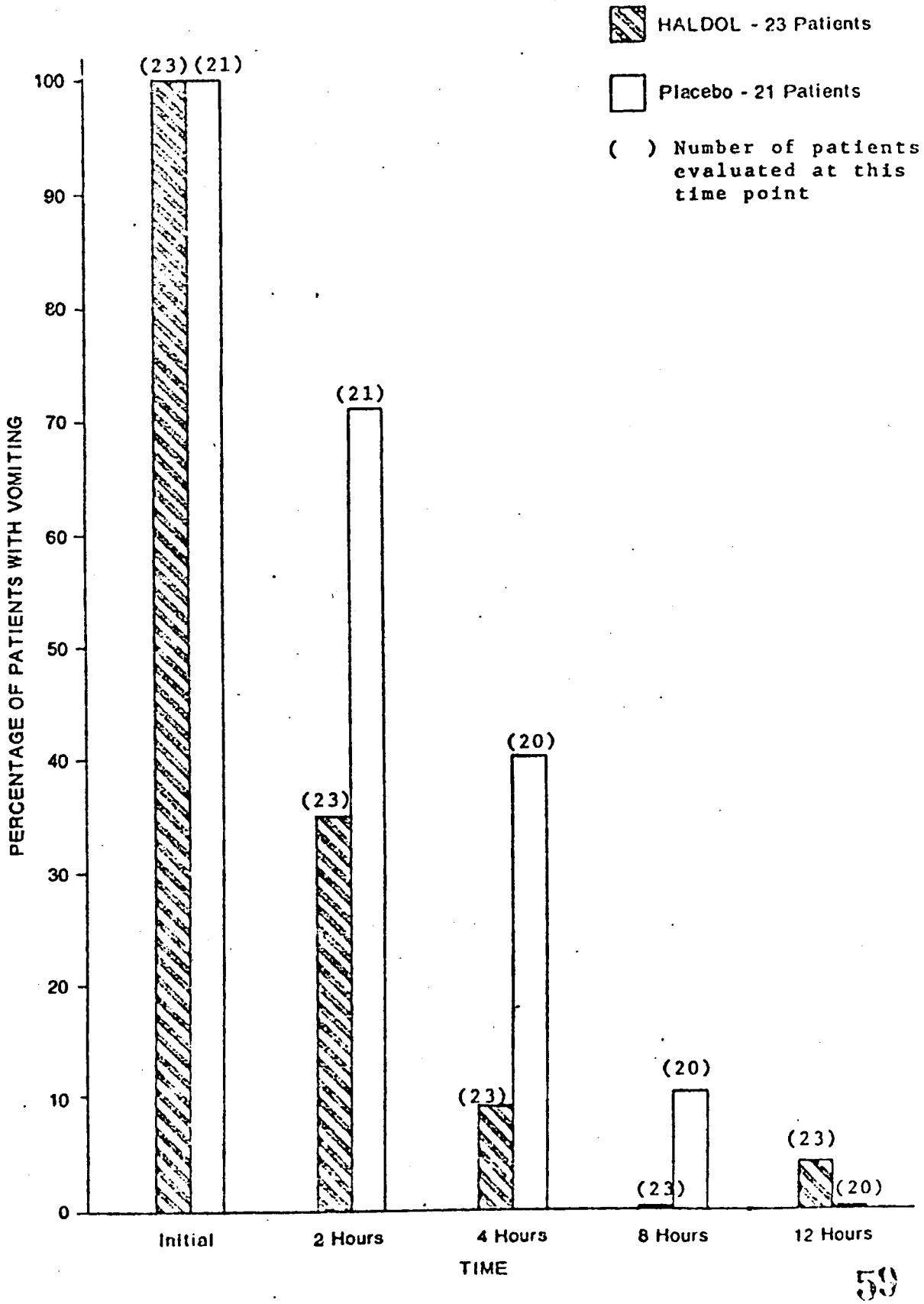
The occurrence of nausea after treatment is presented in Table XLVI.

Table XLVI
Occurrence of Nausea

Time of Observation	Drug Group	Severity*of Nausea				Total Patients
		0	1	2	3	
Initially (Pre-Study Drug)	HALDOL	0	2	18	3	23
	Placebo	0	0	21	0	21
During First Two-Hour Post-Study Drug	HALDOL	11	9	3	0	23
	Placebo	3	15	3	0	21
During Two-Hour to Four-Hour Period	HALDOL**	21	2	0	0	23
	Placebo	10	10	0	0	20
During Four-Hour to Eight-Hour Period	HALDOL	21	2	0	0	23
	Placebo	17	3	0	0	20
During Eight-Hour to 12-Hour Period	HALDOL	22	1	0	0	23
	Placebo	19	1	0	0	20

*0=None, 1=Mild, 2=Moderate, and 3=Marked
**Statistically significant less nausea among HALDOL patients ($P<.01$)

Figure 7


HALDOL - 23 Patients
Placebo - 21 Patients
( ) Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH VOMITING
100
90
80
70
60
50
40
30
20
10
0
(23) (21)
(23)
(21)
(23)
(20)
(23)
(20)
(23)
(20)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

There were fewer occurrences of nausea among the HALDOL patients than among the placebo patients at each evaluation point. The difference in the occurrence of nausea between the two treatments is significant ($P < .01$), favoring HALDOL, during the 2 to 4-hour evaluation point.

A pattern for the reduction of the incidence of nausea is similar to that of vomiting presented in Fig. 8.

A review of the two cumulative severity score distributions made by summing each patient's nausea rating during the 12-hour observation period shows that the severity of nausea for the placebo patients is significantly ($P < .01$) higher than that of the HALDOL patients.

The investigator's global or overall evaluation at the end of therapy is presented in Table XLVII.

Table XLVII
Global Evaluation

Drug Group	Evaluation				Total Patients
	Marked	Moderate	Minimal	Unchanged	
HALDOL	19	3	1	0	23
Placebo	11	5	2	3	21

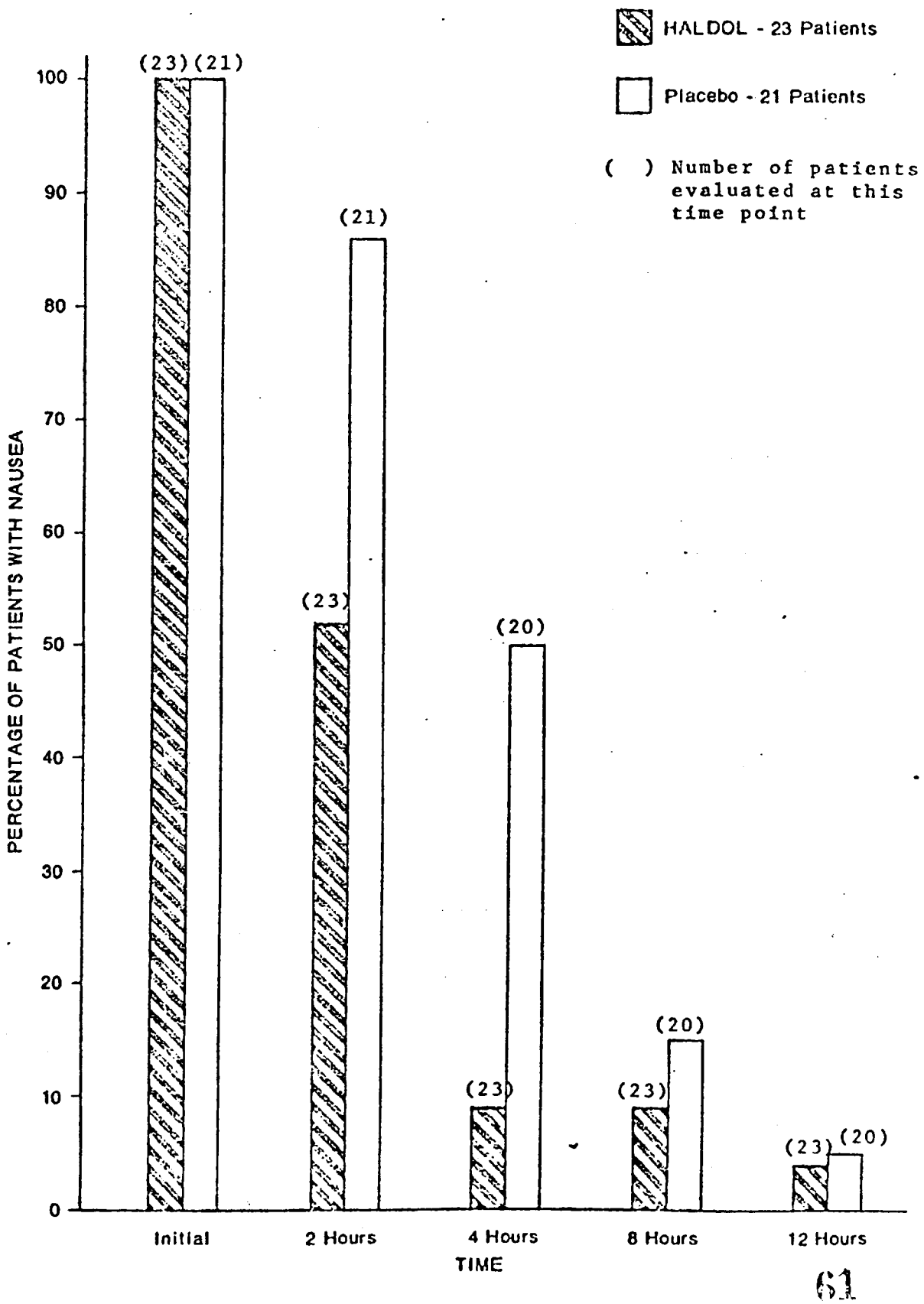
An analysis of the data shows the statistical difference between the therapeutic responses to the two treatments to be $P < .05$ in favor of HALDOL.

The vital signs obtained 2 hours after administration of the drug demonstrated no significant difference between the treatment groups.

No side effects were observed in either drug group during the course of the study.

One patient, who had received placebo, continued to have nausea and vomiting to a degree requiring immediate

Figure 8


HALDOL - 23 Patients
Placebo - 21 Patients
( ) Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH NAUSEA
100
90
80
70
60
50
40
30
20
10
0
(23) (21)
(21)
(23)
(20)
(23)
(20)
(23)
(20)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

treatment. He was considered a treatment failure and dropped from the evaluation. The patient was then administered 1.0 mg of uncoded parenteral HALDOL and exhibited a marked therapeutic response.

In summary, the intramuscular injection of 1.0 mg HALDOL was safe and significantly ($P < .05$ and in some instances $P < .01$) more effective than was placebo in controlling nausea and vomiting as a result of gastrointestinal disorders.

2. Weinstein, R.A., M.D. (13)
A double-blind evaluation of the antiemetic properties of HALDOL in hospitalized and nonhospitalized patients with nausea and vomiting as a result of gastrointestinal disorders.

Forty-three patients who required antiemetic treatment for moderate to severe vomiting with nausea were entered into the study.

The characteristics of the 43 patients are shown in Table XLVIII. Either HALDOL 1.0 mg or placebo was administered intramuscularly as a single dose within four hours of an episode of vomiting.

Table XLVIII
Patient Characteristics

Drug Group	Age		Sex		Weight		Total Patients
	Mean	Range	Male	Female	Mean	Range	
HALDOL	52.0	22-80	2	21	142.1	92-175	23
Placebo	40.7	18-74	4	16	141.5	110-195	20

Patients were evaluated for 12 hours post-drug administration.

The incidence of vomiting was recorded initially and every two hours for the first four hours and every four hours for the next eight hours (up to 12 hours). The data are presented in Table XLIX.

Table XLIX
Episodes of Vomiting

Time of Observation	Drug Group	Frequency						Total Patients
		0	1	2	3	4	> 5	
Initially (Pre-Study Drug)	HALDOL	0	2	4	5	7	5	23
	Placebo	0	1	5	5	7	2	20
During First 2-Hour Post-Study Drug	HALDOL*	6	4	3	0	0	0	13
	Placebo	2	0	6	1	1	0	10
During 2-Hour to 4-Hour Period	HALDOL*	14	4	4	1	0	0	23
	Placebo	7	0	10	3	0	0	20
During 4-Hour to 8-Hour Period	HALDOL**	22	1	0	0	0	0	23
	Placebo	8	4	7	0	0	0	19
During 8-Hour to 12 Hour Period	HALDOL**	22	0	0	0	0	0	22
	Placebo	7	7	3	0	0	0	17

*Statistically significantly fewer episodes of vomiting during this period ($P < .05$, Rank "t" Test); **$P < .01$

The data demonstrate that the response to HALDOL, in a single 1.0 mg dose administered intramuscularly, was significantly ($P < .05$ and in some instances $P < .01$) greater at each evaluation point than to placebo.

The data are presented graphically in Figure 9. Of the 23 HALDOL patients, 12 (52%) were free of vomiting during the entire 12-hour period of evaluation; whereas, only 6 (30%) of the placebo patients remained free of vomiting.

An evaluation of the incidence of vomiting reveals significantly ($P < .01$) less vomiting in the HALDOL-treated group than in the placebo-treated group during the 12-hour observation period.

The duration of effectiveness is further demonstrated by an evaluation of the incidence of vomiting during the 4 to 12-hour observation period. This observation reveals a significant ($P < .01$) difference in the cumulative score between the two treatments in favor of HALDOL.

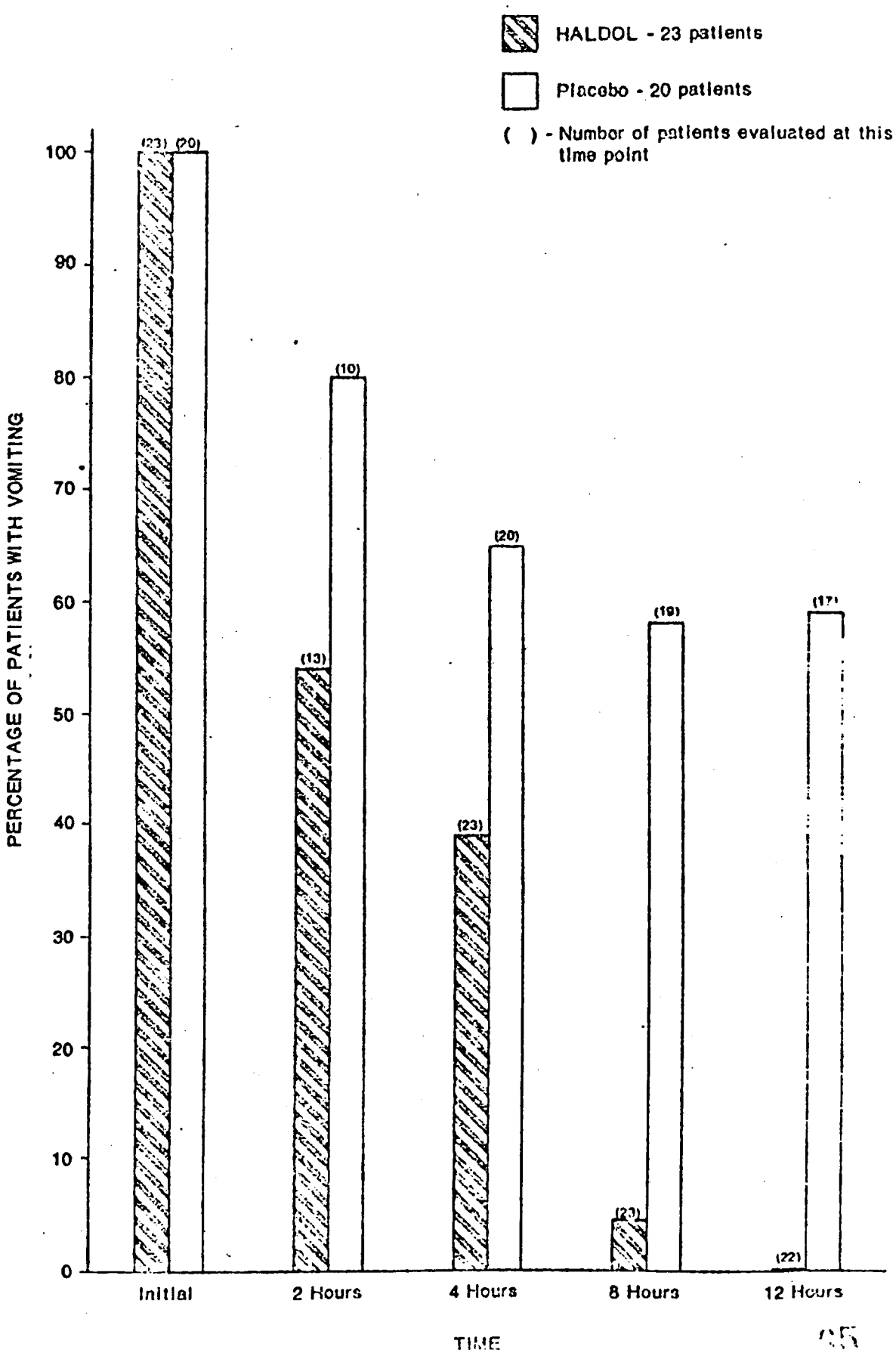
The occurrences of nausea during the 12-hour post-treatment period are presented in Table L.

Table L
Occurrences of Nausea

Time of Observation	Drug Group	Severity† of Nausea				Total Patients
		0 +	1	2	3	
Initially (Pre-Study Drug)	HALDOL	0	0	6	17	23
	Placebo	0	0	6	14	20
During First 2-Hour Post-Study Drug	HALDOL	3	3	7	0	13
	Placebo	1	1	6	2	10
During 2-Hour to 4-Hour Period	HALDOL	3	9	8	3	23
	Placebo	3	2	9	6	20
During 4-Hour to 8-Hour Period	HALDOL*	15	6	0	2	23
	Placebo	5	1	13	0	19
During 8-Hour to 12-Hour Period	HALDOL*	19	2	0	1	22
	Placebo	5	4	6	2	17

†0=None, 1=Mild, 2=Moderate, and 3=Marked
*Statistically significantly less nausea among HALDOL patients ($P < .05$, Rank "t" Test)

Figure 9


HALDOL - 23 patients
Placebo - 20 patients
( ) - Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH VOMITING
100
90
80
70
60
50
40
30
20
10
0
(23)
(20)
(10)
(13)
(20)
(23)
(19)
(23)
(17)
(22)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

An evaluation of these data clearly demonstrates that the severity of nausea experienced by the HALDOL-treated patients was significantly less than that experienced by the placebo-treated patients at the 8 and 12-hour evaluation points. The data are presented graphically in Figure 10.

The investigator's global or overall evaluation at the end of therapy is presented in Table LI.

Table LI
Global Evaluation

Drug Group	Evaluation				Total Patients
	Marked	Moderate	Minimal	Unchanged	
HALDOL	7	15	1	0	23
Placebo	2	3	7	8	20

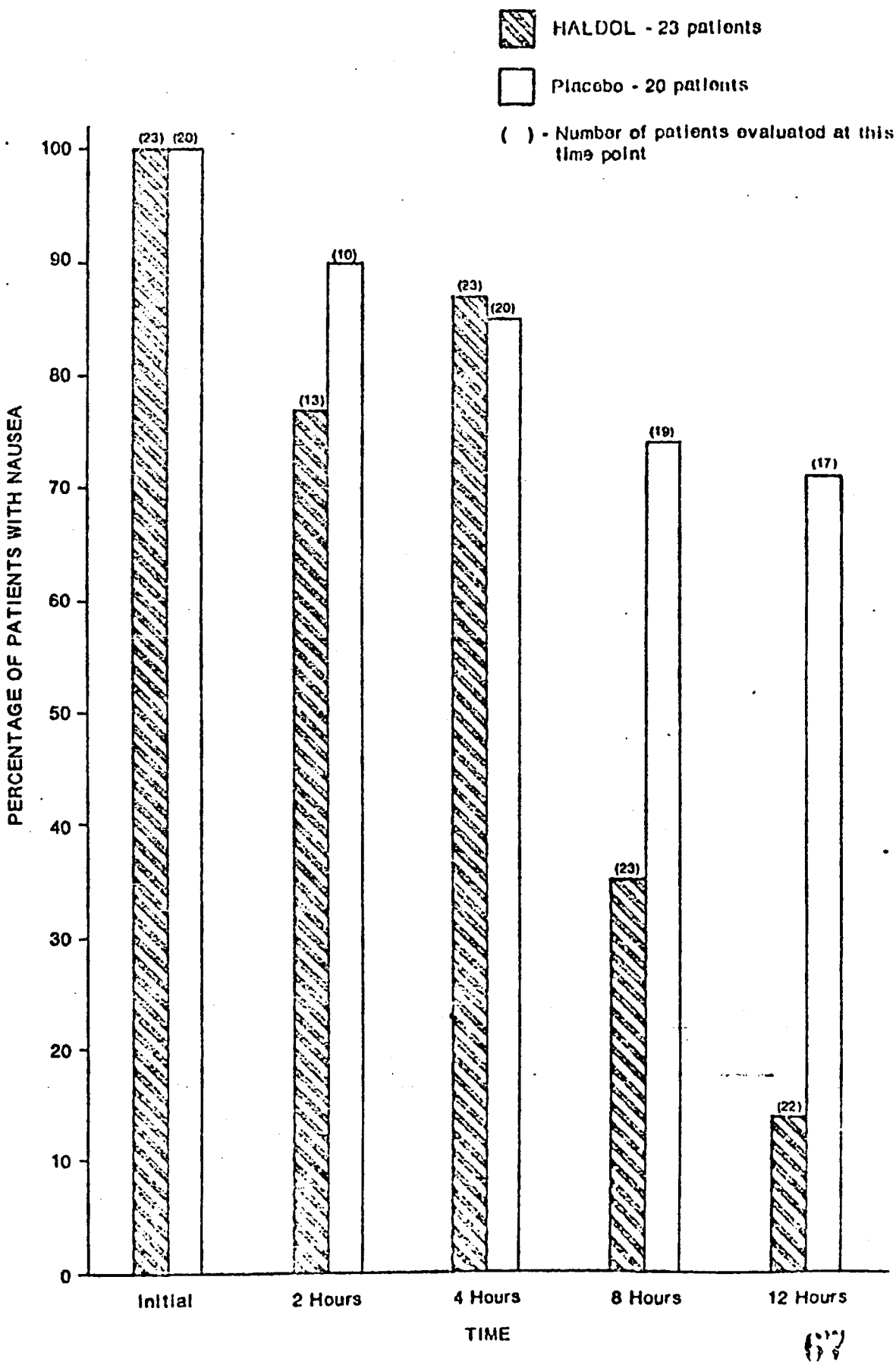
A review of these data clearly reveals that the response of the patients to HALDOL treatment was significantly ($P < .01$) superior to that on placebo treatment. Marked to moderate responses to treatment were experienced by 22 (96%) of the 23 patients receiving HALDOL but by only 5 (25%) of the 20 patients receiving placebo.

Vital signs were observed initially and after 2-hours, and except for a small, but statistically significant difference in respiration between the two groups, no other significant differences were noted.

No side effects were observed in either drug group during the course of the study.

In summary, the intramuscular administration of HALDOL in a single dose of 1.0 mg was shown to have superior effectiveness to placebo in the treatment of the nausea and vomiting as a result of gastrointestinal disorders. The prolonged effect of HALDOL is demonstrated by the significant difference in response during the 4 to 12-hour period in favor of HALDOL.

Figure 10


HALDOL - 23 patients
Placebo - 20 patients
( ) - Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH NAUSEA
100
90
80
70
60
50
40
30
20
10
0
(23) (20)
(13) (10)
(23) (20)
(23) (19)
(22) (17)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

3. Christman, R.S., M.D. (14)
A double-blind evaluation of the antiemetic properties of nonhospitalized patients with nausea and vomiting as a result of gastrointestinal disorders.

Fifty patients who required antiemetic treatment for moderate to severe vomiting with nausea were entered into the study.

The characteristics of the 50 patients are shown in Table LII. Either HALDOL 1.0 mg or placebo was administered intramuscularly as a single dose within four hours of an episode of vomiting.

Table LII
Patient Characteristics

Drug Group	Age		Sex		Weight		Total Patients
	Mean	Range	Male	Female	Mean	Range	
HALDOL	50.2	21-70	8	17	152.3	120-214	25
Placebo	44.0	32-67	7	18	153.0	101-218	25

Patients were evaluated for 12 hours post-drug administration.

The incidence of vomiting was recorded initially and every two hours for the first four hours and every four hours for the next eight hours (up to 12 hours). The data are presented in Table LIII.

Table LIII
Episodes of Vomiting

Time of Observation	Drug Group	Frequency						Total Patients
		0	1	2	3	4	≥5	
Initially (Pre-Study Drug)	HALDOL	0	2	4	7	8	4	25
	Placebo	0	0	5	14	4	2	25
During First 2-Hour Post-Study Drug	HALDOL**	16	9	0	0	0	0	25
	Placebo	3	21	1	0	0	0	25
During 2-Hour to 4-Hour Period	HALDOL*	24	1	0	0	0	0	25
	Placebo	17	7	1	0	0	0	25
During 4-Hour to 8-Hour Period	HALDOL	24	1	0	0	0	0	25
	Placebo	24	0	0	0	0	0	24
During 8-Hour to 12-Hour Period	HALDOL	25	0	0	0	0	0	25
	Placebo	24	0	0	0	0	0	24

*Statistically significantly fewer episodes of vomiting during this period ($P < .05$, Rank "t" Test), **$P < .01$

The data demonstrate that the response to HALDOL in a single 1.0 mg dose administered intramuscularly was significantly ($P < .05$ and in some instances $P < .01$) greater at the 2 and 4-hour post-treatment periods than was placebo. The effectiveness of HALDOL was maintained at the 8 and 12-hour observation periods, however, the responses to placebo were also high at these points resulting in lack of significant differences.

The data are presented graphically in Figure 11.

During the 12-hour observation period, 16 (64%) of the 25 patients receiving HALDOL were free of vomiting, whereas, only 3 (12%) of the 25 patients receiving placebo were free of vomiting.

An evaluation of the incidence of vomiting during the 12-hour observation period reveals that the HALDOL group vomite significantly ($P < .01$) less often than did the group on placebo

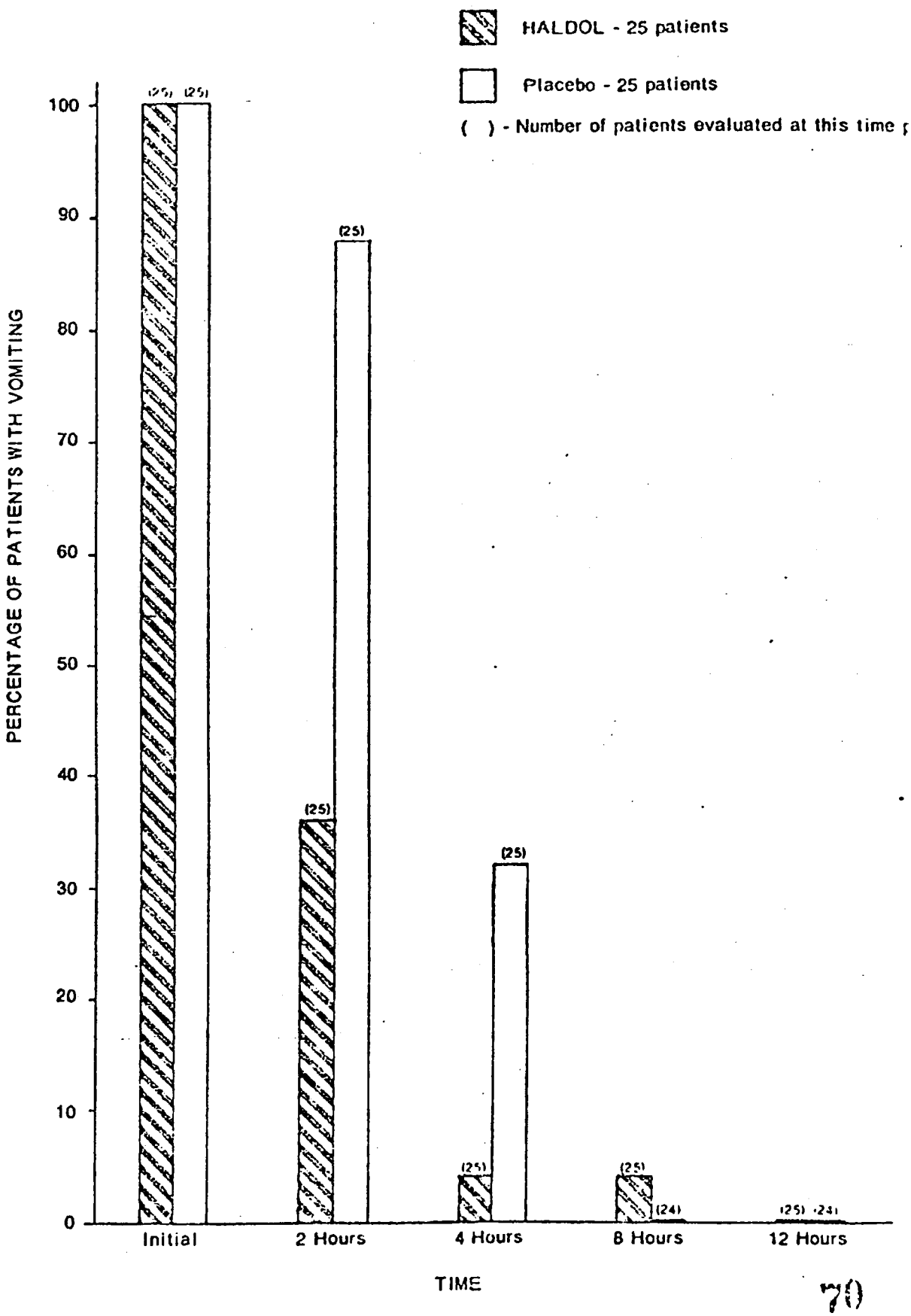
The occurrences of nausea during the 12-hour post-treatment period are presented in Table LIV.

Table LIV
Occurrences of Nausea

Time of Observation	Drug Group	Severity† of Nausea				Total Patients
		0	1	2	3	
Initially (Pre-Study Drug)	HALDOL	0	1	12	12	25
	Placebo	0	1	20	4	25
During First 2-Hour Post-Study Drug	HALDOL*	0	21	4	0	25
	Placebo	0	14	10	1	25
During 2-Hour to 4-Hour Period	HALDOL**	8	16	1	0	25
	Placebo	0	21	4	0	25
During 4-Hour to 8-Hour Period	HALDOL*	16	9	0	0	25
	Placebo	8	16	0	0	24
During 8-Hour to 12-Hour Period	HALDOL	24	1	0	0	25
	Placebo	22	2	0	0	24

† 0 - None, 1 - Mild, 2 - Moderate, and 3 - Marked.
*Statistically significantly less nausea among HALDOL patients ($P < .05$, Rank "t" Test), **$P < .01$

Figure 11


HALDOL - 25 patients
Placebo - 25 patients
( ) - Number of patients evaluated at this time
PERCENTAGE OF PATIENTS WITH VOMITING
100
90
80
70
60
50
40
30
20
10
0
(25) (25)
(25)
(25)
(25)
(25)
(24)
(25) (24)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

An evaluation of these data demonstrate that the severity of nausea experienced by the HALDOL group was significantly ($P < .05$ and in some instances $P < .01$) less than that experienced by the placebo group at the 2, 4 and 8-hour observation points. The data are presented graphically in Figure 12.

The data may also be compared by summing each patient's post-drug cumulative nausea rating over the 4-hour and 12-hour observation periods. These comparisons show that the severity of nausea scores for the patients on placebo were significantly ($P < .01$) higher (and the nausea, therefore, more severe) than for the patients on HALDOL in both time periods.

The investigator's global or overall evaluation at the end of therapy is presented in Table LV.

Table LV
Global Evaluation

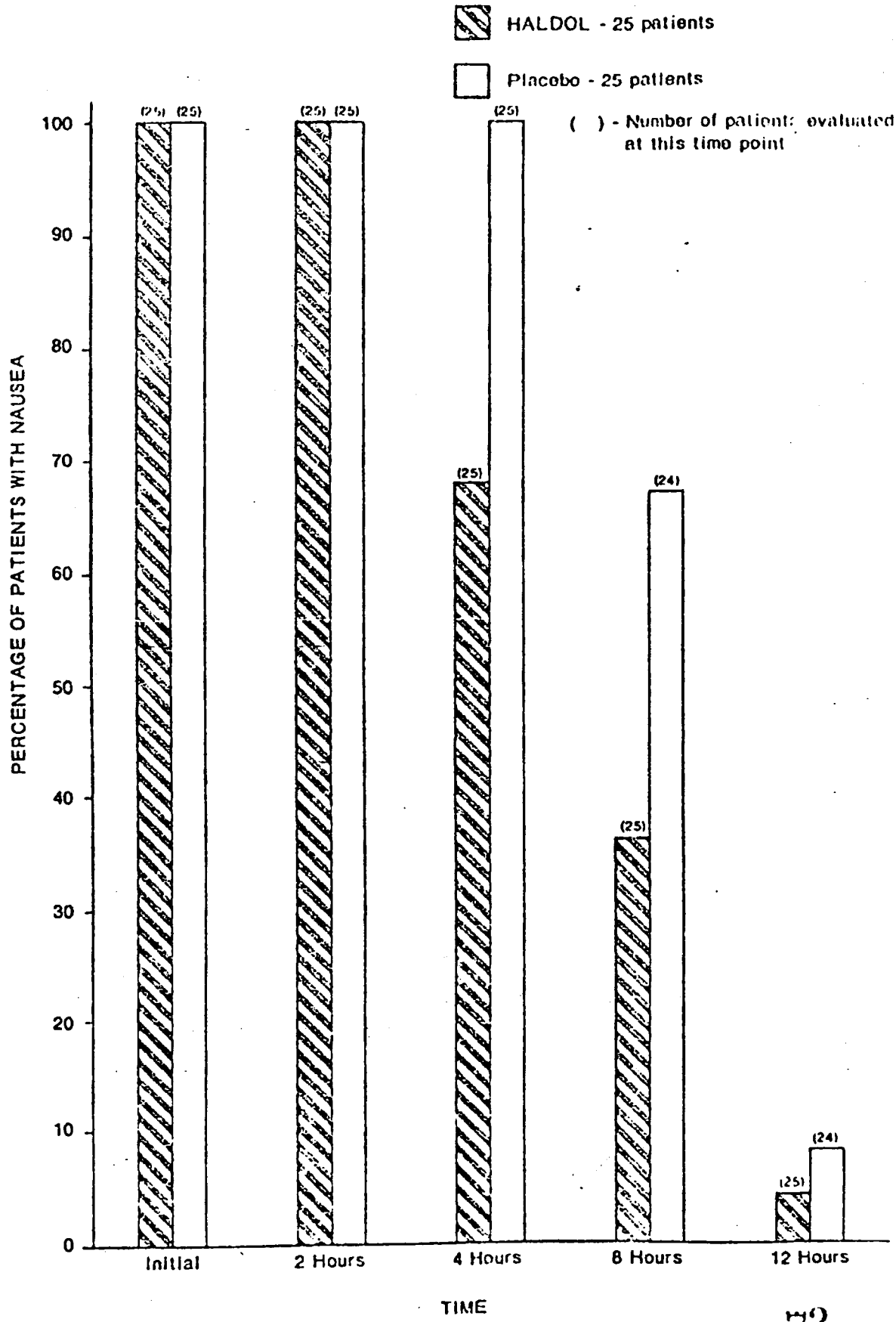
Drug Group	Evaluation				Total Patients
	Marked	Moderate	Minimal	Unchanged	
HALDOL	10	11	4	0	25
Placebo	1	10	13	1	25

An analysis of these data clearly reveals that the response of the patients to HALDOL treatment was significantly ($P < .01$) superior to that of placebo. Marked to moderate responses to treatment were experienced by 21 (84%) of the 25 patients receiving HALDOL but by only 11 (44%) of the 25 patients receiving placebo.

Vital signs were observed initially and after 2-hours with no significant difference being observed between the two groups

Two patients in the HALDOL drug group reported side effects one reported blurred vision and the other reported drowsiness.

Figure 12


HALDOL - 25 patients
Placebo - 25 patients
( ) - Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH NAUSEA
0
10
20
30
40
50
60
70
80
90
100
(25) (25)
(25) (25)
(25)
(25)
(24)
(25)
(24)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

In summary, the intramuscular administration of HALDOL in a single dose of 1.0 mg was shown to have superior effectiveness to placebo in the treatment of nausea and vomiting due to gastrointestinal disorders. The reduction of vomiting during the first 4-hours and nausea during the first 8-hours by HALDOL was significantly greater than that by placebo.

4. Robbins, E.L., M.D. (15)
A double-blind evaluation of the antiemetic properties of HALDOL in institutionalized geriatric patients with nausea and vomiting as a result of gastrointestinal disorders.

Thirty patients from a nursing home population were selected for study. All required antiemetic treatment for moderate to severe vomiting with nausea.

Two patients were excluded from the analysis because of failure to vomit prior to drug administration as required by protocol. The characteristics of the remaining 28 patients are shown in Table LVI. Either HALDOL 1.0 mg or placebo was administered intramuscularly as a single dose within four hours of an episode of vomiting.

Table LVI
Patient Characteristics

Drug Group	Age		Sex		Weight		Total Cases
	Mean	Range	Male	Female	Mean	Range	
HALDOL	81.7	72-91	2	12	120.6	88-157	14
Placebo	85.0	76-95	1	13	119.8	90-169	14

Patients were evaluated for 12 hours post-drug administration.

The incidence of vomiting was recorded initially and every two hours for the first four hours and every four hours for the next eight hours (up to 12 hours). The data are presented in Table LVII.

Table LVII
Episodes of Vomiting

Time	Drug Group	N*	No. of Episodes of Vomiting or Retching				
			0	1	2	3	≥ 4
Previous 12 Hours	HALDOL	14	0	9	4	1	0
	Placebo	14	0	10	3	0	1
+ 2 Hrs.	HALDOL	14	13	1	0	0	0
	Placebo	14	10	2	0	1	1
+ 4 Hrs.	HALDOL	14	13	1	0	0	0
	Placebo	11	8	3	0	0	0
+ 8 Hrs.	HALDOL	12	12	0	0	0	0
	Placebo	8	6	2	0	0	0
+ 12 Hrs.	HALDOL	12	12	0	0	0	0
	Placebo	6	6	0	0	0	0

*N=Number of patients

A review of the table indicates that the frequency of vomiting was reduced in both groups within two hours. The number of episodes of vomiting during the several observation periods was lower in the HALDOL group but not significantly different from the placebo group. This lack of difference in groups may have been due to the fact that a known antiemetic was administered whenever a patient developed vomiting after the study medication had been given. This action was taken because of the advanced age (mean 83 years) of the patients. For that reason, nine patients (2-HALDOL, 7-placebo) were dropped from the study prior to completion of the 12-hour period. Fifty percent of the placebo patients (7 of 14) but only 14% of the HALDOL patients (2 of 14) required supplemental antiemetic medication during the study. This difference is statistically significant ($P < .05$) in favor of HALDOL.

During the 12-hour observation period, 12 (86%) of the 14 HALDOL-treated patients, but only 6 (43%) of the 14 placebo patients were free of vomiting. This difference is statistically significant ($P < .05$) in favor of HALDOL.

The occurrences of nausea during the 12-hour post-treatment period are presented in Table LVIII.

Table LVIII
Occurrences of Nausea

Time	Drug Group	N*	Severity of Nausea			
			None	Mild	Moderate	Marked
Previous 12 Hours	HALDOL	14	0	4	6	4
	Placebo	14	1	2	8	3
+ 2 Hrs.	HALDOL	14	12	1	1	0
	Placebo	14	8	3	1	2
+ 4 Hrs.	HALDOL	14	12	0	2	0
	Placebo	11	6	3	1	1
+ 8 Hrs.	HALDOL	12	12	0	0	0
	Placebo	8	6	1	1	0
+ 12 Hrs.	HALDOL	12	12	0	0	0
	Placebo	6	5	1	0	0

*N=Number of patients

A significant ($P < .05$) difference in the severity of nausea occurred in the 4-hour observation period in favor of HALDOL. As with the data on vomiting, the lack of significance at other evaluation points may be attributed to the high incidence of placebo drop-out.

The investigator's global evaluation at the end of therapy is presented in Table LIX.

Table LIX
Global Evaluation

Drug Group	Evaluation					Total Patients
	Marked	Moderate	Minimal	Unchanged	Worse	
HALDOL	12	0	0	2	0	14
Placebo	5	3	0	4	2	14

Review of the global data reveals a significant ($P < .05$) difference between the therapeutic responses of the two treatments in favor of HALDOL.

Vital signs were observed initially and after 2-hours, and, except for a small but statistically significant difference in body temperature between the two groups, no other significant differences were noted.

With the exception of one placebo patient who showed a significantly increased pulse rate, no adverse reactions were reported.

In summary, the intramuscular administration of HALDOL in a single dose of 1.0 mg was shown to be statistically more effective than placebo in the reduction of nausea and vomiting due to gastrointestinal disorders in a geriatric population during the 12-hour period following antiemetic therapy.

5. LaRose, J.B., M.D. (16)
A double-blind evaluation of the antiemetic properties of HALDOL in nonhospitalized patients with nausea and vomiting as a result of gastrointestinal disorders.

Twelve patients who required antiemetic treatment for moderate to severe vomiting with nausea as a result of gastrointestinal disorders were entered into the study and accepted for analysis. Seven patients received HALDOL 1.0 mg administered intramuscularly, and five patients received placebo as a single dose within four hours of an episode of vomiting. Because of the small sample in this study, the details of the data are not presented in this summary but can be found in the tabulation and analysis of this investigator's study.*

During the 12 hours post-drug administration, a greater reduction in frequency of vomiting and the occurrence of severity of nausea was apparent in the HALDOL drug group as compared to the placebo drug group; however, the difference was not statistically significant.

A review of the global evaluations by the investigator shows that 6 of the 7 HALDOL-treated patients and 3 of the 5 placebo patients experienced "marked" to "moderate" responses; however, the difference was not statistically significant.

Vital signs were not significantly different between the two treatment groups, and no side effects were reported by either group.

In summary, the sample was too small to demonstrate a significance of the differences which were shown to exist in favor of HALDOL (1.0 mg, I.M.) in reducing the episodes of

* See exhibit Vol. 16 Pg. 4648

vomiting and the severity of nausea in patients with gastrointestinal disorders.

6. Combined Analysis of Five Investigators (Leslie, R., Weinstein, R., Christman, R., Robbins, E., and LaRose, J.) (17)

A double-blind evaluation of the antiemetic properties of HALDOL in hospitalized and nonhospitalized patients with nausea and vomiting as a result of gastrointestinal disorders.

The above named investigators used the same protocol and case report form to study the intramuscular administration of HALDOL at a single dose of 1.0 mg in the therapeutic treatment of nausea and vomiting due to gastrointestinal disturbances.

The patient population used in the combined analysis of these five studies is shown in Table LX.

A total of 189 patients were entered into the five studies. Of these patients, 12 were excluded as explained in the individual analyses. The final analysis included 92 patients in the HALDOL and 85 in the placebo group.

Table LX
Patient Population

Investigator's Name	Number of Patients			
	Excluded		Included	
	HALDOL	Placebo	HALDOL	Placebo
R. Leslie, M.D.	7	3	23	21
R. Weinstein, M.D.	0	0	23	20
R. Christman, M.D.	0	0	25	25
E. Robbins, M.D.	0	2	14	14
J. LaRose, M.D.	0	0	7	5
Total	7	5	92	85

The characteristics of the patients analyzed are presented in Table LXI.

Table LXI
Patient Characteristics

Drug Group	Age		Sex		Weight		Total Patients
	Mean	Range	Male	Female	Mean	Range	
HALDOL	55.9	21-91	20	72	147.7	88-301	92
Placebo	54.4	17-95	17	68	142.1	90-253	85

Patients were evaluated for 12 hours post-drug administration. The episodes of vomiting were recorded initially and every two hours for the first four hours and every four hours thereafter up to 12 hours. These data are presented in Table LXII.

Table LXII
Episodes of Vomiting

Time of Observation	Drug Group	N+	Frequency					
			0	1	2	3	4	≥5
Initially (Pre-Study Drug)	HALDOL	92	0	13	20	28	19	12
	Placebo	85	0	11	16	26	22	10
During First 2-Hour Post-Study Drug	HALDOL**	82	53	22	7	0	0	0
	Placebo	75	22	34	13	4	2	0
During 2-Hour to 4-Hour Period	HALDOL**	92	78	8	4	2	0	0
	Placebo	81	49	16	13	3	0	0
During 4-Hour to 8-Hour Period	HALDOL**	90	87	2	0	1	0	0
	Placebo	75	59	8	8	0	0	0
During 8-Hour to 12-Hour Period	HALDOL*	88	85	3	0	0	0	0
	Placebo	71	61	7	3	0	0	0

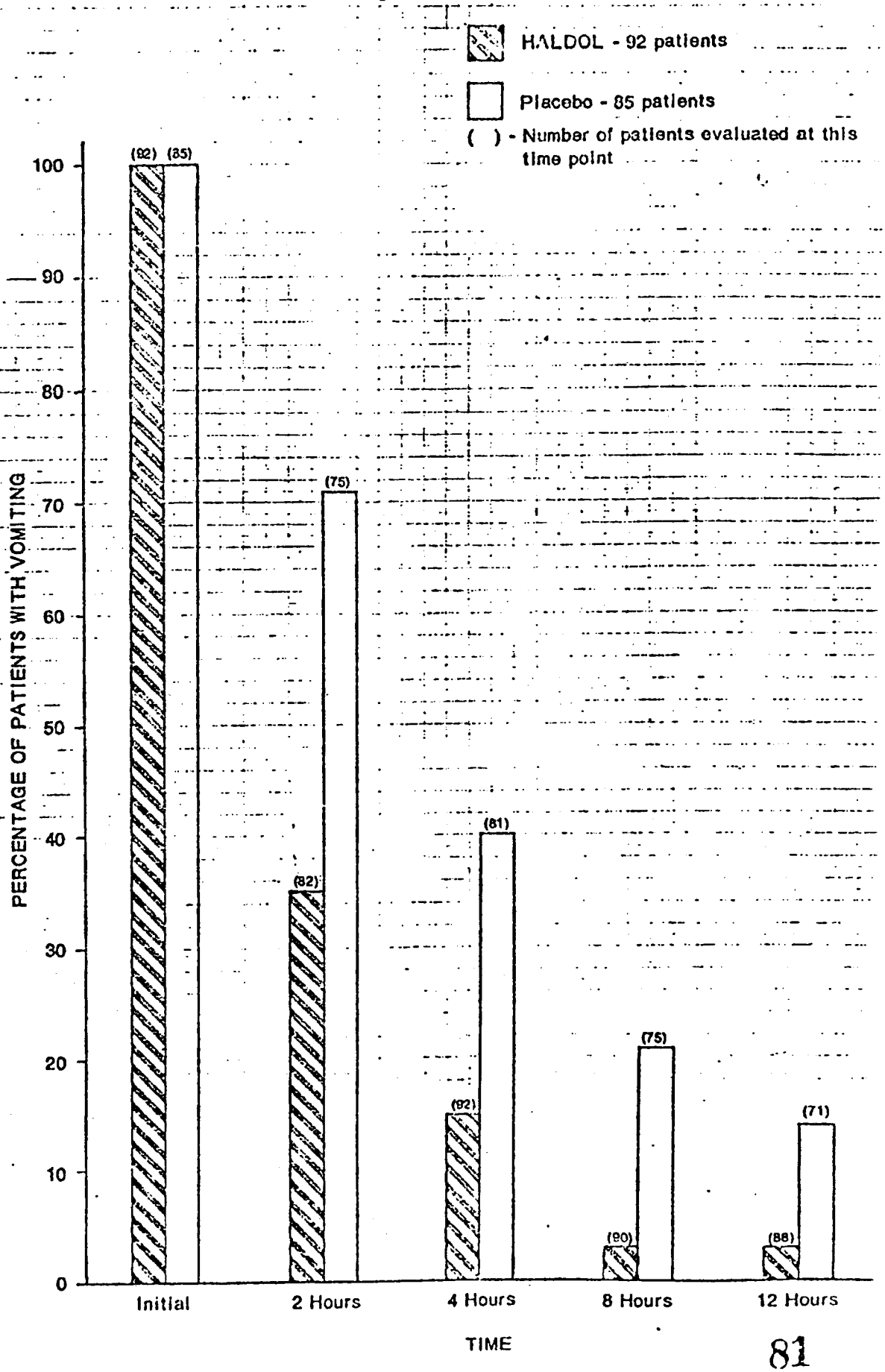
+Number of patients evaluated during this period
*Statistically significantly fewer episodes of vomiting during this particular period ($P < .05$, Rank "t" Test) **$P < .01$

A review of the data shows that there were fewer episodes of vomiting in the HALDOL-treated group than in the placebo group. The difference between the two treatments in the episodes of vomiting was significant ($P < .01$) for the first three evaluation periods and ($P < .05$) for the fourth evaluation point favoring HALDOL. The data are presented graphically in Figure 13.

The incidence of vomiting in the HALDOL drug group was significantly ($P < .01$) less than in the placebo group over the 12-hour evaluation period.

During the 12-hour observation period, 59 (64%) of the 92 HALDOL patients but only 21 (25%) of the 85 placebo patients were free of vomiting. This difference between the two treatments is statistically significant ($P < .01$) in favor of HALDOL.

Figure 13


HALDOL - 92 patients
Placebo - 85 patients
( ) - Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH VOMITING
0
10
20
30
40
50
60
70
80
90
100
(92)
(85)
(82)
(75)
(92)
(81)
(90)
(75)
(88)
(71)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME

The occurrence of nausea after treatment is presented in Table LXIII.

Table LXIII
Occurrence of Nausea

Time of Observation	Drug Group	N+	Severity† of Nausea			
			0	1	2	3
Initially (Pre-Study Drug)	HALDOL	92	0	7	45	40
	Placebo	85	1	3	56	25
During First 2-Hour Post-Study Drug	HALDOL	82	21	34	26	1
	Placebo	75	12	36	22	5
During 2-Hour to 4-Hour Period	HALDOL	92	28	29	28	7
	Placebo	81	9	41	24	7
During 4-Hour to 8-Hour Period	HALDOL**	90	49	18	19	4
	Placebo	74	21	21	32	0
During 8-Hour to 12-Hour Period	HALDOL*	88	60	6	19	3
	Placebo	71	35	9	25	2

+Number of patients evaluated during this period
†0=None, 1=Mild, 2=Moderate, and 3=Marked
*Statistically significantly less nausea among the HALDOL patients ($P < 0.05$, Rank "t" Test) **$P < 0.01$

There were fewer occurrences of nausea among the HALDOL patients than among the placebo patients. The difference between the two treatments in the occurrence of nausea was significant ($P < .01$) at the 8-hour evaluation point and ($P < .05$) at the 12-hour evaluation point favoring HALDOL. The data are presented graphically in Figure 14.

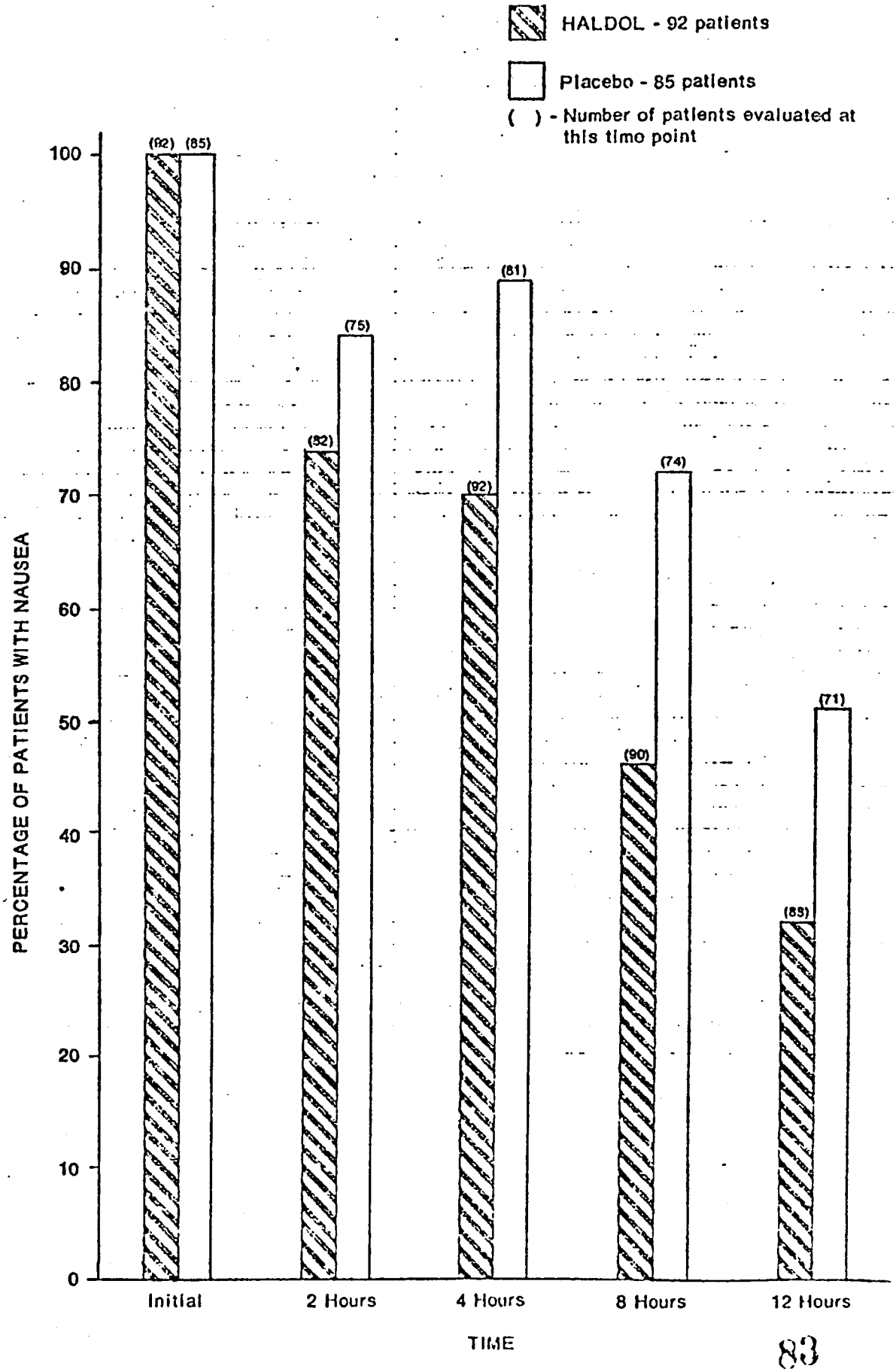
According to the two cumulative severity score distributions made by summing each patient's nausea rating during the 2 to 12-hour observation periods, the severity of nausea for the placebo patients is significantly ($P < .01$) higher than that of the HALDOL patients.

The investigators' global evaluations recorded at the end of therapy is presented in Table LXIV.

Table LXIV
Global Evaluation

Drug Group	Final Evaluation					Total Patients
	Marked	Moderate	Minimal	Unchanged	Worse	
HALDOL	51	32	6	3	0	92
Placebo	19	24	24	16	2	85

Figure 14


HALDOL - 92 patients
Placebo - 85 patients
( ) - Number of patients evaluated at this time point
PERCENTAGE OF PATIENTS WITH NAUSEA
100
90
80
70
60
50
40
30
20
10
0
(92) (85)
(82)
(75)
(92)
(81)
(90)
(74)
(83)
(71)
Initial
2 Hours
4 Hours
8 Hours
12 Hours
TIME