

## CONTROL OF VOMITING DUE TO DITHIAZANINE, AN ANTIPARASITIC DRUG

Francisco BIAGI-F., Oscar PINZÓN and Alfonso MARTUSCELLI-Q.

### SUMMARY

Three special dithiazanine preparations were compared by the "double blind" method, including also the preparation available at present on the market.

It was found that the four preparations were equally effective against each of the five intestinal parasitoses studied, but that one of the special preparations was very well tolerated by the patients, not causing vomiting at any time in the 133 patients treated.

### INTRODUCTION

The effectiveness of dithiazanine against various parasitoses has been reported recently. In a previous paper<sup>2</sup> we gave the bibliographical references that had appeared on the subject and other simultaneous or subsequent publications<sup>1, 4, 5, 6</sup> have corroborated the initial observations.

Unfortunately, this drug used to cause vomiting rather frequently as the most severe manifestation of intolerance. In a total of 304 treatments, there was vomiting in 33 persons, or 10.9%<sup>2, 4</sup>, thus limiting the use of the drug.

It was thought that with certain coatings that would retard the dissolution of the tablets the frequency of the vomiting would be decreased; however, it would be necessary to demonstrate in an objective manner: (a) that vomiting would decrease in frequency and (b) that the drug would maintain its effectiveness against the parasitoses.

### MATERIAL AND METHODS

Four dithiazanine\* preparations of identical appearance and designated A, B, C, and

D, were used. Tablets A had multiple coatings of methylcellulose; tablets B had multiple coatings of polyvinyl-pyrrolidone; and tablets C had several coatings of methylcellulose but with a special granulation. The disintegration time of these tablets varied between 60 and 45 minutes in the Stowl-Bershberg (Vanderkamp, U.S.P.) apparatus. Tablets D were identical to the tablets now available on the market.

Treatments were administered at the rate of 10 mg per kg. of body weight per day (without exceeding 600 mg.) for 5 days. The "double blind" method was used to avoid false results.

Prior to treatment three egg counts in feces were made, figuring the average egg count per gram of feces for each parasite. Eight days after the end of the treatment the study was repeated in the same manner and the percentage of the drop in the egg count was figured. Considering persons having a reduction of 70% in the egg count as really benefitted by the drug, its effectiveness was compared according to the frequency with which a 70-100% reduction in the egg count was obtained in the various groups of persons treated.

Pathology Unit, School of Medicine, U.N.A.M., Hospital General — México 7, D.F., México.

\* Partel (Lilly).

TABLE I

Age and number of persons treated with various dithiazanine preparations, the control of which was completed.

Dithiazanine	Number of cases treated	Age Groups			
		Infants	Pre-school age	School age	Adults
A	106	—	9	72	25
B	79	1	0	56	16
C	62	—	6	38	18
D	71	—	7	53	11
Total .....	318	1	28	219	70

The FERREIRA 1:10 method was used because it is a quantitative concentration method, useful for egg counts and exceptionally offering negative results if there are eggs in the feces, even in very scarce numbers<sup>3</sup>.

The control of 318 treatments (one treatment per case) was finished. Table I gives the data relative to the age of the persons treated and the number of treatments corresponding to each preparation. Actually, more treatments were given, but the patients did not deliver their control samples; a higher number of cases were questioned as to intolerance phenomena.

and that preparation A caused vomiting with less frequency than B and C ( $P < 0.05$ ).

TABLE II

Frequency of vomiting in cases treated with various dithiazanine preparations.

Dithiazanine	No. of cases treated	Vomiting	
		No. of cases	%
A	133	—	—
B	103	3	2.9
C	88	2	2.3
D	76	8	10.5

#### RESULTS AND COMMENTS

An analysis of the incidence of vomiting is shown in table II. Preparation D continued to cause vomiting with great frequency. By applying tests of statistical significance it was demonstrated that forms A, B, and C caused vomiting with much less frequency

Other intolerance phenomena are shown in table III. As can be seen, what happened with the vomiting also happened with all the other intolerance phenomena, and preparation A was the best tolerated, since it only produced disorders of little importance.

TABLE III

General table of intolerance phenomena in cases treated with various dithiazanine preparations. The percentage of frequency is given.

Dithiazanine	No. of cases	% with intolerance phenomena				% without disorders
		Vomiting	Nausea	Dizziness	Abdominal pain	
A	133	—	0.7	9.8	11.3	79.7
B	103	2.9	5.8	9.7	16.5	69.9
C	88	2.3	6.8	12.5	17.0	73.8
D	76	10.5	21.1	23.7	36.8	55.2

TABLE IV

Effectiveness of various dithiazanine preparations in cases of hymenolepiasis. Cases with a reduction of over 70% in egg count per gram of feces (70-100% ↓) are tabulated.

Dithiazanine	No. of treatments	Cases with a reduction over 70% in egg count	
		No.	%
A	25	11	44.0
B	20	8	40.0
C	20	13	65.0
D	24	12	50.0

Differences statistically not significant.

An analysis of the effectiveness of the different preparations against five intestinal helminthiasis is presented in tables IV to VIII. Tests of statistical significance ( $\chi^2$ ) were applied and it was found that the four preparations had practically the same effectiveness against each parasitosis. It is especially interesting to note that the coatings that retarded the dissolution of the tablets did not decrease the effectiveness of the drug against the parasites localized in the duodenum (hookworm and *Strongyloides*).

TABLE V

Effectiveness of various dithiazanine preparations in cases of ascariasis. Cases with a reduction of over 70% in egg count per gram of feces (70-100% ↓) are tabulated.

Dithiazanine	No. of treatments	Cases with a reduction of over 70% in egg count	
		No.	%
A	93	45	48.4
B	67	36	53.7
C	57	26	45.6
D	59	33	55.9

Differences statistically not significant.

TABLE VI

Effectiveness of various dithiazanine preparations in cases of trichocephaliasis. Cases with reduction of over 70% in egg count per gram of feces (70-100% ↓) are tabulated.

Dithiazanine	No. of treatments	Cases with a reduction of over 70% in egg count	
		No.	%
A	64	39	60.9
B	45	24	53.4
C	32	14	43.7
D	47	29	61.7

Differences statistically not significant.

TABLE VII

Effectiveness of various dithiazanine preparations in cases of hookworm infection. Cases with a reduction of over 70% in egg count per gram of feces (70-100% ↓) are tabulated.

Dithiazanine	No. of treatments	Cases with a reduction of over 70% in egg count	
		No.	%
A	35	14	40.4
B	21	12	57.1
C	16	9	56.3
D	20	10	50.0

Differences statistically not significant.

TABLE VIII

Effectiveness of various dithiazanine preparations in cases of strongyloidiasis. Cases with a reduction of over 70% in larvae count per gram of feces (70-100% ↓) are tabulated.

Dithiazanine	No. of treatments	Cases with a reduction of over 70% in larvae count	
		No.	%
A	5	5	
B	5	5	
C	1	1	
D	7	6	

The lesser effectiveness of dithiazanine found by us (if our figures are compared with those of other authors) is due to the FERREIRA method, which shows the eggs even when they remain in a very scarce quantity after the treatment.

#### RESUMO

*Contrôle do vômito devido à ditiázanina, uma droga antiparasitária.*

Três preparados especiais de ditiázanina foram comparados, pelo "double blind método", com um preparado atualmente existente no mercado.

Chegou-se à conclusão de que os quatro preparados eram igualmente eficientes contra todas as cinco parasitoses estudadas. Entretanto, apenas um dos preparados especiais, com revestimentos múltiplos de metilcelulose, era bem tolerado, não causando vômitos em nenhuma ocasião aos 133 pacientes tratados por ele.

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