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ARTÍCULO ORIGINAL

Evaluation of the efficacy and security of quinfamide administered in a single dose of 300 mg in adult patients with intestinal amebiasis

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ABSTRACT

Quinfamide is an intraluminal amebicidal with high therapeutic efficacy and low toxicity. Its mechanism of action consists in the intraluminally immobilization of the ***Entamoeba histolytica*** *trophozoite, and gets its maximum concentration blood level in about 7 hours. The objective of this paper is to evaluate the therapeutic action of quinfamide with a single dose in patients having sub-acute or chronic intestinal amebiasis parasitologicaly demonstrated, and to probe its security. Adults with a coproparasitoscopic exam mean concentration-flotation, as well as a complete clinical study were sudied. The cases that result positive because of the identification of parasite forms of* ***E. histolytica*** *and that fulfill the inclusion requirements besides signing the consent letter were given a single 300 mg dose of quinfamide and were kept in the following days under strict observation with coproparasitoscopic control studies realized the next five, six, seven, fourteen and twenty one days. From 568 persons studied, 221 (38.9%) were positive to the presence of intestinal* ***E. histolytica****. The coproparasitoscopic control studies showed that in 35 persons (15.84%), the parasite forms continued to be in the feces; and 186 persons (84.16%) corresponded to negativized cases. The clinical follow up never revealed the presence of secondary effects with the administration of this drug. In conclusion, the therapeutic efficacy of a single dose of quinfamide in the treatment of* ***E. histolytica*** *infection was good in comparison with the quinfamide administration of the same dose but in three intakes a day.*

Key words: Entamoeba histolytica, *intestinal amebiosis, quinfamide, therapeutic.*

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INTRODUCTION

Intestinal parasites diseases represent a public health problem on many places of the world, as they are very frequent and affect all ages, especially children, with consequent health damage, from minimal to mortal, economic repercussion for all direct and indirect expenses they sponsor and for the impaired productivity of the sick person; the family socioeconomic damage is also important[1].

Intestinal amebiasis is a parasitic illness, endemic of big planet areas and more frequent on undeveloped countries; where the epidemic chain is supported by many factors. It is considered the third mortality cause of parasitological diseases, paludism and schistosomosis are above it[1,2]. The frequency of intestinal amebiasis in our environment is extensively variable between 2 to 39%, with an age distribution of: 22% on newborns pediatrics, 30% on preschool children and 20% on school children; 2-15% of all cases of diarrhea that require hospitalization have been associated to *Entamoeba histolytica*[2-4].

There have been great advances on amebiasis treatment, no doubt on that, 5-imidazols brought superior control of the illness, but an important problem is the treatment abandonment which turns patients into chronic carriers and illness propagators[5,6]. At this moment there are drugs that can eradicate *E. histolytica* after some days of treatment, but none of them are considered ideal because of the long term treatment administration needed and side effects[7].

Recent products reach their objective on less time. For specific cases of amebiasis the therapeutic option is the use of 5-nitroimidazoles that goes from 1 to 10 days of administration, but side effects with short term treatments are more frequent[5].

Some other drugs that have been denominated as contact-drugs, like diyodohidroxiquinolein, etofamide, clefamide and newer quinfamide, reduce the treatment time to 20-5-3 and finally 1 day treatment with minimal side effects[8-13]. These characteristics make it possible to apply massive control programs since they are accepted by population because there are no uncomfortable side effects and its very short scheme of administration.

Quinfamide is a dicloroacetilquinolinol with intraluminal amebacidal action that after completed several stages of clinical investigation is considered to have good therapeutic efficacy and nearly no toxicity, this characteristics make it different from all other drugs introduced in to the medical practice, its easy administration line and specially the fact that is a single dose treatment with no side effects, end the treatment abandonment attitudes[14]. It is a crystalline white powder, odorless, chloroform but not water soluble. Its empiric formula is 16H 13C 12No4 with 354.19 of molecular weight [14]. *In vitro* studies have demonstrated that quinfamide at a 20 mcg/ml concentration inhibits ameba growth and motility. This drug controls ameba propagation. On animal testing it has been demonstrated that oral administration for 3 days has eliminated *Entamoeba criceti* from hamster's bowel. Quinfamide showed to be more effective than etofimate, diloxamide and teclozan[15,16].

About its pharmacokinetics, we know that the highest blood level concentration is reached after 7 hours, urine radioactivity was higher (84%) after intravenous administration compared with the oral use (48%); drug tissue concentrations were low. No intolerance symptoms were observed with a 10 g/kg of weight on mice, hamsters or rats; toxicity or other disorders were not present on postmortem studies on quinfamide treated dogs and monkeys[5,13,14]. Quinfamide did not show mutagenic action in Ames test with and without *Salmonella* activation but on lymphoma mutagenic assay on mice, quinfamide produced more mutations on micronuclei test. Of all the studied clinical tests quinfamide administrated on split doses of one day demonstrated a high efficacy to eliminate *E. histolytica* trophozoites of fecal samples, with cure index of 77.8% to 100%. The side effects where headache and nausea, most of them minimal[13,14].

Dosage that's been used on adults is one 100 mg drop every 8 hours to a total of 300 mg a day. On children from 3 to 6 years: half drop every 12 hours (100 mg a day), from 7 to 9 years: one drop every 12 hours (200 mg a day)[7,9-12,15,16].

Considering these characteristics, the objective of this study is to evaluate the therapeutic action of quinfamide using one single dosage on carrier patients of intestinal sub-acute or chronic amebiasis, demonstrated with parasitological studies and to evaluate the security of the product.

MATERIALS AND METHODS

These work has been done on the Motors and Refactions S.A. company, located on the industrial complex of the Industrial Vallejo zone on the north of México City, the study was made directly with the workers of the company, on the production area, all of them were adult people who freely accepted to participate on the investigation. A coprology study was made to all participants by flotation-concentration, besides a complete health study. To all positive cases for *E. histolytica* who reached the inclusion criteria, besides signing a consent letter, we administered 300 mg of quinfamide in a single intake; on the next days we clinically followed them, extra coprology studies were made the 5,6,7,14 and 21 days after the administration.

RESULTS AND DISCUSSION

Of a 568 group of persons studied, 221 (38.9%) were positive to one or more parasitic forms of intestinal *E. histolytica* (39%); 185 were male and 36 female.

The control coprology studies after the treatment, showed that 186 (84.16%) patients have no longer *E. histolytica*, compared to 35 persons (15.84%), that were still excreting the parasite and for that they still have infection. Clinical follow never showed side effects to the administration of the drug in this study.

With the results obtained, we can say that the efficacy of quinfamide on *E. histolytica* treatment with a single dose was good and in comparison with the results on patients treated with quinfamide at the same dose, but with three intakes a day, the results were very similar with minimal differences with no statistical significance.

So we can say, that there is no difference in to treat adult patients with intestinal amebiasis with 300 mg of quinfamide orally administrated on single intake, than in three intakes at the same dosage, that are 100 mg every day. The therapeutic effectiveness of the quinfamide in our study were very similar to the one obtained in other investigation works in different cities and countries[5-9,13-19].

RESUMEN

La quinfamida es un amebicida intraluminal, con alta eficacia terapéutica y baja toxicidad. Su mecanismo de acción consiste en la inmovilización intraluminal del trofozoito de *Entamoeba histolytica* y alcanza sus niveles máximos de concentración sanguínea en aproximadamente 7 horas. El objetivo de este trabajo fue evaluar la acción terapéutica de la quinfamida con una dosis única en pacientes con amibiasis intestinal sub-aguda o crónica demostrada parasitológicamente; además de comprobar su seguridad.

Se estudiaron a 568 personas a quienes se practicaron exámenes coproparasitoscópicos por concentración-flotación, además de un estudio clínico completo. A los individuos que resultaron positivos por la identificación de formas parasitarias de *E. histolytica* y llenaron los requisitos para su inclusión en el estudio, además de haber proporcionado su consentimiento por escrito, se les administró una dosis única de 300 mg de quinfamida y se hizo un riguroso seguimiento con exámenes coproparasitoscópicos de control durante los 5, 6, 7, 14 y 21 días postratamiento.

De las 568 personas estudiadas, 221 (38,9%) fueron positivos a la presencia de *E. histolytica* en el intestino. Los exámenes coproparasitoscópicos de control demostraron que 35 personas (15,84%), continuaban excretando al parásito en las heces mientras que 186 (84,16%), se negativizaron. El seguimiento clínico demostró la ausencia de efectos secundarios a la administración del fármaco.

Se concluye que la eficacia terapéutica de la quinfamida en dosis única en el tratamiento de la infección por *E. histolytica* fue buena en comparación con la administrada durante 3 días a la misma dosis.

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