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TREATMENT OF HERPESVIRUS VARICELLAE INFECTIONS WITH THE INTERCALATING COMPOUND QUINACRINE

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It is well known (5, 7) that the acridine derivatives, inclusive of quinacrine (8), inactivate and eliminate the R-plasmids from the bacteria bearing them. It became clear that capacity of eliminating plasmids is a group property of the so-called intercalative compounds which bind to double-standed DNA through intercalation between the adjacent base pairs (1, 4). To this class of compounds belong the phenanthridine deri-

vatives ethidium and propidium, acridine derivatives (inclusive of quinacrine), some heterocyclic sulfur-containing compounds (such as the phenothiazines, methylene blue), derivatives of 4-aminoquinoline, tilorone, some antitumoral compounds (e.g. actinomycin D, mitamycin) etc.

We have succesfully used the quinacrine in several severe urinary and pleuropulmonary infections caused by R-plasmid bearing multiresistant Enterobacteria and staphylococcus strains, respectively, combining it with an antibiotic previously used without any effect. Hypothesising that the quinacrine as a potent intercalataing compound would act in a similar manner on the double-stranded DNA of the Herpesviruses as it does on the DNA of the plasmids, we tried it in the treatment of varicella and zoster.

In an uncontrolled study, 12 successively hospitalized patients with varicella and 13 with zoster were treated with quinacrine. The quinacrine was used as 0.10 g containing tablets of Mepacrin. After an initial loading dose of 20 mg kg in the first 24 hours, divided in four equal doses (i.e. 4×3 tablets of Mepacrin for an adult of 60 kg body weight, given by mouth with 200 ml of water after four successive principal meals), for the following three days we administreted only a minimal dose (0,10 g die for adults) with the aim to compensate the renal excretion. The alkalinization of the urine during the treatment by ingestion of 3×1 g sodium bicarbonate decreases the renal elimination of the drug.

The therapeutical effects observed in varicella can be summarized as follows: The evolution of the rash is stopped; no new crops appear; the macules and papules disappear within 24 hours without transforming in vesicles; the content of the vesicles at the beginning of the treatment is resorbed in 2—3 days; the crusts formed are smaller, thinner than usually, they become sooner detached; the resorption of the content of the vesicles is often complete, without of scab formation.

The quinacrine therapy modifies and shortens the evolution of the zoster in a similar manner: The diffuse erythema and infiltration fades and disappears, respectively, in 2—4 days; from the second day of the treatment begins the absorption of the content of the vesicles; the vesicles dry up in a few days, with forming of thin crusts which fall off within 7—10 days.

Quinacrine as an intercalating agent affects both the structure and the function of DNA (6).

The intercalating agents bind to DNA by intercalation between two adjecent pairs of bases causing an unwinding of the double helix and form covalent cross-links of the two strands of the DNA (1, 4). Intercalation binding to DNA results in template toxicity, as it inhibits the DNA and RNA biosyntheses (2, 3). Acting in this manner on double standed DNA of Herpesvirus varicellae, the quinacrine acts as an antiviral agent.

As recently stated by *Hahn* (3), no intercalating substance was yet used for the treatment of viral intections in human. Quinacrine proved to be an efficacious antiviral drug in Herpesvirus varicellae infections. It has several other advantages: It has a high chemotherapeutic index; it is devoid of toxicity in therapeutical doses; it is a well-known drug; it is administered perorally; the treatment is simple and short-lasting.

References

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