THE TREATMENT OF HUMAN TAPEWORM INFECTIONS WITH 'YOMESAN'

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'Yomesan', N-(2'-chloro-4'-nitrophenyl)-5-chlorsalicylamide, is a drug which has recently been introduced for the treatment of human tapeworm infections, and in this paper we report on its efficacy. The drug is an insoluble, tasteless solid and is poorly absorbed from the gastro-intestinal tract. In animal studies it has been found to have a direct lethal action on cestodes[1] and to be virtually non-toxic.[2]

Our initial results with yomesan in 30 African patients with tapeworm infection were totally unsatisfactory. This was contrary to the findings of other clinical trials, and the manufacturers of the drug, who proceeded to investigate the discrepancy, submitted the following explanation. Incorporated in the yomesan tablets is a substance, the function of which is the production of a stable suspension, and hence an adequate and uniform concentration, of the water-insoluble yomesan in the aqueous contents of the intestine. It was discovered that the activity of this stabilizing agent varied markedly, unless its incorporation during the manufacturing process was rigidly standardized and controlled. Failure to appreciate this led to the production of batches of yomesan tablets of variable potency, which accounted for the discrepancy between our results and those of other workers.

Together with this explanation and an assurance that the manufacturing difficulty had been fully overcome, the makers sent us another batch of yomesan tablets, and it is these which constitute the subject of the following report.

SUBJECTS AND METHODS

Thirty-nine African subjects (20 males and 19 females), and 1 white male were studied. All were infected with *T. saginata*. Thirty-three of the 40 subjects were between the ages of 17 and 51, 6 were between 10 and 14, and 1 was 2½ years old.

All subjects were treated as outpatients. Yomesan was administered after an overnight fast of about 12 hours. The dose for all except the infant aged 2½, was 1 G., repeated after 1 hour, i.e. a total dose of 2 G. The infant received half this amount. The drug is put up as vanilla-flavoured 0·5 G. tablets and patients were instructed to chew these well before swallowing with a little water. The infant took the drug as an aqueous suspension. Two hours after the second dose of yomesan a purgative was given and all stools passed over the next 2 - 3 hours were collected and examined for the presence of the head of the worm. In half the cases the purgative used was magnesium sulphate; in the other half it was pitressin, 0·5 ml. by intramuscular injection.

Where the head was not found, an attempt was made to follow-up the patient for at least 4 months after therapy. For this purpose we employed an African social worker, who visited the patients in their homes, questioned them carefully about the passage of segments in the stool, and collected specimens of stool which were examined for segments and ova. All stool specimens were concentrated by the merthiolate-iodine-formalin method before examination for ova. Segments were recovered by washing the stool through a fine sieve.

Proof of cure was based on the generally accepted criteria of (*a*) the finding of the head, or (*b*) where the head could not be found, the absence of segments in the stool for a period of at least 4 months after therapy.[3] Since the latter criterion is dependent on the patient's testimony, which may not be entirely reliable, we attempted to confirm cure by demonstrating that stools obtained at 4 or more months after therapy were free of both segments and ova. In a number of cases, stools obtained at 2 months after therapy were also examined for ova and segments.

RESULTS

Following the purge, 2 patients passed the whole worm including the head, 11 passed the whole worm except the head, and 11 a varying number of segments – in 4 of these the segments were in a partly digested state. In a further 11 cases no segments were detected in the stools. In the remaining 5 the purgative failed to yield a stool for examination.

Follow-up of the 38 subjects in whose stools the head was not found, yielded the following results:

1. Thirty-one patients passed no segments in the stool for a period of 4 - 8 months after therapy. In 29 of these, specimens of stool were obtained at 4 or more months after therapy, and all were found to be free of both segments and ova. In 12 of these 29 cases, stools were also examined at 2 months after therapy and these, too, were free of segments and ova.

2. In 1 subject, a female aged 19 years, segments reappeared in the stool at the end of the 4th month after therapy.

3. In the remaining 6 cases the effect of therapy could not be assessed. All had moved from their original addresses, and despite an exhaustive search by our social worker, neither they nor their relatives could be traced.

In summary, then, the effect of yomesan therapy could be assessed in 34 of the 40 subjects in the series, and in all but 1 proof of cure was obtained.

The vanilla-flavoured yomesan tablets were exceptionally well taken by both adults and children, and side-effects were noted in only 1 patient. This was an adult male, who complained of intestinal colic about 1 hour after the second dose of yomesan.

DISCUSSION

The results of this trial show that yomesan is an effective, safe and simple remedy for *T. saginata* infections in man. It cured all but 1 of 34 subjects in whom its effects could be assessed. Even the exception may not represent a yomesan failure, since segments reappeared in the stool only at the end of the 4th month after therapy; this raises the possibility of reinfection rather than recurrence of the original infection. *T. saginata* grows from the scolex to the point at which segments are excreted in about 3 months. Thus, while the appearance of segments *within* this period after therapy generally means a recurrence, their appearance *after* this time may be due to reinfection as well as recurrence.

Our favourable results are in accord with the findings of other trials with yomesan.[4-9] In these, representing a total of about 120 cases, the cure rate varied between 90 and 100%, and side-effects were slight or absent. It is noteworthy, however, that in the present study the head of the worm was found in only 2 of the 40 subjects treated, whereas in most other trials it was found in the majority. The reason for this difference is probably an organizational error on our part, whereby yomesan and the purgative were administered on a Friday morning, but the stools were not examined until the following Monday. There is good evidence that the action of yomesan is taenicidal, which means that, unless the dead worm is rapidly expelled by purging and immediately removed from the stool for examination, it will be digested by the enzymes of the intestine and the faecal flora. This applies particularly to the head, which is the smallest part of the worm, and, because it is situated most proximally in the gut, is the first to be exposed to the lethal action of the drug.

We had no examples of *T. solium* infection in our series, but it is generally accepted that any drug which will remove *T. saginata* will also expel *T. solium*. However, it is important to note that the lethal action of yomesan does not extend to the ova contained within the tapeworm segments. This means that the use of yomesan in *T. solium* infections may expose the patient to the risk of developing cysticercosis, since, following digestion of the dead segments, viable ova will be liberated into the

gut lumen. This is not a contraindication to yomesan therapy in *T. solium* infections, but it does make it mandatory that a powerful purge be given within 1-2 hours after the second dose of yomesan to clear the bowel of all dead segments before they can be digested. In *T. saginata* infections, in which there is no risk of cysticercosis, purging is unnecessary unless immediate proof of cure by finding the head is desired.

Other Drugs

Yomesan would appear to be the drug of choice in the treatment of tapeworm infections. Its principal rivals are male fern, mepacrine and dichlorophen. Male fern and mepacrine, with cure rates of about 80%, are less effective than yomesan.[3] Both have a higher incidence of side-effects, one of which, vomiting, may be responsible for the development of cysticercosis in *T. solium* infections. Male fern is also liable to produce serious toxic effects such as blindness, jaundice and convulsions.

Dichlorophen, like yomesan, is reported to be taenicidal, but its use has given variable results. In one trial 92% of 104 cases were said to have been cured,[10] but in 4 others the cure rates were 69%,[11] 69%,[12] 64%[13] and 30%.[14] Seaton[9] attributed most dichlorophen failures to underdosage, and claimed that provided a single dose of 6 G. is given, a 90% cure rate may be expected. Schneider,[11] however, administered 6 G. on each of two successive days, followed by 3 G. on the third day, and obtained cures in only 69% of 61 cases. Furthermore, dichlorophen has a higher incidence of side-effects, such as colic and diarrhoea, than yomesan.

SUMMARY

Forty subjects with tapeworm infection were treated with a new drug, yomesan. Its efficacy could be assessed in 34 of the subjects, and all but 1 were cured. The drug was simple to administer, and side-effects were virtually absent.

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