separation of the aponeuroses occurs within the first few days. This is a question yet to be answered.

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Combination chemotherapy is more effective in postspillage prophylaxis for hydatid disease than either albendazole or praziquantel alone

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Recurrence is one of the most significant postoperative complications following surgery in man for *Echinococcus granulosus*, occurring in approximately 10 per cent of patients[1]. When recurrence occurs, further surgery is associated with increasing morbidity and mortality[2]. It has previously been reported that a short course of oral albendazole after spillage of viable protoscolices can significantly reduce the risks of cyst development in a gerbil model[3] and that the timing of albendazole prophylaxis to spillage was of great importance[4]: it was ineffective when given 15 days later. The isoquinoline praziquantel has been found to be a more effective scolicidal agent in *in vitro* cultures of *E. granulosus*[4]. We have previously shown that combinations of albendazole and praziquantel are more effective than either agent alone in *in vitro* culture[5]. In this paper we study *in vivo* results in an animal model of peritoneal spillage.

Materials and methods

Thirty-nine gerbils were each injected intraperitoneally with approximately 4000 viable protoscolices obtained from viable ovine cysts of *E. granulosus*. The gerbils were divided into a control and three treatment groups: ten received a 1-month course of albendazole ($50\,mg\,kg^{-1}\,day^{-1}$), ten received a 1-month course of praziquantel ($500\,mg\,kg^{-1}\,day^{-1}$) and ten gerbils received 1 month of a combination of praziquantel ($500\,mg\,kg^{-1}\,day^{-1}$) and albendazole ($50\,mg\,kg^{-1}\,day^{-1}$). All drugs were given by once daily gavage starting within 24 h of intraperitoneal infection. The remaining nine animals became the infected untreated controls. Eight months after inoculation, the gerbils were killed. The number of cysts in each animal in each group was measured at necropsy. The Mann–Whitney *U* test was used.

Results

All the gerbils survived until the end of the experiment. It was found that the number of cysts developing in any of the three test groups (albendazole treated mean (s.d.) 22·6(10·0) cysts per gerbil, praziquantel treated 5·9(1·09) and combination treated 0·8(0·29)) was significantly less ($P<0·01$) than the number developing in the controls (67·6(12·8) cysts per gerbil). It was also found that a combination of the two drugs was significantly more effective ($P<0·001$) than when either drug was given alone. Praziquantel alone showed a trend to more effective reduction of the number of cysts at this particular dosing regimen, compared with albendazole ($P<0·1$).

Discussion

We have previously shown that even 7 days treatment with albendazole after intraperitoneal inoculation of protoscolices of *E. granulosus* in a gerbil model host can reduce the number of cysts that develop.

In vitro culture of protoscolices has shown their sensitivity to the isoquinoline praziquantel[6,7]. We have also defined the minimum concentrations and time of drug exposure[8,9]. Praziquantel is an active scolicidal agent at concentrations as low as $20\,\mu g\,litre^{-1}$ (compared with $250\,\mu g\,litre^{-1}$ of albendazole sulphoxide) and exposure time can be as low as 30 min at a high concentration[10]. Albendazole does however have a proven effect on the germinal layer of the parasite[11], and this drug may be useful in the postoperative patient where tiny undetected cysts may remain. This study clearly demonstrates that combined chemotherapy with albendazole and praziquantel in an animal model is more effective than either agent when given alone, and should be considered in clinical practice.

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