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Povidone-iodine in experimental peritoneal hydatidosis

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The effect of polyvinylpyrrolidone-iodine (PVP-I) on experimental peritoneal hydatidosis was evaluated in this randomized blind controlled study. Seventy-five white, 3-month-old rats were subjected to laparotomy. After the intraperitoneal inoculation of viable scolices, the rats were randomly divided into three groups. Their peritoneal cavities were irrigated with either 1 per cent PVP-I solution (the PVP-I group), hypertonic saline (the HS group) or Ringer's lactate (the control group). Each group was assigned a separate code number; observers blind to the meaning of the code numbers noted all findings during a period of 4 months, after which the rats were killed to allow assessment of the abdominal cavity. The results were decoded after the statistical analyses were completed. The incidence of peritoneal cysts was found to be lower (8·7 per cent) in the PVP-I group compared with the HS (50 per cent) and control (90·9 per cent) groups; the mean number of hydatid cysts per animal was also lower in the PVP-I group compared with the other two groups. We conclude that the scolicidal activity of PVP-I is significantly higher than that of hypertonic saline and that it can be employed as a prophylactic agent against peritoneal hydatidosis.

Hydatid disease continues to be an important and endemic problem in many parts of the world. Surgical intervention is still the preferred method of treatment but carries the risk of intraoperative spillage of scolices. Furthermore, preoperative spontaneous rupture of, or leakage from, cysts occurs quite frequently. Irrigation of the intracystic or pericystic space with a scolicidal agent is often employed to prevent the emergence of recurrent hydatidosis as a consequence of these complications.

Povidone-iodine (polyvinylpyrrolidone-iodine, PVP-I) is a local antiseptic with activity against a wide spectrum of microorganisms[1], including protoscolices, as revealed by an *in vitro* trial[2]. Prophylactic peritoneal lavage with PVP-I solution has been demonstrated to be an effective and safe measure against intra-abdominal infections in animals, as well as in humans[3–6]. The effect of intraperitoneal PVP-I on experimental peritoneal hydatidosis was investigated in this study.

Materials and methods

Seventy-five albino rats, 3 months old, randomly selected from a population of rats bred under similar conditions, were used in this study. All of the manipulations described below were performed with strict compliance to antiseptic principles. The rats were subjected to a median laparotomy of 2 cm length performed with a scalpel under ether anaesthesia; the peritoneum was exposed and opened to reach the intraperitoneal cavity, in which 1 ml concentrated hydatid 'sand' was instilled with a pipette. All rats received samples of a single concentrate of hydatid sand, which was prepared from the fresh hepatic hydatid cysts of sheep by collecting cyst fluid into a glass container and allowing it to stand for 10 min at 37°C, after which the supernatant was discarded. The remaining sediment (hydatid sand) contained approximately 15 000 scolices/ml, which were 95 per cent viable immediately before inoculation as determined from their motility characteristics under the light microscope. Two minutes after the inoculation of scolices, the rats were randomly divided into three equal groups identified as the PVP-I, control and hypertonic saline (HS) groups. They were put into three separate compartments bearing different code numbers, where they remained for the rest of the study. Using an injector, 10 ml of one of three solutions was instilled into the peritoneal cavity of each rat: the PVP-I group received a mixture containing 1 ml 10 per cent PVP-I solution and 9 ml Ringer's lactate solution (final solution of 1 per cent PVP-I, free iodine concentration 1 ppm)[7]. The HS and control groups received 20 per cent saline and Ringer's lactate, respectively. All workers participating in the subsequent steps of the investigation were ignorant of how each rat had been treated. Two minutes later, 4 ml of the excess fluid in the lower part of the abdominal cavity was gently aspirated with an injector to facilitate the closure of the laparotomy incision with a continuous subcuticular 4/0 polyglactin suture. None of the rats received any medication before or after this operation. The rats were kept under continuous observation in identical maintenance conditions. Four months later, the surviving rats were killed under ether anaesthesia and a second laparotomy was performed. The intermesenteric areas and all peritoneal surfaces were examined with the aid of a dissection microscope to determine the number of hydatid cysts.

Statistical analysis

All data were entered into a computerized database (Works DataBase, Productivity Software Incorporated, Boston, USA) in the form of three sets of results designated by the previously assigned code numbers. Data were generally expressed as the mean (s.e.m.). Statistical analyses were realized with the StatView package (BrainPower Incorporated, California, USA) and consisted of Student's t and Fisher's χ^2 tests. A P value $<0{\cdot}05$ was accepted as significant. The results were decoded after the statistical analyses were completed.

Results

No statistically relevant difference was encountered in the weight, age and sex ratio of the groups. Two rats from the PVP-I, five from the HS and three from the control group died in the early postoperative period, presumably because of anaesthetic complications. Sixty-five rats survived without weight loss, general deterioration or impaired wound healing and were killed 4 months later. The differences in the survival rates of the PVP-I, HS and control groups were not significant (*Table 1*). The percentage of rats with at least one hydatid cyst was 90·9 per cent in the control group; this was moderately reduced to 50 per cent in the HS group, but showed a striking decrease to 8·7 per cent in the PVP-I group. The mean number of cysts per animal also displayed a statistically significant reduction in the PVP-I group, as compared with the other two groups. The ratio of rats with more than 10 cysts to rats with 0–10 cysts was higher in the control group, in contrast to the PVP-I and HS groups, which had comparable results.

Discussion

Surgical intervention remains the primary mode of treatment for hydatid disease. The various surgical methods employed

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Table 1 *Findings at the end of the trial*

	Povidone-iodine group	Hypertonic saline group	Control group
Surviving rats (*n*)	23	20	22
Survival rate (%)	92	80	88
Weight (g) (mean(s.e.m.))	172(6)	170(4)	165(6)
Male:female ratio	13:10	12:8	13:9
Rats with hydatid disease (%)	8·7†	50*	90·9
No. with >10 cysts/0–10 cysts	1/22‡	5/15‡	20/2
No. of cysts per rat (mean(s.e.m.))	0·6(0·5)†	4·7(1·4)*	23·3(2·5)

* $P \leqslant 0{\cdot}01$ *versus* control group; † $P \leqslant 0{\cdot}01$ *versus* hypertonic saline group and $P \leqslant 0{\cdot}001$ *versus* control group (Student's *t* test); ‡ $P \leqslant 0{\cdot}01$ *versus* control group (Fisher's χ^2 test)

for the treatment of hydatid cysts[8–14] can be classified into two basic alternatives: resection and evacuation. Resection is obviously more desirable but is often not technically feasible, and evacuation combined with scolicidal irrigation of the intracystic or pericystic space has to be preferred[9]. Formaldehyde[12], hypertonic saline[8–11], silver nitrate[13,14], cetrimide[9] and other solutions have been used as scolicidal agents, but most have unacceptable side-effects[15–18] limiting their use. None of these agents can be safely employed for intraperitoneal irrigation.

PVP-I is a synthetic polymer of *N*-vinylpyrrolidone strongly complexed to iodine. It is devoid of the problems inherent in the use of free iodine, such as serious toxicity to tissues as well as instability and insolubility in water, while retaining and enhancing its microbicidal properties[1]. The following discussion refers to the solution form of PVP-I.

Although the beneficial effects of intraperitoneal PVP-I in the prevention of experimental peritonitis were reported quite early[3–5], the use of this route of administration in humans was late to follow owing to concerns about its possible systemic, especially renal, iodine-related toxicity or interference with wound healing suggested by some workers[19,20]. Interest in using intraperitoneal PVP-I to treat peritonitis and prevent postoperative intra-abdominal bacterial infections has revived recently with the development of PVP-I solutions containing PVP polymers of relatively homogeneous and lower molecular weights as compared with the formerly used preparations. This change has proved to be extremely important as it is associated with the rapid renal clearance of polymers, making it possible to avoid their storage in solid organs[1,21]. In the randomized, saline-controlled human trial of Sindelar *et al.*[6], intraperitoneal irrigation with low molecular weight 1 per cent PVP-I solution during contaminated abdominal procedures led to a significant decrease of postoperative intra-abdominal infectious complications; evidence of local or systemic iodine toxicity or impairment of wound healing was not reported.

Our results show that PVP-I has potent *in vivo* scolicidal activity which is of prophylactic value against secondary peritoneal hydatidosis and is superior to hypertonic saline used for the same purpose. Evacuation combined with irrigation of the intracystic and/or pericystic space with PVP-I can be regarded as an effective method for the surgical treatment of hydatid cysts. We suggest a 1 per cent solution because it has an attendant free iodine level[7] of only 1 ppm, is not associated with the adverse effects of higher concentrations[22], and has been previously used for intraperitoneal irrigation without significant harm in humans[6].

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