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The Protoskolicidal Effect of 1% Polyvinylpyrrolidone-Iodine (Pvp-1) and 2% Taurolidine on Abdominal Hydatidosis

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SUMMARY: The aim of this study is to determine the efficacy of 1% polyvinylprolidone-iodine (Betadine, PVP-I) and 2% Taurolidine as scolicidal agents for the prevention of abdominal hydatidosis defined as the rupture of the echinococcal cyst spontaneously or traumatically. The study was carried out in fifty mice randomly assigned into 5 treatment groups as following: group with no expose to any scolicidal agent, groups with 1% PVP-I for 2 and 5 minutes; groups with 2 % Taurolidine for 2 minutes, and 5 minutes. PVP-I has found to be effective according to results of staining with the eosin dye in vitro and abdominal hydatidosis in vivo, while Taurolidine was ineffective as a scolicidal agent.

Key Words: Abdominal hydatid cyst, polyvinylpyrrolidone - iodine (PVP-I), Taurolidine, scolicidal effect

%1'lik Polivinilprolidon - İyot (Pvp-1) ve %2'lik Taurolidinin Abdominal Hidatidosis Üzerine Protoskolisidal Ajan Olarak Etkileri

ÖZET: Bu çalışmanın amacı ekinokok kistlerinin spontan veya travmatik olarak intraabdominal yırtılması sonucu olarak tanımlanan abdominal hidatik kist hastalığının önlenmesinde %1'lik polivinilprolidon-iyot (Betadin, PVP-1) ve %2'lik Taurolidin'in etkisini araştırmaktır. Çalışma hiçbir ajana maruz kalmayan, 2 ve 5 dakika %1'lik PVP'ye; 2 ve 5 dakika %2'lik Taurolidin'e maruz kalan gruplar olarak beş gruba ayrılmış 50 rasgele seçilmiş farede yapılmıştır. *In vitro* eozin boya ile boyanmasına ve in vivo abdominal hidatidosise göre PVP-I'in skolisidal etkiye sahip olduğu ve Taurolidinin etkisi olmadığı görülmüştür.

Anahtar Sözcükler: Abdominal hidatik kist, polivinilprolidon-iyot (PVP-I) , Taurolidin, skolisidal etki.

INTRODUCTION

Hydatidosis is a parasitic infection caused by the larval stage of *Echinococcus granulosus*. It is endemically seen in many parts of the world and the most common site of occurrence in humans is the liver (3, 16). Surgery is the current therapy now; however it has several complications. One of the most serious complications of the surgery is secondary hydatidosis (abdominal hydatid cyst) which is defined as the rupture of the echinococcal cyst spontaneously or traumatically before/during the surgical procedure (9, 11). The main principles of protection of this complication are to use swabs soaked with scolicidal agents, inactivation of the scolex with a scolicidal solution and finally treating the cavity (26). Although there are many scolicidal agents available, an optimal agent effective in lower concentrations without systemic or local side effects, easily prepared and protected, cheap moreover convenient for surgical usage is not available (10). In our study, we tried to identify the scolicidal efficacy of Taurolidine, an antiendotoxic, antiseptic formaldehyde agent with safe usage intraabdominally, and polyvinylpyrrolidone-iodine (PVP-I, Betadine®) which is currently available for hydatid cyst surgery.

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MATERIAL AND METHODS

This study was made in Istanbul University, Cerrahpasa Medical School Animal Laboratory. Fifty mice weighed between 25-28 grams were used. Study designed as two stages, *in vivo* and *in vitro*.

An aseptic cystic fluid without calcification and with no fistulisation to biliary tract was obtained from operated patients with liver hydatid cyst disease. The fluid was aspirated and secondary hydatidosis was formed in laboratory animals. The cystic ingredients were gained in steril-

ized conditions before scolicidal agent injection. Gained material was put in a glass tube and kept waiting for precipitation. Following precipitation, obtained sediment washed with normal saline two times and a suspension of 1000-12000 scolex per one milliliter was achieved. Samples taken from suspension were treated with eosin dye and examined under light microscope on behalf of staining features. The oval shaped scolex with ameboid movement, as well as devoid of eosin dye was documented as alive; immobile, disc shaped ones with un-remarkable rostellum and stained with eosin documented as dead. We used live cystic water in our study.

The study design for section two was in vitro. Suspensions mixed with certain experimental materials were listed as follows:

Section I (*in vitro*)

Group 1: Scolex suspension treated with normal saline solution for two and five minutes evaluated microscopically.

Group 2: Scolex suspension treated with %1 PVP-I for two minutes evaluated microscopically.

Group 3: Scolex suspension treated with %1 PVP-I for five minutes evaluated microscopically.

Group 4: Scolex suspension treated with %2 Taurolidine for two minutes evaluated microscopically.

Group 5: Scolex suspension treated with %2 Taurolidine for five minutes evaluated microscopically.

We put 5 drops of scolex suspension, which has 1000-1200 scolex per one milliliter, to every four tubes. Then we mixed five milliliters of 10% PVP-I into two of them and five milliliter of 2% Taurolidine with the other tubes. Samples were taken after two or five minutes. They were washed with normal saline solution. Subsequent to that procedure, live scolexes were investigated under microscope with 1% eosine dye.

Section II (*in vivo*)

Group 1: The scolex suspension with no expose to any scolicidal agent given intraabdominally (n: 10).

Group 2: The scolex suspension treated with 1% PVP-I for two minutes given intraabdominally (n: 10).

Group 3: The scolex suspension treated with 1% PVP-I for five minutes given intraabdominally (n: 10).

Group 4: The scolex suspension treated with 2% Taurolidine for two minutes given intraabdominally (n: 10).

Group 5: The scolex suspension treated with 2% Taurolidine for five minutes given intraabdominally (n: 10).

Following this procedure 0,5 cc gained suspension given intraabdominally as Group 2, 3, 4 and 5. 0,5 cc scolex suspension without any scolicidal expose was given in Group 1.

Following 90 days after inoculation, laboratory animals were sacrificed with high ether anesthesia. Abdominal hydatid disease was examined.

RESULTS

The viability ratios of *Echinococcus granulosus* scolex after exposure to Taurolidine, PVP-I and NaCl for certain time periods are shown in Table 1. Betadine 1% seemed to have stronger scolicidal effect in 5 min than Taurolidine. Although 99-100% of scolexes lost viability in 5 min with betadine 1%, Taurolidine 2% did not have enough scolicidal effect in the same time period. Approximately 8-10% of the scolex lost viability in 5 minutes with Taurolidine.

Section I; scolex stained with eosin dye and live scolex were investigated microscopically. We observed that 8-10% of the scolex of Group 2 stained by eosin dye after two minutes, and after five minutes 99-100% of them stained by the dye. (Figure I). We did not detect any scolex stained by eosin in Group 4 and 1 while 8-9% of scolex stained by eosin in Group 5.

Section II; following 90 days the animals were sacrificed and autopsies were performed. We detected intraabdominal cyst development in nine of the animals sited in Group 1 and 4 and eight of Group 5 (Table 1) (Figure 2). The mean diameters of the cysts were 3 mm (2-5 mm). One of the animals in Group 3 died after two days.

Table 1. Results of *in vivo* and *in vitro* experimental groups

	Time (min)	Colored by eosine dye	*In vivo* hydatid disease
%10 PVP-I group	2 min	+ (9-10 %)	7/10
	5 min	+ (100 %)	0/10
%2 Taurolidin group	2 min	- (0 %)	9/10
	5 min	+(8-9 %)	8/10
Control group (0.9% NaCl)	5 min	0 %	9/10

DISCUSSION

Surgery and percutaneous aspiration are the main treatment modalities of hydatidosis (16, 23). Recurrence is one of most important complication of surgical procedure and is associated with cystic ingredient spillage. During open surgery spillage can be controlled but in laparoscopic procedure there is an increased risk of contamination of the abdominal cavity with difficulty in aspirating viscid organic cyst content (2).

Recurrence and secondary hepatic hydatidosis has been reported as 10-30% (11, 20). The risk of spillage of scolexes cannot be underestimated. Use of effective scolicidal agents during puncture, aspiration or injection of a scolicidal agent and reaspiration (PAIR) is essential to reduce the recurrence rate. Prevention of secondary hydatidosis by killing

scolexes in the cyst during the procedure is the secondary but an important aim of the surgery because the cyst fluid contains thousands of scolexes and each one has the potential to grow into a new hydatid cyst (4). Thus, there is special interest in research on scolicidal agents in order to inhibit the formation of secondary hydatid cysts.

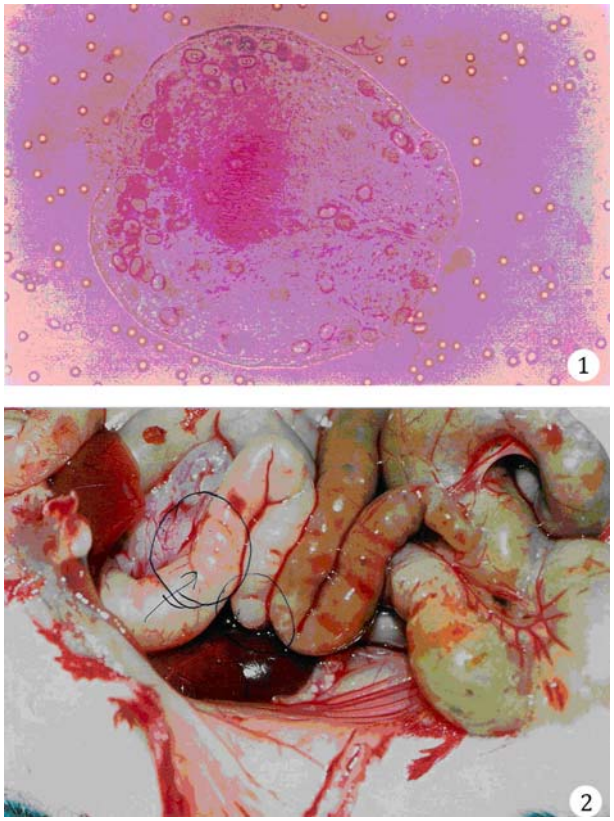

Fig 1. Uptaken eosine dye scolex. A dead scolex
2. Hydatidosis on the bowel surface

For this purpose intracystic and pericystic irrigation is recommended with various scolicidal agents such as formaldehyde, cetrimide, hypertonic saline, chlorhexidine and silver nitrate (8, 18, 23, 32).

Betadine (10% povidone iodine) is a disinfectant used as a scolicidal agent by many surgeons. PVP-I which has antiviral, anti fungal, antiprotozoal and antibacterial activity including anaerobic and spore producing microorganisms, used by Shelanski in 1956 as an antiseptic solution (25, 30). Bosanac et al (5) performed percutaneous drainage with 10% povidone iodine that allowed acting within the cyst for 30 minutes before drainage on 52 consecutive of the disease. Gokce *et al* (15) also concluded that PVP-I can be applied to the patients with hydatid cysts in the liver. 6-9 year follow up showed no local recurrence or spread as a prophylactic agent against peritoneal hydatidosis. Besim et al (4) investigated 20% saline, 3% hydrogen peroxide, 1.5% cetrimide-0.15% chlorhexidine (10% Savlon), 95% ethyl alcohol, 10% PVP-1 (Betadine®) in their study. They concluded that chemical agents are more effective than mechanical ones. Puryan *et al*. concluded in their study that clorhexidine gluconate affected in a short time (24). Ozcelik *et al*. showed the scolicidal effect of garlic in both direct and daughter vesicules (22).

Although formol/formaldehyde is an effective scolicidal agent and used for hydatid treatment, it has many unwanted side effects like local tissue damage (28, 32, 33) Taurolidine which has formol derivate was not tested previously against common causes of hydatidosis. Taurolidine [Taurolidine; bis (1,1-dioxoperhydro-1,2,4-methylene thiadiazinyl-4) methane] is a nonantibiotic antimicrobial agent which has antiendotoxic, antiadhesive, antitumor, antifungal and antilipopolysaccharide properties (7, 13, 14, 19, 29). As a dimer molecule, it exists in equilibrium with two monomeric forms, taurultam and hydroxymethyltaurultam. The latter one undergoes hydrolysis to liberate formaldehyde and taurultam (21). After adsorption onto the bacterial cell, Taurultam undergoes hydrolysis and liberates antimicrobially inactive metabolite taurinamide and the potent biocide, formaldehyde (17, 34). Its activity is due to the presence of formaldehyde in Taurolidine solutions (17). Owing to its antimicrobial activity, Taurolidine is used for irrigation of peritoneal cavity in localized and generalized peritonitis also it has been introduced previously for intraoperative peritoneal lavage in reducing abscess formation, decreasing morbidity , accelerating recovery time in patients with peritonitis (1, 12, 27). The use of a Taurolidine/citrate haemodialysis catheter-locking agent on haemodialysis population has significantly reduced the line sepsis rate, with a positive impact on morbidity, mortality and cost (6, 31). With this knowledge, we aimed Taurolidine and Betadine to investigate its efficacy on abdominal hydatidosis in this experimental study.

There is no consensus about the ideal scolicidal agent. Authors think that the properties of the ideal scolicidal agent should include the ability to kill the scolexes during a short time and should be nontoxic to the patient. For effective and efficient surgery, five minutes were thought to be proper in scolicidal exposion, so the authors did not wait any longer.

In conclusion, we suggest that PVP-I may be used as a scolicidal agent both perioperatively and in the PAIR method because it has rapid and strong scolicidal effectiveness on protoscolex. It may be to reduce recurrence. But further study is needed to investigate more specific scolicidal agents in clinical usage.

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