Hydrogen Peroxide Versus Povidone Iodine as Intra-Operative Scolicidal Agents to Attack Hydatid Cysts

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Abstract: *Objectives*: A prospective randomized study designed to compare results of intra-operative applications of povidone-iodine with those of hydrogen peroxide during surgery for hydatid cysts.

Methods: This study includes 160 patients with pulmonary and/or hepatic univesicular hydatid cysts. Group A consisted of 80 patients for whom we used hydrogen peroxide; Group B consisted of 80 patients for whom we used povidone-iodine. Each cyst was examined both macroscopically and microscopically to identify effects of the used scolicidal agent on the wall. Post-operatively, patients received Albendazole as a scolicidal drug for one year. Follow up times ranged between 48 and 84 months. Chest x-rays and abdominal ultrasound examinations were performed every six months to detect any recurrences.

Results: There was no peri-operative mortality in either of the two groups. Group A: one case of postoperative prolonged air-leak and two cases of wound infection. No recurrences were reported. Mean hospital stay was 5.5 ± 1.1 days. Group B: two cases of prolonged air leak, three cases of persistent cough and hemoptysis, one developing broncho-pleural fistula that healed (air leak ceased after 19 days), two cases of wound infection, one had subphrenic abscess, nine cases of recurrences, one on the diaphragmatic pleura, two with deep chest wall cysts at sites of thoracostomy tubes, four intraperitonial recurrences, two in the same liver lobe. Recurrences occurred in 11% of the subjects (9/80; p value = 0.028). Mean hospital stay was 9.6 ± 1.5 days.

On histologic examination of Group A, the cyst wall lost its integrity, luster and viability and became friable. In Group B the cyst wall maintained most of its luster, integrity, viability and did not become friable.

Conclusions: Hydrogen peroxide is a more effective and safer scolicidal drug than povidone-iodine as shown by the differences in mean duration of hospital stay and postoperative recurrence rate significance.

Keywords: Hydatid cysts, scolicidal agents, hydrogen peroxide as a scolicidal agent. povidone iodine, albendazole.

INTRODUCTION

Pulmonary echinococcosis is caused by the small tapeworm Taenia echinococcus which commonly produces hydatid cystic disease of the liver. As hydatid cysts enlarge, they compress the surrounding parenchyma, damaging the surrounding tissues by mechanical and toxic factor means. Secondary bacterial infections complicate the picture in 10 to 25% of cases [1], with either spontaneous or traumatic rupture in 5-10% of the cases [2]. Rupture can lead to anaphylactic shock and/or disseminated pulmonary or peritoneal disease [3]. As rupture can occur at any time, therapeutic intervention as early as possible is indicated. The principles of surgical therapy of hydatid cysts include: prevention of contamination of the operative field, the injection of a scolicidal agent into the partially evacuated cyst, extrusion of the cyst into a basin and closure of the residual cavity. Several scolicidal agents have been described but serious complications have been reported after using most of them [4].

OBJECTIVE

The aim was to evaluate and compare the safety and efficacy of hydrogen peroxide 3% and povidone iodine 10% as scolicidal agents during surgical therapy of hydatid cysts.

METHODS

The study included 160 patients with pulmonary and/or hepatic univesicular hydatid cysts, who were admitted between 1st March 2004 through 29th February 2008, at the Unit of Chest Surgery, Hadhramout University Hospital, Almukalla, Yemen. Group A included 80 patients on whom hydrogen peroxide was used and group B included 80 patients on whom povidone-iodine was applied. Patients were randomized to hydrogen peroxide 3% (group A) or povidone iodine 10% (group B) based on their medical records number (even Group A, odd Group B). The two groups were evenly distributed with respect to age, sex, weight, height, smoking status, side and site of involvement, surgical indications and surgical approaches. Patients allergic to iodine, with thyroid disease, or with

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preoperatively ruptured hydatid cysts were excluded from the study. After muscle-sparing minithoracotomy or upper midline laparotomy, the field around the cyst was packed with scolicidal agent-soaked green packs to deal with any spillage of cyst fluid. About half of the cyst fluid was aspirated by inserting a needle down to the middle of the cyst cavity, then injecting a similar volume of scolicidal agent. After a few minutes the pericyst was incised to extract the cyst with its contents and was completely removed with sponge forceps. In every case there was a non-adherent tissue layer between the cyst wall and the pericyst, making extrusion using a spoon or into a basin a simple procedure. The residual cavity was inspected for communicating bile ducts (in case of hepatic cysts) or bronchial tree tubules/tissue (in case of pulmonary cysts), while ensuring adequate hemostasis. Closure of any tubular communications was completed and the cavity was totally collapsed and closed with 3-0 polypropilene (proline) suture material. Omentoplasty was not needed to close cavities, even those with very large cysts. No patient in this series with univesicular hydatid cysts had either a lobectomy or segmentectomy during surgery. The cyst wall was examined macroscopically and microscopically.

Post-operatively all patients used albendazole (10 mg/Kg daily) as a scolicidal drug for one year. Follow up was for 48 to 84 months. Chest x-rays and abdominal ultrasound examinations were performed every six months (n = 6), then annually to look for signs of complications. The mean follow up period for all patients was 71 ± 4 months.

Statistical Analysis

Sample and data percentages, mean and the standard deviation were used to report data variations, using a bivariate analysis (SPSS Ltd, Quarry Bay, Hong Kong).

RESULTS

Age of patients ranged between 40 months and 60 years with more males than females, but both males and females were equally distributed between the groups as near as possible. 89 cases had cysts in the liver, 54 cases in the lung and 17 cases with cysts in both liver and lung. Among the last category, 12 cases were operated *via* a mini-thoracotomy and trans-diaphragmatic approach, three *via* a thoraco-abdominal approach and two patients had thoracotomy and laparotomy (See Table **1**).

There was no perioperative mortality in either of the two groups (See Table **2**), while in Group A there was one case of postoperative prolonged air-leak after pulmonary cyst surgery and two cases of wound infection which were controlled. No recurrences were reported despite the fact that one left apical peripheral cyst ruptured intra-operatively, requiring repeated washing of the pleural cavity with hydrogen peroxide. Group B included two cases of prolonged air leaks, three cases of persistent cough and hemoptysis, one of them developing broncho-pleural fistula that healed with cessation of air leak on day 19 after onset of postoperative symptoms. There were nine cases of recurrences (11%), one on the diaphragmatic pleura, two with multiple chest wall cysts at sites of thoracostomy tubes, four intra-peritoneal disseminations and two in the same liver lobe. Two patients had superficial wound infection, and one subphrenic abscess developed after surgery on hepatic hydatid cyst. Statistical analysis showed significant correlation between applied scolicidal agent and recurrences (p=0.028; Table **2**).

Fig. (**1**) compares the gross and tissue sections from inner wall of cysts after five minutes-exposure to scolicidal agents, showing that after hydrogen peroxide the inner wall lost its integrity, luster and viability and became friable (1B), while after povidone-iodine exposure the inner wall maintained its luster, integrity, viability, was non-friable, and retained an overall healthy appearance (1A).

Microscopic examination of sections in the wall of cysts postoperatively showed that in cysts injected with 10 % povidone-iodine the inner layer of cyst wall contained not only germinal pyknotic cells, but also some cells with nuclear fragmentations (karyorrhexis). Cysts injected with 3

Table 1. Characteristics of Patients

Feature	Hydrogen Peroxide	Povidone Iodine
Number	80 (100%)	80 (100%)
Age	40 months to 60 Y.	4- 60 Y
Males Females	45 35	43 37
Hepatic cysts	47 (58%)	42 (52%)
Pulmonary cysts	24 (30%)	30 (37%)
Pulmonary and hepatic cysts	9 (12%)	8 (11%)
Pre-op. events: cyst infection Fever	 2 (5%) 2	 1 (4%) 2
Intra-op. events: - Rupture of cyst -Moderate hypotension.	 1 (4%) 2	 0 (1%) 1
Mean period of postoperative follow up	71 ± 4 months	71 ± 4 months

Table 2. Comparison of Outcomes in Groups A & B

Group A	Group A	Group B	P Value
Prolonged air leak	1 (1%)	2 (2%)	0.0737
Wound infection	2 (2%)	2 (2%)	
Productive cough and hemoptysis	0	3 (4%)	
Subphrenic abscess	0	1 (1%)	
Hospital stay	5.5±1.1 days	9.6±1.5 days	0.019*
Recurrences	0	9 (11%)	0.028*
Perioperative mortality	0	0	

% hydrogen peroxide however showed a great deal more cellular degeneration.

DISCUSSION

Echinococcosis is a serious problem in Australia, New Zealand, South America and the Mediterranean [5]. In Hadhramout-Yemen, many farmers suffer from hydatid disease. We found that most of their family members exhibited the same problem.

Current study presents findings from 160 patients operated upon in a four year period in a single surgical center. The youngest patient in this current study was a forty months old girl. She had two huge cysts, one in right lobe of liver near the superior surface and another in the right lung. She was operated upon through right muscle-sparing thoracotomy, and the hepatic cyst was approached through an incision into the diaphragm. The oldest patient was a 60 year old farmer with seven children, five of whom had hydatid cysts. His youngest son fell and died suddenly while he was playing and he had a ruptured hydatid cyst into the bronchial tree.

Uncontrolled puncture of an hydatid cyst can be followed by spillage of hydatid fluid leading to anaphylaxis and pulmonary or peritoneal dissemination of the disease. Under anesthesia, no shock or severe hypotension was reported in our patients, though we did have three cases of mild to moderate intra-operative hypotension of unknown origin. In order to prevent contamination and subsequent dissemination of scolices, the surgeon must replace the removed hydatid fluid in a careful and controlled manner, totally filling the cyst cavity with an equivalent volume of scolicidal agent. There are many such agents with variable degrees of effectiveness and subsequent rates of complication and clinical and experimental studies have shown that intracystic injection of scolicidal agents may cause sclerosis and chemical cholangitis or bronchiolitis. Moreover, one report stated that fatal cholangitis might occur when scolicidal solutions are introduced into the biliary system, if communication exists from the hydatid cyst to the biliary system, with chemical cholangitis possibly causing sclerosing cholangitis. The highest frequency and greatest severity of inflammatory reaction or late stricture formation of bile ducts was seen with formalin, whilst the lowest was with silver nitrate solutions. Hypertonic saline and cetrimide solutions were also irritating to the bile ducts but with moderate severity, while severe hypernatremia was reported following hypertonic saline solution injection. Also, it was shown that the bronchial tree can be affected in a similar manner to the biliary tract following the use of scolicidal agents [5].

Two readily available agents, hydrogen peroxide (3%) and povidone iodine (10%), were selected for current study. It has been reported that halogens act by oxidizing SH-

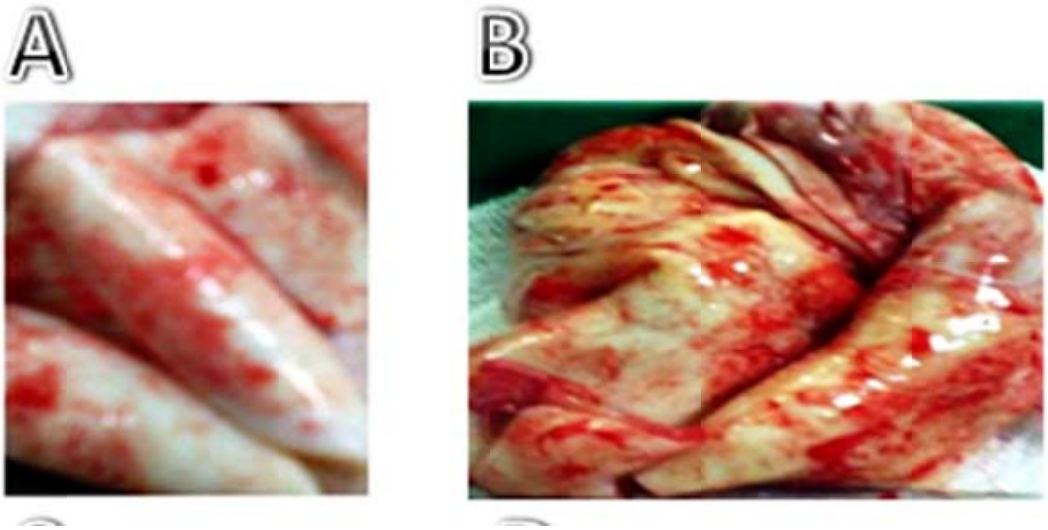

Fig. (1). (**A**) After exposure to povidone iodine, (**B**) After exposure to hydrogen peroxide.

groups (6). Povidone- iodine (Betadine®) is an iodophor containing 0.75% available iodine and in 10% solutions it is primarily used as an antiseptic agent and is a safe sclerosing agent [7]. The chief disadvantage of this type of agent is susceptibility to quenching by organic matter, becoming inactivated by organic contents in the hydatid cyst. Hydrogen peroxide (H_2O_2) always decomposes into water and oxygen and has been used as an antiseptic and anti-bacterial agent for many years. Three percent H_2O_2 is used medically for cleaning wounds, removing dead tissue, and as an oral deriding agent. Hydrogen peroxide is a Generally Recognized As Safe (GRAS) antimicrobial agent and oxidizing agent by the United States- Food and Drug Administration [6]. Significance differences were noted between the outcomes of these two. The rate of postoperative complications (other than recurrences) was 4% in group A *vs* 10% in group B; Hospital stay was longer in group B than in group A (9.6 ± 1.5 *vs* 5.5 ± 1.1 days), indicating that hydrogen peroxide is safer than povidone iodine. The recurrence rate was 11% in group B, but zero in group A over the same period of regular postoperative follow up (p=0.028), 48 and 84 months post surgery (mean 71±4 months). This might be considered as evidence that hydrogen peroxide is much more effective than povidone iodine as a scolicidal agent.

Postoperative mortality of hydatid cyst treatment shown the in literature is stated as 1-3%, while the recurrence rate did not exceed 10 % in any of these published studies, even with thoracoscopic management of the cysts [1]. Cemal *et al.* [8] reported cyst recurrence after treatment of ventricular myocardial echinococcosis, and while these investigators used polyvinyl pyrolidone iodine solution as a scolicidal agent and prescribed Albendazole for 5 years, they still reported a 10% recurrence rate [9, 10], stating that recurrences were mostly due to daughter cysts even though treatment with Albendazole in doses of 10 mg/ kg daily produced therapeutic levels in hydatid fluid [11].

A statistically significant number of recurrences in group B, indicates that administration of the scolicidal drug Albendazole might not be the best procedure to use in such treatments, seeming to be of minimal help when used for one year. We suggest that further research needs to be performed using higher doses of Albendazole for much longer time periods, up to several years. However, we recommend that Albendazole be administered in high doses in all cases of recurrence that develop during the first year. Impact of this infectious disease in endemic areas is such that continuous, focused research is warranted.

CONCLUSIONS

Hydrogen peroxide (3%) is a more effective and safer scolicidal drug than povidone-iodine (10%). Statistical significance of recurrent cases among patients treated with povidone iodine indicates that it is inferior to hydrogen peroxide in this study.

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CONFLICT OF INTEREST

Declared none.

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