Yeditepe Medical Journal 2011;5(17):379-384

SCOLICIDAL AGENT USE IN HYDATID CYSTS AND COMPLICATIONS

HIDATIK KISTTE SKOLOSIDAL AJAN KULLANIMI VE KOMPLIKASYONLARI

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ABSTRACT

Hydatid disease or cyst is an old endemic condition in many countries all over the world caused by tapeworm echinococcus embryo in sheep, cattle, pig, rat and human. Surgery is generally accepted as the most effective treatment method for the hydatid cyst. Since the possibility of spread of the cyst always exists, the vital scolices should be killed at first. The aim should be the prevention of the secondary hydatidosis by killing the vital scolices inside the cyst during this intervention. It is well-known that the agents used during the hydatid cyst surgery may lead to sclerosing cholangitis in the postoperative period. The aim of this article is to review the agents used in the treatment of hydatid cyst and their complications.

Key words:*Hydatid disease;treatment, complications.*

ÖZET

Hidatik hastalık ya da kist koyunlarda, büyük baş hayvanlarda, domuzlarda ve insanlarda ekkinokokus embriyosunun yol açtığı tüm dünyada bir çok ülkede görülen eski bir salgın hastalıktır. Cerrahi hidatik kistin tedavisi için en etkili yöntem olarak kabul görmektedir. Kistin yayılma ihtimali her zaman mevcut olduğundan canlı skoleksler öldürülmelidir. Amaç, bu girişim sırasında kist içerisindeki canlı skoleksleri öldürerek sekander hidatitozun önlenmesi olmalıdır. Hidatik kist cerrahisinde kullanılan ajanların postoperative dönemde sklerozan kolanjite neden olabileceği bilinmektedir. Bu çalışmada kist hidatikte kullanılan ajanlar ve komplikasyonları derlenmiştir.

Anahtar kelimeler: *Hidatik kist hastalığı, tedavi, komplikasyonları.*

Hydatid disease or cyst is an old endemic condition in many countries all over the world caused by tapeworm echinococcus embryo in sheep, cattle, pig,

rat and human (1). This parasite is usually observed as larva in the intestines of dogs or some carnivorous animals eating meat contaminated with hydatid cyst (2,3). Thousands of eggs are spread out with the animal feces. These eggs resistant to environmental conditions hatch into embryos in the stomach and duodenum of human and herbivorous animals that ate contaminated food. Then, they transform into invasive active form. Passing through the jejunum mucosa, embryos reach liver with portal circulation and then hook to sinusoids. Occasionally embryos pass the first filtration and settle in lungs or bone, brain and other organs (4-9). Embryos lose their hooks in the organ where settled. They grow and go through larvae phase and then turn into their typical shape for hydatid cyst. The intermediate host, who ate contaminated food or had close contact with the carrier animal, has the disease by this way. Scolex grows into adult tapeworm in the intestine of definitive host (**Figure 1**).

Hydatid cyst found in the intermediate host is filled with clear and odorless fluid as rock water. The present lesion appears to be tense and spherical with the fluid pressure. It grows slowly with constant expansion while exerting pressure to surrounding tissues. This fluid contains millions of scolex originating from germinative membrane. When scolices pass into the cyst fluid, they form a white sediment known as hydatid sand (1,10,11).

Today, surgery is generally accepted as the most effective treatment method for the hydatid cyst (12,13,14). The selection of the surgical method depends on the diseased organ, the location of the cyst, its number and size (15, 16, 17). Medical treatment of hydatid cyst may be utilized pre- or postoperatively in residual and inoperable cases (16).

The principles of the surgical treatment of hepatic echinococcosis are as follows,

1. The neutralization of the parasite.
2. The removal of germinal layer and drainage of the cyst.
3. Intervention to residual cavity (17, 18, 19).

Since the possibility of spread of the cyst always exists, the vital scolices should be killed at first. Killing vital cysts with intra-cystic procedures is an applicable method prior to surgery. Even though surgical intervention is the key point of the treatment, it has been reported that the preoperative use of scolicidal agents is unnecessary for ruptured, degenerated or secondarily infected cysts (20,21,22). The aim should be the prevention of the secondary hydatidosis by killing the vital scolices inside the cyst during this intervention (23). But, the side effect is the development of sclerosing cholangitis due to the chemical agents used.

It is well-known that the agents used during the hydatid cyst surgery may lead to sclerosing cholangitis in the postoperative period. This condition particularly occurs when the solutions come into contact with bile duct through their injection into the cyst opening. This is a rare, but a chronic condition affecting the bile ducts totally or partially and characterized by inflammatory reaction without bacteria (24). Sclerosing cholangitis associated with the surgical treatment of hydatid cyst may occur in a week or within a year (25,26,27). The most common solutions accounting for this condition are formalin, hypertonic

salt, silver nitrate, ethanol and hydrogen peroxide (25).

The macroscopic pathological findings related with sclerosing cholangitis depend on the duration, invasion and the localization of the cyst structure. Some histological alterations may be found after biopsy in liver which is observed as normal macroscopically in the early period. Even though the incidence of the dominant strictures resulting with icterus, itching, cholangitis or pain in the upper right quadrant is 15-20%, the worst complication of sclerosing cholangitis is cholangiocarcinoma with the incidence of 7-30% (28). In a study evaluating caustic sclerosing cholangitis that occurred clinically following the surgical treatment of hydatid disease, the occurrence of this condition was associated with 4 factors; a) the injection of the scolicidal agent into the cystic space, b) the relationship between cyst and bile ducts, c) contact of bile ducts with this scolicidal agent for a definite time, and d) specificity of the agent used. The symptoms of caustic sclerosing cholangitis begin earlier than primary sclerosing cholangitis and have a fast progression trend (29).

The relationship with scolicidal agents and sclerosing cholangitis.

The scolicidal agents including formaldehyde (22), hypertonic salt solution (30-33), silver nitrate (30,33), cetrimide (34), chlorhexidine (35), hydrogen peroxide, povidone iodine and ethyl alcohol have been used. However, these agents have many toxic effects limiting their usage (36,37,38). Particularly, secondary sclerosing cholangitis or caustic sclerosing cholangitis may develop due to the injection of these agents into the cyst opening to bile ducts and moreover, this may cause a clinical situation involving secondary biliary cirrhosis and death (39-47).

Formalin is toxic to biliary epithelium (36,37). In addition, the leakage of formalin to peritoneum and adjacent tissues may lead chemical peritonitis, necrosis of serosa, and chemical pneumonia of lungs. Furthermore, its leakage to systemic circulation may lead cardiac arrest due to toxic effect (38,48,49). Such adverse effects of formalin have influenced the researchers to develop novel agents. It was suggested that 96% ethyl alcohol is more efficient on scolices in 10 minutes and less detrimental than formalin (38,48,50). Ethyl alcohol has long been used for percutaneous aspiration and drainage (51,52). The adverse effect termed sclerosing cholangitis also occur with ethyl alcohol (26).

Many studies suggested that the use of silver nitrate as a scolicidal agent might be associated with sclerosing cholangitis (53). Eyüpoğlu et al. (54) observed slight portal inflammation in liver, necrotizing areas in parenchyma, slight stasis and Kupffer's cell hyperplasia following histopathological evaluation.

Recently, many surgeons have used hypertonic salt solution and this enables eradication of the cyst totally. Moreover, its application to peri-cystic area prevents inoculation to peritoneal cavity (9,30,35,49). The researchers have commonly accepted that hypertonic salt solution does not cause any toxic effect even if they infiltrate the blood vessels (9,49). Since Heslop (35) showed the scolicidal effect of concentrated sodium chloride solution, sodium chloride in 5-33% concentration has gained interest. However, hypernatremia associated with the use of sodium chloride was reported (55,56). Krige et al. (57) found fatal hypernatremia due to the use of hypertonic salt solution in a patient with hepatic hydatid cyst and resulted with mortality. Kayaalp et al. (42) investigated the efficiency of hypertonic salt solution in hydatid disease and concluded that the scolicidal effect was limited to low doses and toxic effects might arise with high doses. Hypertonic salt solution was reported to be ineffective in preventing the recurrence of this disease. Sclerosing

cholangitis was also described with the use of sodium chloride (58,59,60).

Özmen et al. (61) used 10% hydrogen peroxide as a scolicidal agent to patients having surgical treatment in a case series and reported no recurrence after regular follow-ups. Sathyanarayana et al. (62) described metabolic acidosis associated with the use of cetrimide-chlorhexidine in a patient with a large hydatid cyst in the left lobe of the liver. It was reported that the application of 0.5% cetrimide might cause methemoglobulin and result with the gas embolism with H2O2 (63). Furthermore, Belghiti et al. (64) described 6 mortalities after treating for the prevention of spread into abdomen and killing the vital cysts. They reported that one patient treated with 10% H2O2 died due to shock and the other patients treated with 2% formalin or 20% hypertonic salt solution developed sclerosing cholangitis. In another study, Belghiti et al. (65) showed caustic sclerosing cholangitis in 2 patients treated with 2% formaldehyde and in 3 patients treated with 20% hypertonic salt solution having cysts associated with bile duct. The cholangiography revealed strictures in intrahepatic bile duct in 2 patients and also showed strictures in both intrahepatic and extrahepatic bile duct in 3 patients.

In a study on povidone iodine (PVP-I), Sungur (66) reported that it was an effective scolicidal agent and showed adequate effect in 5 minutes in 1% concentration. Besides hypersensitivity and irritation was decreased due to iodine associated with PVP. However, cholangitis was observed in 50% of animals in this study. Gokce et al. (40) showed the efficiency of PVP-I in experimental peritoneal (secondary) hydatidosis. In an experimental study with 10% PVP-I, Coşkun et al. (67) reported marked stasis in liver, "spotty" necrosis in parenchyma, "piecemeal" necrosis, moderate portal inflammation and mild proliferation in bile duct. In another study, with the use of the same agent, renal shut-down due to systemic absorption, sterile peritonitis associated with local use, sclerosing serositis and constrictive pericarditis were described in addition to these pathological findings (68). Eyüpoğlu et al. (54) found statistically significant increase in ALT and AST levels and prominent histopathological alterations in liver and bile ducts despite the use of 5% PVP-I. These findings indicate the toxic effects of PVP-I on hepatobiliary system even in low concentrations. Alcohol-iodine solution was also described to be effective (30,32, 35,37,48) but it also has the disadvantages of being irritant and hypersensitivity risk to iodine.

The ideal scolicidal agent for hydatid cyst should kill vital scolices present, not have local or systemic adverse effects, and not be toxic to bile duct if the cyst opens. Yet, there is no ideal scolicidal agent involving such effects. Nevertheless, today there are many agents in use for the treatment of hydatid cyst. Further prospective comparative studies are needed to develop an ideal scolicidal agent.

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