INTRODUCTION

Echinococcus granulosus, which causes cystic echinococcosis, is one of the smallest members of the Taenia family. In the larval stage, it causes zoonosis in humans.\(^1\)

The hydatid disease is widespread around the globe but is unevenly concentrated, being more common in rural areas, and more prevalent among shepherds, butchers and cattle breeders. The disease is considered endemic in the following areas: the Mediterranean, Middle East, Eastern Europe, Africa, Argentina, Australia, Chile, China and New Zealand.\(^2,3\)

In Romania, the number of cases is increasing due to increases in livestock numbers and to current diagnostic possibilities.\(^4\)

Diagnosis is usually the result of paraclinical investigations such as ultrasound, X-ray, CT, hematologic and immunohistochemical tests. It is rarely established by clinical examination as the disease has a slow, insidious evolution and, in the absence of complications, is accompanied by minimum and non-specific clinical manifestations.\(^5,6\)

The treatment of hepatic hydatid cysts includes drugs such as albendazole or mebendazole, classical or laparoscopic surgery and the PAIR method (puncture, aspiration, injection, re-aspiration).\(^7\)

The treatment is usually mixed, but in the case of small, young cysts with thin walls, only medical methods can be used. Some studies have shown that high doses and long term use of drugs can lead to reversible...
neutropenia and, in some cases, to modifications of the hepatic and renal functions. 8, 11

Open surgery is especially useful in difficult to reach locations, in the cases of giant cysts or in the presence of adhesions, but it has a higher rate of complications and leads to longer hospitalization. Laparoscopy, recommended only when the cyst is easily accessible, ensures a high visibility, a safe hemostasis and a shorter hospitalization. 10, 11, 12

The ultrasound-guided transcutaneous puncture is a method that caught on very quickly due to its relatively easy execution and to its incontestable advantages compared to surgery, in terms of postoperative mortality and duration of hospitalization. 10, 11

However, the method also involves a number of risks, such as bleeding accidents, injuries of other viscera, secondary seeding caused by leaks of the hydatid fluid into the abdominal cavity and infections. Also, allergic reactions including anaphylactic shock may occur.

We report here the preliminary results of this treatment used on 217 patients presenting 268 hepatic hydatid cysts.

MATERIAL AND METHODS

Between April 1996 and December 2011, 319 patients with hepatic hydatid cysts were admitted to the Department of General Surgery No. 2, of the Timisoara County Emergency Hospital. Out of these, 46 were operated laparoscopically, 56 were operated through classical methods and 217 were treated using ultrasound-guided transcutaneous puncture. (Fig. 1)

As a detection method for hydatid cysts, all patients undertook abdominal ultrasounds. The hepatic cysts were classified according to the criteria developed by Gharbi and Niron. 13, 14

The abdominal ultrasound was followed by computed tomography for a more accurate cyst evaluation, with superior results regarding size and location. Casona intradermoeactions were also performed in 67 cases, with serological diagnosis based on echinococcosis antibodies.

The 217 patients were selected for treatment by ultrasound-guided transcutaneous puncture according to the following criteria:

- Types I and II according to the Gharbi classification;
- Patients for whom drug treatment had failed;
- Patients for whom surgical treatment was contraindicated due to the multiple comorbidities;
- Cysts in difficult to reach locations;
- Patients who accepted this treatment as an alternative to the surgical treatment;

This treatment was unsuitable for:

- Patients with hydatid cysts classified from the ultrasound point of view as Gharbi types III, IV and V;
- Patients whose cysts were infected or broken in the bile ducts or in the peritoneum.

After the certitude diagnosis of hepatic hydatid cysts, therapeutic protocols must be prepared. At the moment, the protocol for the percutaneous puncture is standardized and is unanimously approved and applied by specialists in all the countries that have accepted it.

The minimally invasivePAIR treatment protocol of the hydatid cyst 15, 17

The puncture site was chosen under ultrasound guidance. Most often, it was the same intercostal space recommended by most of the authors as having the lowest risk of peritoneal seeding. 18, 20

The steps of the PAIR minimally invasive treatment protocol of hydatid cysts were observed.

![Graph 1: Distribution of cases according to the type of surgery.](image)

1. The patient’s informed consent.
2. Serologic tests (IHA, ELUSA), ultrasound, CT, ERCP, MRI only for research purposes.
3. Treatment with albendazole or albendazole + cimetidine 4 hours before the procedure and after the surgery, during the first week or first month (treatment duration depends on the size of the cyst and its ultrasound aspect, more or less solid).
4. The presence of the anesthetist. Patient with a venous line.
5. Ultrasound-guided puncture with or without catheter.
6. Aspiration of the intra-cystic liquid (10-15 ml) for parasitological and biochemical examinations.
7. If protoscoleces are present and still viable – aspiration of the hydatid liquid.
8. In the absence of protoscoleces:
   a. If the clinical, epidemiological data and the fluid biochemistry are positive – the next step;
   b. If the clinical, epidemiological data and the fluid biochemistry are negative, the procedure ends (probably a non-parasitic cyst non-parasitic cysts are injected with alcohol only if symptomatic).
9. Intra-cystic introduction of the contrast medium and re-aspiration.
10. Injection of ethyl alcohol 35% (1/3 of the quantity of aspirated liquid).
11. Aspiration of the alcohol solution after 15 minutes.
12. Repetition of the parasitological examination (to check the viability of protoscoleces).
13. Evaluation of blood alcohol content (Gas chromatography). This is no longer performed as starting with the first patient treated, the results were constantly negative.
14. Parasitological, biochemical, serological, immunological and ultrasound monitoring, weekly up to one month, monthly up to 6 months and yearly up to 5 years.
15. Thorax radiography after one year and after 2 years from the procedure. Complete CT after 5 years.

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RESULTS

The age of the 319 patients under study was between 16 and 67 years, with an increased incidence in 21 – 30 and 31 - 40 years age groups. (Fig. 2) The female/male ratio was 1.4/1 (187 cases found in females and 132 cases found in males). (Fig. 3)

Table 1. Ultrasound classification of hepatic hydatid cysts of the entire group, according to Gharbi criteria.

<table>
<thead>
<tr>
<th>Ultrasound type</th>
<th>Patients (no.)</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I = well-delimited cyst, clear liquid inside</td>
<td>120</td>
<td>37.61</td>
</tr>
<tr>
<td>II = well-delimited cyst, with double contour of the walls, with clear liquid</td>
<td>97</td>
<td>30.41</td>
</tr>
<tr>
<td>III = cyst with multiple septa inside</td>
<td>85</td>
<td>26.64</td>
</tr>
<tr>
<td>IV = cyst with multiple hyperechogenic images inside</td>
<td>13</td>
<td>4.07</td>
</tr>
<tr>
<td>V = cyst with calcified walls</td>
<td>4</td>
<td>1.26</td>
</tr>
</tbody>
</table>

Out of the 319 patients, we shall further refer only to those selected for the PAIR method (217 patients, presenting 268 cysts).

Table 2. Clinical parameters of the study group.*

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>Patients (no.)</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>132</td>
<td>60.82</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>59</td>
<td>27.18</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>83</td>
<td>38.24</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>55</td>
<td>25.34</td>
</tr>
</tbody>
</table>

*The patients experienced one or more symptoms.

Table 3. Cysts parameters.

<table>
<thead>
<tr>
<th>Number of cysts/patient</th>
<th>Patients (no.)</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 cyst</td>
<td>174</td>
<td>80.18</td>
</tr>
<tr>
<td>2 cysts</td>
<td>35</td>
<td>16.12</td>
</tr>
<tr>
<td>3 cysts</td>
<td>8</td>
<td>3.68</td>
</tr>
</tbody>
</table>

Localisation of cysts

<table>
<thead>
<tr>
<th>Type of cyst</th>
<th>Patients (no.)</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right hepatic lobe</td>
<td>158</td>
<td>72.81</td>
</tr>
<tr>
<td>Left hepatic lobe</td>
<td>24</td>
<td>11.05</td>
</tr>
<tr>
<td>Both lobes</td>
<td>35</td>
<td>16.13</td>
</tr>
</tbody>
</table>

The cysts’ diameter varied from 2.5 cm up to giant size of 15.8 cm. The average diameter of the treated cysts was 5.8 cm.

All cysts were successfully treated using the PAIR method. The results are presented in Table 4.

Table 4. Results.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Average value</th>
<th>Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity of aspirated fluid (ml)</td>
<td>88</td>
<td>10 – 1400</td>
</tr>
<tr>
<td>Duration of hospitalization (days)</td>
<td>3.5</td>
<td>2 – 6</td>
</tr>
<tr>
<td>Monitoring period (months)</td>
<td>15.8</td>
<td>6 - 36</td>
</tr>
<tr>
<td>Postprocedural decrease in cyst diameter (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>74</td>
<td>58 – 100</td>
</tr>
<tr>
<td>3 months</td>
<td>86</td>
<td>69 – 100</td>
</tr>
<tr>
<td>6 months</td>
<td>90</td>
<td>72 – 100</td>
</tr>
<tr>
<td>12 months</td>
<td>93</td>
<td>75 - 100</td>
</tr>
</tbody>
</table>

Following this procedure, five (2.3%) cases of allergic reactions were recorded, which responded very well to treatment with hydrocortisone hemisuccinate and anti-allergic medication. In this series 232 cysts (86.56%) disappeared, 16 (5.97%) needed to undertake the puncture procedure again, due to the stagnation of diameters for 3 months, and 20 cysts (7.46%) relapsed, so surgical interventions were subsequently required.

DISCUSSIONS

Transcutaneous ultrasound-guided puncture entered the therapeutic arsenal for hydatid cysts starting with the mid 80s.

Today, most experts believe that the first choice in the treatment of the univesicular hydatid cyst is drug therapy with albendazole in the usual doses. If this treatment fails, the PAIR method is to be associated, and if the technique cannot be used, traditional laparoscopic treatment or conventional surgery shall be applied.
PAIR benefits are related to the fact that this is a minimally invasive maneuver, with a low risk compared to surgery, as well as much lower costs and hospitalization times. Also, it improves the effectiveness of chemotherapy before and after the puncture, most likely by increasing the penetrability of the drug substance within the cystic cavity.

As with any puncture, there is a risk of hemorrhagic accidents, injuries of adjacent viscera and, if the recommended protocol is not observed, secondary seeding due to the rupture of the pericyst and leakage of hydatid fluid into the abdominal cavity. Also, rupture of the hydatid cysts can lead to allergic reactions, ranging from mild symptoms to anaphylactic shock. The frequency of their occurrence is however not sufficiently studied. Due to the allergic potential of echinococcosis, prophylactic antihistamines and anti-inflammatory steroids were administered to the patients in our study before anesthesia, and only 5 cases (2.3%) of mild allergic reactions were recorded. In similar studies, authors also recorded small numbers of mild allergic reactions and no cases of anaphylactic shock, giving 20 minutes before the puncture H1 antihistamines and an anti-inflammatory steroid (Prednisone). As with conventional surgery, this method brings into discussion the possibility of sclerosing cholangitis, through the injection of a parasiticide into a cyst with a cystic-biliary communication. Thus, if a cystic-biliary fistula is suspected following the analysis of the aspirated fluid, the procedure is aborted.
In such cases, some authors recommend the introduction of drainage tubes into the cavity, by means of dilators on the initial tract of the puncture. Drainage tubes are maintained until the externalized secretion diminishes and disappears.\textsuperscript{26} Their results were mostly good, but in some cases surgery was still necessary in order to perform an external biliary drainage before closing the biliary fistulas of the residual cavity. Today, this disadvantage can also be eliminated by performing an endoscopic papilosphincterotomy.\textsuperscript{26,27}

Mueller et al. were the first to report a case of a patient who, after the PAIR procedure, was left with a drainage tube for three months. Subsequently, it turned out that maintaining a catheter for a longer period of time can lead to superinfection and clogging of the lumen drainage tube with fragments of the germinative membrane.\textsuperscript{21} Also, the routine use of catheterization for the drainage of the remaining cavity largely extended the duration of hospitalization, that reached to an average of 8.73 days with limits between 2 and 30 days, and, in the case of concurring infection, to an average of 25 days with limits between 20 and 30 days.\textsuperscript{26}

All cysts punctured by us were of types I and II according to the Gharbi classification, and their treatment was performed in a single step, without subsequent drainage.

The cavity that results from the procedure was found to gradually reduce in diameter. This is due to the use of alcohol, which ensures the sclerosis of the germinative membrane and its fibrous transformation. Through content aspiration, the intracystic pressure disappears and the hepatic parenchyma expands, leading to a gradual collapse of the cavity.

There are cases in which, due to the large size of the cavity, liquid secretion increases from transudation through the cyst walls, impeding the cavity’s collapse. In these cases, a puncture repetition may be required if the diameter of the cavity appears constant for over 3-6 months.

Other authors used the PAIR method for some cysts of types III and IV under the Gharbi classification and experienced complications – both major (anaphylactic shock in 0.1 to 0.2% of cases) and minor (rash, jaundice, fever, cyst superinfection or biliary system rupture in 10-30% of cases).\textsuperscript{28}

Even with cysts of types I and II and no complications, cysts were found to relapse in up to 4% of patients.\textsuperscript{29,30}

The results of our study are only preliminary, as the monitoring period necessary to draw safe conclusions about the effectiveness of the PAIR treatment has not ended.

We believe that the PAIR method is not sufficient in the case of multivesicular, infected or calcified cysts, but it represents an efficient and safe solution for the treatment of the hydatid cyst in carefully selected cases. Surgical treatment remains the main alternative.

**CONCLUSIONS**

The PAIR method is increasing in popularity for the treatment of hydatid cysts because it is easy to apply and is linked to low mortality.

The advantages of this method are most obvious when compared to surgery, in terms of trauma, post-operative mortality, hospitalization duration, use in difficult to reach locations and post-surgery relapses. The combination of medical treatment using anthelmintic drugs with percutaneous puncture is a viable alternative to surgery for removing hepatic hydatid cysts.\textsuperscript{31}

Still, the PAIR method is limited in its’ applicability and requires careful patient selection.

**REFERENCES**


