



PRE-OPERATIVE MEDICAL TREATMENT FOR LIVER HYDATIDOSIS: A 5 YEAR PROSPECTIVE COHORT STUDY

Y. BAKALI MD, *S. BENAMMI MD, O. BOUSLAM MD, F. SEBBAH MD, M. RAISS MD, Abdelmalek HRORA, M. ALAOUI MD

Surgical Department, IbnSina University Hospital, 10000, Rabat, Morocco UM5

ARTICLE INFO

Article History:

Received 4th June, 2020

Received in revised form 25th June, 2020

Accepted 23rd August, 2020

Published online 28th September, 2020

Key words:

Hydatidosis; Liver hydatidosis ;Albendazol;
General Surgery;

ABSTRACT

Background : Hydatid cyst is a cosmopolitan anthro pozoonosis resulting from the development of larval form of *Echinococcusgranulosus* in human tissue. The aim of our study is to evaluate the effectiveness of preoperative treatment with albendazole in cyst sterilization and prevention of recurrence.

Methods : This was a prospective cohort study conducted in surgical department of University Hospital IbnSina Morocco, from January 2013 to December 2018. Anthropometric, comorbidity, clinical characteristics, surgical approach and post-operative evolution data were collected. Radiology characteristics and biology markers using IFI and ELISA technics before and after pre-operative medical treatment were compared. And finally data of viability of parasite in surgical specimen were collected. All patients were started on Albendazole; accordingly 10 mg/kg/day divided on two takes, for 6months consecutively.

Results: 50 patients were included. Mean age was 45 years ; 68% were female. 20 patients had past history of surgical intervention for hydatid cyst prior to the last 10 years. Clinical symptoms were dominated by abdominal pain (90%). Right localization was predominant in 60% with segment VI involvement on abdominal CT. 40% presented hepatic cytolysis during treatment course. Clinical and radiological improvement was reported in 80% and 62% respectively. Finally non-viable scolex on surgical excision were observed in 82%. Resection of the prominent dome was the most used technique (92%). No recurrent cases were reported.

Conclusion: The effectiveness of Albendazole is demonstrated when administered for a period of 6 months. Cytolysis is not an indication to discontinue Albendazole therapy permanently. In case of cytolysis, therapeutic windows are a standard practice until normalization of transaminases.

Copyright©2020. Y. BAKALI MD et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Hydatidosis or cystic echinococcosis is a parasitosis caused by the development in humans of the larval form of dog taenia, *Echinococcusgranulosus* [1]. This parasitosis have a life cycle balancing between canids (essentially dogs) who are definitive host, and ungulates (essentially sheep), which are the intermediate host (A). Humans can get infected via eggs ingestion though infested dogs faeces, though humans are aberrant infective hosts, or “dead-end” intermediate hosts (A). This parasitosis can affect all organs without exception, but hepatic localization is the most frequent (2/3 of cases) which can be related to the digestive portal circulation [2, 3].

Hydaticechinococcus is considered an endemic disease in Morocco with mostly a rural distribution, and constitute a significant public health issue. Morocco is highly endemic for CE as the prevalence of infection in animals has been reported to be up to 58.8% in dogs, 19.3% in sheep and 48.7% in cattle (4, 5). A total of 23,512 human surgical interventions were reported by the Ministry of Health of Morocco from 1980–1992 and 2003–2008 (6). And in 2006, 1403 operated cases for hydatid cyst representing an average incidence of 4.55 cases per 100,000 inhabitants (7). Morocco officially launched in 2008 a national program to retaliate against hydatidosis(8).

If the diagnosis has been facilitated by developments diagnostic means, either biological and radiological explorations, treatment remains a subject of discussion and nonetheless an important matter considering the risk of recurrence. Indeed, treatment approach varies between exclusive surgical approach, conservative medical treatment,

*Corresponding author: S. BENAMMI MD

Surgical Department, IbnSina University Hospital, 10000, Rabat, Morocco

or a combination of both. Until recent years, surgical treatment was the only solution to treat hydatidosis. The lack of effective chemotherapy made this condition a worrying condition with a poor overall prognosis. Indeed, surgical treatment of hydatidosis carries a significant risk of per-operative dissemination promoting the recurrence, but also risk of anaphylactic reaction.

The aim of our study was to evaluate the effectiveness of preoperative treatment with albendazole in cyst sterilization and prevention of recurrence.

METHODS

We conducted a prospective cohort study including patients admitted in the surgical department « C » of the University Hospital Ibn-Sina in Morocco. Data were collected between January 2013 to December 2018. Patient presenting liver hydatidosis were included. Of each patient included, sociodemographic and anthropometric characteristics were collected. Data of patient's health characteristics that were collected included clinical symptoms before and after pre-operative medical treatment; radiology characteristics such as location, classification and dimension of liver hydatidosis before and after pre-operative medical treatment; biology tests such as liver function test and hydatid serology using IFI and ELISA technic ; surgical approach ; and finally viability of parasite in surgical specimen. Data was collected using a survey prospectively. Patients included followed pre-operative medical treatment protocol of albendazole, accordingly 10 mg/kg/day divided on two takes, for a period of 6 months consecutively. Women of childbearing potential were advised of the teratogenicity effect of treatment of albendazole, and consecutively contraceptive treatment was initiated. Monitoring throughout medical treatment protocol was conducted via clinical examination and biological examination on a pace of once per month. Treatment was discontinued in the event of severe neutropenia (<500). Moreover if liver function test were two times more than normal range the treatment course was suspended. Biological check up were conducted three weeks later, and medical treatment resumed after normalization of liver functions. We excluded patients who reported past history of hydatid cyst treatment either medical or surgical within last 10 years, and who interrupted their pre-operative treatment protocol.

Continuous variables are presented as mean \pm standard deviation for variables with a normal distribution, and as median and interquartile range (IQR) for variables with skewed distributions. The normality of the distribution was tested by the Kolmogorov-Smirnov test with Lilliefors correction. For categorical variables, the percentages of patients in each category were calculated.

RESULTS

We included 50 patients over a period of 5 years. The age of our patients varied between 16 and 76 years with an average age of 45 years old. 68% of included patients were female. Contact with dogs was reported 60% (n=30), 24% reported absence of contact (n=12), and 16% (n=8) noted an unclear contact. Hydatid cyst was symptomatic in almost all of our patients with 92% of patients, and n=4 were diagnosed with

liver hydatidosis incidentally upon clinical workup. The main functional signs that prompted the medical consult was abdominal pain with 90% of cases (n=45). Asthenia and weight loss were observed in 30% (n=15). Fever was related in 16% (n=8) and finally chest pain with respiratory discomfort was reported in 4% (n=2). Physical examination was uneventful in 70% (n=35). Abdominal sensitivity upon examination was found in 12% (n=6). And finally hepatomegaly was in (n=9) cases (18%).

Overall 92% totalized a period of 6 months of pre-operative treatment with Albendazole. In our cohort study, 60% received a consecutive 6 months of treatment without a free interval. 40% had interrupted the 6 months course as hepatic cytolysis was observed (n=40) of patients. Within 40%, four of our included patients received only 4 months of treatment due to intolerance of the treatment (digestive disorder; significant cytolysis). Finally in 4 patients (8%) live scolices were recovered in surgical specimen. Hence medical treatment was continued for 6 months after surgery in 4 cases.

Surgical treatment

All admitted patients received surgical treatment. Right subcostal laparotomy was the most used approach in our study with 72% of operated cases (n=36). Supra-umbilical median laparotomy was recommended in (n=14) patients. Resection of the protruding dome was the most recommended surgical procedure for the treatment; performed in 46 cases (92%). And perikectomy was performed in 4 cases (8%). In order to detect biliary fistula and prevent infection of residual cavity, drainage of the cavity was performed in 96% of patients.

Impact of preoperative treatment

On clinical follow-up 80% of patients showed improvement, judged by comparison of previous reported signs prior to start of treatment. While 10% of cases showed no visible change. On radiology evaluation conducted at completion of the 6 months treatment period, it showed a reduction of 45 \pm 15% in the size of the cyst in (n=31) cases, (n=15) cases remained stable and (n=4) cases increased in size. On post-operative evolution 2 patients developed a secondary infection at the residual cavity. Postoperative mortality was null

DISCUSSION

Since 1977 when first successful use of medical treatment in humans was achieved, management protocol of hydatidosis evolved (9). Medical treatment has since then rapidly gained weight in hydatidosis treatment along side the surgical management, due to the significant risk of dissemination, possible complications of any surgical intervention, and complexity of surgery in patient with multiple hydatid localization (2, 3). Several studies using the leading benzimidazole carbamates Mebendazole and Albendazole proved their efficiency regarding down-sizing of cysts prior surgery, or even complete remission (10).

Medical treatment therapy was initially indicated for patients deemed inoperable. Nowadays, medical treatment is considered due to its proven properties, in particular down-sizing and sterilization of cyst's contents before surgery. Thus avoiding the risks of dissemination, anaphylactic, and

surgically unattainable cyst (10). Over the past two decades, several studies have shown the efficiency of albendazole by using it as a neoadjuvant and adjuvant therapy in the framework of surgery [11, 12]. Its preoperative administration aims to reduce the viability or even sterilize the cysts, thereby significantly reducing the risk of intraoperative dissemination and reducing the rate of recurrence due to exovesiculations [11, 12, 13, 14].

Albendazole is prescribed per os in 400mg per tablet format, or as solution at 400mg / 10ml (10ml bottle); according to a daily dosage of 10 to 12 mg/kg divided in 2 take [15]. Albendazole can be prescribed according to two protocols: sequential protocol with repeated courses of one month, one daily take, and with 15 days of free interval; or continuous protocol for 3 months at a dosage of 10 to 12 mg/kg/day divided into 2 daily takes, without exceeding 800 mg / day, both approved by the WHO (16, 17). The duration of treatment varies in literature and remains imprecise, ranging from 4 weeks to 6 months (Morris *et al*, Coulaud, Rosa, Horton (18, 19, 20)). However, other data suggests greater efficacy of continuous treatment for 3 to 6 months in obtaining a favourable result (negation of serological tests, and reduction in the volume of CT images (21)). Finally our study shows that cytolysis is not an indication for permanently stopping treatment with albendazole. In the event of cytolysis, therapeutic windows are practiced until the normalization of transaminases, thus making it possible to total the 6 months of treatment.

CONCLUSION

To this day, the radical treatment of hydatidosis remains surgical. However, medical treatment is of interest in the prevention of secondary dissemination and recurrence adjuvant to operative or percutaneous act. However, there is no consensus regarding the duration of preoperative treatment and its modalities. In literature, the results of the studies cannot be generalized or extrapolated to all groups of patients, as there was variability in the duration of preoperative treatment and in the general condition of patients between the different studies. The results of this work show the role of preoperative treatment with albendazole in the management of liver hydatid cyst.

Conflict of Interest

None to declare

Ethical consideration & disclosure

Study protocol was approved by Rabat ethic committee, and informed consent was obtained from all participants

Bulleted Keys

- The results of this work show the role of preoperative treatment with albendazole in the management of liver hydatid cyst over a period of 6 months
- Abdominal pain is the major clinical symptoms of liver hydatid cyst
- Resection of the protruding dome was the most recommended surgical procedure for the treatment

- Neoadjuvant medical treatment efficiently reduce risk of hydatid dissemination and hydatid metastasis
- Cytolysis is not an indication for permanently stopping treatment with albendazole. In the event of cytolysis, therapeutic windows are practiced until the normalization of transaminases, thus making it possible to total the 6 months of treatment.

References

1. P. L. Moro and P. Cantey, 281 - Echinococcus Species: Agents of Echinococcosis, Fifth Edit. Elsevier Inc., 2018.
2. P. Aubry, "Hydatidose :Kystehydatique," pp. 2–6, 2013.
3. F. Noomen, A. Mahmoudi *et al*. Traitement chirurgical des kystehydatiques du foie. EMC- Techniques chirurgicales – Appareil digestif 2013 ; 8(2) :1-18 [Article 40- 775].
4. Chebli H, Laamrani El Idrissi A, Benazzouz M, Lmimouni BE, Nhammi H, Elabandouni M, *et al*. (2017) Human cystic echinococcosis in Morocco: Ultrasound screening in the Mid Atlas through an Italian-Moroccan partnership. PLoSNegl Trop Dis 11(3): e0005384. doi:10.1371/journal.pntd.0005384
5. Azlaf R, Dakkak A. Epidemiological study of the cystic echinococcosis in Morocco. Vet Parasitol. 2006; 137(1–2):83–93. doi: 10.1016/j.vetpar.2006.01.003 PMID: 16473466
6. Derfoufi O, Akawa E, Elmaataoui A, Miss E, Esselmani H, Lyagoubi M, *et al*. Epidemiological profile of cystic echinococcosis in Morocco from 1980 to 2008. Ann Biol Clin. 2012; 70(4):457–61.
7. "Les HELMINTHOSES," pp. 1–55, 2018.
8. D.E.L.M. Guide de lutte contre l'hydatidose 2007. Disponibles sur internet :URL: <http://www.sante.gov.ma>.
9. Biomnis, "hYDA TIDOSE," PRÉCIS Biopathol. Anal. MÉDICALES SPÉCIALISÉES, pp. 1–3, 2012.
10. E. G. Singounas, A. S. Leventis, D. E. Sakas, D. M. Hadley, D. A. Lampadariou, et P. C. Karvounis, « Successful treatment of intracerebral hydatid cysts with albendazole: case report and review of the literature », Neurosurgery, vol. 31, no 3, p. 571-574, sept. 1992.
11. Dervenis C., Delis S., Avgerinos C., Madariaga J., Milicevic M. Changing concepts in the management of liver hydatid disease J Gastrointest Surg 2005 ; 6 : 869-877 [cross-ref].
12. Dziri C., Haouet K., Fingerhut A., Zaouche A. Management of cystic echinococcosis complications and dissemination: where is the evidence? World J Surg 2009 ; 33 : 1266-1273 [cross-ref].
13. Smego R.A., Sebanago P. Treatment options for hepatic cystic echinococcosis Int J Infect Dis 2005 ; 9 : 69-76.
14. Shams U.B., Arif S.H., Malik A.A., Khaja A.R., Dass T.A., Naikoo Z.A. Role of albendazole in the management of hydatid cyst liver Saudi J Gastroenterol 2011 ; 17 : 343-347.

15. Wenbao Z, Jun L, Donald P. Concepts in Immunology and Diagnosis of Hydatid Disease. *Clin Microbiol Rev* 2003;16:18–36
16. Brunetti E., Kern P., Vuitton D.A., Working Panel for the WHOIWGE Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans *Acta Trop* 2010 ; 114 : 1-16.
17. Vuitton D.A. Benzimidazoles for the treatment of cystic and alveolar echinococcosis. What is the consensus? *Expert Rev Anti Infect Ther* 2009 ; 7 : 145-149.
18. Morris DL Albendazole treatment of hydatid disease follow up at 5 years *Tropical doctor*, 1989, 19, 179–180.
19. Coulaud JP Traitement médicamenteux de l'échinococose Le concour médical 1988– 11–06–110–23.
20. R. Horton, « Albendazole in treatment of human cystic echinococcosis: 12 years of experience », *Acta Trop.*, vol. 64, no 1-2, p. 79-93, avr. 1997.
21. R. Singal, K. S. Sandhu, A. Mittal, S. Gupta, et G. Jindal, « A Giant Splenic Hydatid Cyst », *Bayl. Univ. Med. Cent. Proc.*, vol. 29, no 1, p. 55- 57, janv. 2016.

How to cite this article:

Y. BAKALI MD *et al* (2020) ' Pre-Operative Medical Treatment for Liver Hydatidosis: A 5 Year Prospective Cohort Study', *International Journal of Current Advanced Research*, 09(09), pp. 23083-23086.
DOI: <http://dx.doi.org/10.24327/ijcar.2020.23086.4564>
