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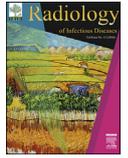


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Research Article

Sonographic assessment of the effect of praziquantel therapy on liver echotexture and diameters of the portal and splenic veins in patients with schistosomiasis

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Abstract

Purpose: To assess the effect of praziquantel (PZQ) treatment on liver echotexture and diameters of the portal and splenic veins.

Materials and methods: This was a prospective study involving 86 known cases of schistosomiasis; these cases were examined via gray-scale sonography in 3-month intervals for a period of 6 months. The patients were categorized into two groups based on whether or not they were treated with PZQ. The liver, spleen, main portal vein (PV), and splenic vein (SV) were evaluated sonographically using 3.5-curved transducers, according to a standard abdominal ultrasound protocol.

Results: The liver echotexture and size were significantly recovered in patients who received PZQ therapy compared to those who did not use the drug (p-values < 0.001). PZQ caused significant reduction in diameters of the PV and SV (p-value < 0.001). **Conclusion:** Liver size and echotexture and diameters of PV and SV improved well as a result of Praziquantel therapy in patients with chronic Schistosoma infection. Treatment of Schistosomiasis is necessary to prevent liver cirrhosis and portal hypertension.

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Keywords: PZQ; Liver echotexture; Portal vein; Splenic vein

1. Introduction

Schistosomiasis is one of the most prevalent parasitic diseases in the world, which affects more than 200 million individuals, and approximately over half suffer from related morbidity [1]. It remains a health problem in many developing countries, and approximately 700 million people worldwide are at risk for this infection [2,3]. In Sudan, the prevalence of schistosomiasis is high, especially in the White Nile river basin. It is closely associated with frequencies of water contact, swimming, taking baths, and wading the stream [4].

Schistosomiasis is one of the common parasitic diseases in Sudan. The epidemiological data revealed that more than 70% of the population were exposed to schistosomiasis, and approximately 7.5 million of them were infected. The majority were below the age of 20 years [5]. The risk for the infection is widespread in different states [6,7]. Moreover, when left untreated, this disease may lead to severe complications such as liver fibrosis, hepatic cirrhosis, and nodular regenerative hyperplasia, and result in portal hypertension [8,9].

Diagnosis and management of schistosomiasis using imaging modalities have mostly been performed using ultrasound (US). The US is an effective imaging method that is frequently used to assess the morbidity associated with infection with *Schistosoma mansoni* and *S. haematobium* and to monitor the changes of fibrosis in the liver, splenomegaly, and dilated main portal vein (PV) and splenic vein (SV) following chemotherapeutic treatment for schistosomiasis [10,11].

Abbreviations: ANOVA, analysis of variance; PV, portal vein; PZQ, praziquantel; SD, standard deviation; SV, splenic vein; US, ultrasound.

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Schistosomal infection frequently causes dilatation of the PV and SV above the average limits [12,13]. Thus, sonographic signs of portal hypertension have been reported as dilatation of the PV and SV, as well as reduction of PV velocity [14,15]. Overall, assessing the changes of diameters of the PV and SV in addition to liver echotexture, are important in the protection against portal hypertension and other suspected complications.

Praziquantel (PZQ) is the drug of choice for treatment against all species of schistosomes. The cure rates of 65% and 90% have been reported after a single dose of medication with PZQ [16]. The assessment of using PZQ is highly needed for health providers and planners. Therefore, identifying the efficacy of PZQ that contribute to such improvements is essential, particularly for the residents of the regions where schistosomiasis is prevalent, who have a higher risk for portal hypertension.

The purpose of this prospective study was to evaluate the effect of PZQ therapy on liver texture and diameters of the PV and SP in known cases of schistosomiasis.

2. Patients and methods

This was a prospective study involving patients with schistosomiasis who were investigated and followed-up for a period of 6 months. Participants with malaria, hepatitis, leishmaniasis, and a history of infectious diseases were excluded from the study. The study was conducted in New Halfa at the East of Sudan from May 2016 to December 2016. A total of 86 patients infected with schistosomiasis mansoni, which was proved clinically and via laboratory tests, were enrolled in this study. They were compared with 85 healthy volunteers (controls). We evaluated the liver echotexture and diameters of the PV and SV in the two groups. The infected group comprised 47 men and 38 women. This group was further classified into two categories: group A, consisting of 49 patients who were treated with PZQ and group B, consisting of 37 patients who were not treated with PZQ during the study period. Group A was examined with ultrasound and administered a single oral dose of PZQ 40 mg/kg body weight. After 3 months, they were examined and administered the same dose of PZQ again. Three months later, the patients were finally investigated. The sonographic findings observed during the three timepoints were compared to evaluate the changes in diameters of the PV and SV for each patient.

2.1. Sonography procedure

Using standard B mode grayscale ultrasound (Mindray 35C50EA, China), abdominal sonography was performed using a portable ultrasound machine equipped with a 3.5-MHz curvilinear transducer. The examination was conducted by two experienced radiologists to reduce interobserver and intra-observer variabilities. Patients were investigated in the supine position with the transducer placed in the epigastrium in both transverse and longitudinal planes. The liver was scanned in the parasagittal scan plane and then subcostal and intercostally

to evaluate the entire liver. The liver size was assessed and interpreted as “normal” and “shrunk.” The normal echotexture of the liver is of medium homogenous echogenicity, and the liver is usually slightly darker than the spleen and slightly brighter than the renal cortex of the right kidney. It was considered coarse when it lost its homogeneous texture by diffuse lesions such as periportal fibrosis. Hepatic tumors and all focal lesions were excluded from the study.

The main PV was examined in an oblique right subcostal view; the diameter was measured from the inner to the outer layer, and then the mean value was obtained. In the control group, the normal mean PV diameter was 13 mm; PVs with a diameter greater than 13 mm were considered dilated. The SV was examined in the transverse and oblique substernal view. It lies behind the tail, body, and head of the pancreas and its upper limit diameter was 10 mm. SVs with a diameter >10 mm were regarded dilated.

The study was approved by the local ethical committee of Alzaiem Alazhari University, Faculty of Radiological Sciences and Medical Imaging. All participants provided oral informed consent and were investigated following the treatment. A designed data collection sheet was used to collect the demographic and clinical data of the participants.

2.2. Statistical analysis

The data were analyzed using SPSS for Windows (Version 16.0; Copyright SPSS Inc., USA). For comparing means, the data were interpreted using independent Student's t-test and analysis of variance (ANOVA). ANOVA was used to compare the means of diameters of the PV and SP at all the three timepoints. Quantitative data were presented as means \pm standard deviation (SD). P-values < 0.05 were considered to be significant.

3. Results

A total of 86 cases of known schistosomiasis were investigated with ultrasound in Halfa region of East of Sudan. They compared of 85 healthy volunteers as control group. The mean age of the infected group was 40.36 ± 10.72 years and that of the control group was 41.34 ± 9.72 years. Of these, 47 were men (54.6%), and 33 (45.4%) were women. Of these patients, 49 (57%) used PZQ regularly while 37 (43%) did not use the drug. Liver cirrhosis was observed in 67 cases (77.9%), as shown in Tables 1 and 2.

Sonography revealed that PV diameter was 14.17 ± 2.44 mm and 12.23 ± 1.44 mm in the infected and control groups, respectively, while SV diameter was 11.52 ± 2.32 mm and 10 ± 0.56 mm in the infected and control groups, respectively. Both PV and SV diameters were significantly higher in the infected group (p-value < 0.001), as shown in Table 1.

PZQ therapy is significantly associated with improvement of liver echotexture and size (p-value < 0.001), as shown in Table 2. Of all patients, 36 (41.8%) who used the drug had normal liver echotexture, while 26 (30.2%) had coarse

Table 1
Comparison of measurements of diameters of PV and SV in the infected group and control.

Variables of the infected group	Infected group Mean \pm SD	control group Mean \pm SD	p-values
Age (years)	40.36 \pm 10.72 years	41.34 \pm 9.72 years	
Diameter of the portal vein	14.17 \pm 2.44mm	12.23 \pm 1.44mm	<0.001
Diameter of the splenic vein	11.52 \pm 2.32 mm	10 \pm 0.56mm	<0.001

Table 2
The ultrasound evaluation of liver in relationship to praziquantel therapy of schistosomiasis.

		PZQ therapy		total	P-value
		yes	No		
Echotexture of the liver	Normal	36	11	47	<0.001
	coarse texture	13	26	39	
	Total	49	37	86	
Size of the liver	Normal	1	22	23	<0.001
	shrunk	48	15	63	
	Total	49	37	86	

Table 3
The sonographic assessment of diameters of PV and SV before and after administration of the PZQ drug.

variables	Before PZQ administration	First interval three months after drug administration	Second interval three months after drug administration	Significance between groups (p-values)
Porta vein diameters	17.13 \pm 1.29mm	14.79 \pm 0.58mm	12.61 \pm 1.7mm	<0.001
Splenic vein diameters	13.70 \pm 2.20	12.21 \pm 1.67mm	10.31 \pm 1.62	<0.001

echotexture. The range of diameters of the main PV decreased by 2.34 mm 3 months after drug administration and further decreased by 2.18 mm at the end of the next 3 months. In addition, the diameters of the SV were reduced by 1.49 mm 3 months after drug administration and further decreased by 1.90 mm at the end of the next 3 months. The results revealed that both PV and SV diameters were significantly reduced after using PZQ (p-value <0.001), as shown in Table 3. Figs. 1–3 are sonograms taken from the patients demonstrating changes in liver echotexture and dilatation of the PV and SV.

4. Discussion

Schistosomiasis is one of the most common parasitic diseases that remains a health problem in Sudan. Several studies in Sudan have reported the epidemiology and effect of schistosomiasis in Sudanese people [17–19]. In 2012, separate estimates reported that the prevalence of schistosomiasis in Sudan had increased to 23.7% [20]. In spite of these studies, to our knowledge, reports demonstrating the evaluation of US findings and its correlation with the effect of PZQ treatment in Sudanese patients are rare.

Liver parenchymal texture is an important characteristic in the evaluation of diffuse hepatic parenchymal diseases and changes such as fibrosis and cirrhosis. Nishiura et al. [21] performed ultrasound-based evaluation of the fibrosis stage in chronic liver diseases. They graded liver echotexture as fine echotexture, mildly coarse, and highly coarse, and reported a statistical correlation of liver echotexture with fibrosis severity. These findings confirmed that infectious diseases influence liver echotexture.

In the current study, we observed that the liver echotexture was coarse, and the liver size was decreased in patients who

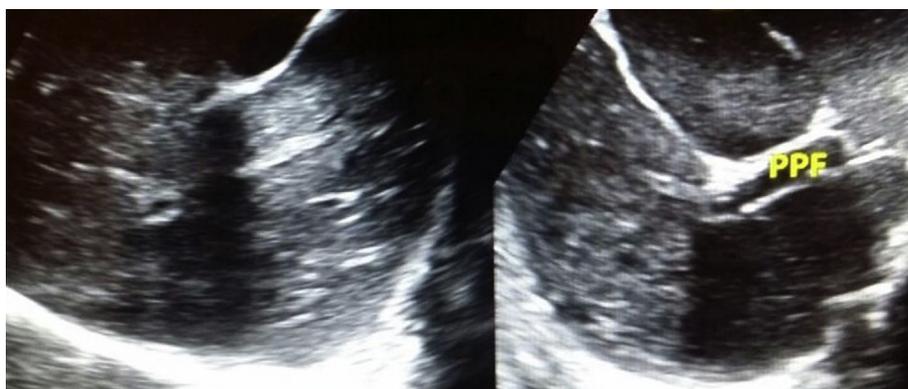


Fig. 1. A sonogram reveals a heterogeneous liver texture due to periportal fibrosis.



Fig. 2. Gray-scale sonogram reveal dilatation of the main portal vein.

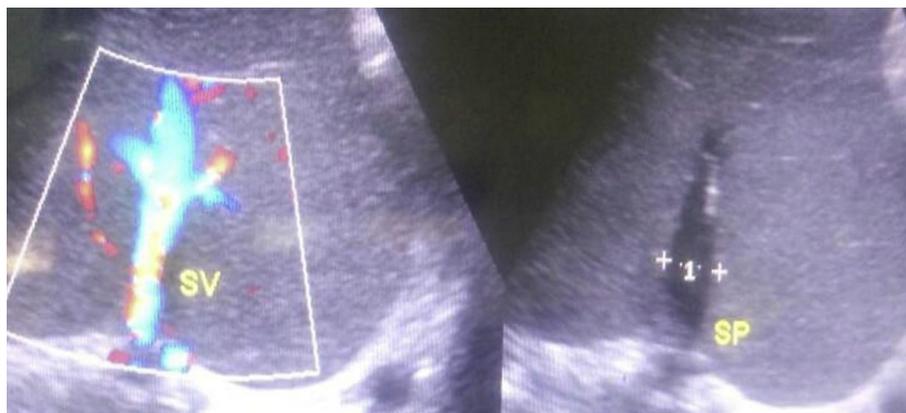


Fig. 3. Gray-scale and Color Doppler sonograms reveal dilatation of the splenic vein.

of the study by Raiza et al., [22] which reported that the SV and PV diameters showed statistically significant reductions ($p < 0.05$) before and after treatment. The benefit of this reduction is essential to prevent portal hypertension.

Therefore, PZQ therapy is effective in the reduction of the morphological changes and other complications of schistosomiasis. It is effective against all species of *Schistosoma*, especially *S. mansoni* and *S. haematobium*, which are prevalent in African regions [24]. However, additional large cohort studies are needed to confirm the initial results of this study.

4.1. Limitation of the study

Although the findings of this study revealed a positive effect of PZQ therapy on liver texture and diameters of PV and SV, the sample size was not large enough and there were lack of published studies regarding sonography of schistosomiasis in Sudanese adults. Most of the studies were review articles and surveys. Moreover, the infected patients have negative belief towards the PZQ drug. Further studies were needed to confirm the initial results of this study.

did not receive PZQ treatment. Liver parenchymal heterogeneity was observed in 15.11% of patients on regular PZQ treatment and 30.23% in those who did not use the drug. It was observed that the liver architecture was significantly improved in those who used the drug. Our result agreed with that of the study by Raiza et al., [22] which evaluated the clinical and ultrasound findings before and after PZQ treatment, and reported that the US-based evaluation of the effect of PZQ treatment showed that the liver disease had improved and the levels of the markers for periportal thickening were reduced [21]. This improvement of liver echotexture is attributed to the effect of PZQ, which paralyzes the worm and exposes it to attack by the host immune system [23]. This mechanism prevents the fibrosis and allows the hepatic tissue to recover to its normal homogeneity in most of the cases.

In the present study, it was observed that the diameters of the main PV and SV were significantly decreased 6 months after PZQ therapy. These findings were consistent with those

5. Conclusion

Liver size and echotexture and diameters of the PV and SV improved well as a result of PZQ therapy in patients with chronic *Schistosoma* infection. Treatment of Schistosomiasis is necessary to prevent liver cirrhosis and portal hypertension.

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