MINISTRY OF EDUCATION AND TRAINING MINISTRY OF HEALTH
**NATIONAL INSTITUTE OF MALARIOLOGY - PARASITOLOGY AND ENTOMOLOGY**

**LE DINH VINH PHUC**

# RESEARCHING CLINICAL, LABORATORY FINDINGS AND TREATMENT OUTCOME OF PATIENTS WITH TOXOCARIASIS BY THIABENDAZOLE IN MEDIC MEDICAL CENTER, HO CHI MINH CITY, VIETNAM (2017-2019)

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## LIST OF THESIS-RELATED PUBLICATIONS OF THE AUTHOR

1. Le Dinh Vinh Phuc, Cao Ba Loi, Huynh Hong Quang, Le Duc Vinh, Cao Truong Sinh, Vu Van Du, Que Anh Tram, Khong Minh Quang, Tang Xuan Hai, Tran Anh Le (2021). Clinical and Laboratory Findings among Patients with Toxocariasis in Medic Medical Center, Ho Chi Minh City, Vietnam in 2017-2019. Iran J Parasitol., 16(4):1-10.

2. Le Dinh Vinh Phuc, Tang Xuan Hai, Cao Ba Loi, Huynh Hong Quang, Le Duc Vinh, Tran Anh Le (2021). The kinetic profile of clinical and laboratory findings and treatment outcome of patients with toxocariasis. Trop Med Int Health., 00:1-8.

# INTRODUCTION

Toxocariasis is the clinical term applied to infection in the human host with either *Toxocara canis* or *Toxocara cati*.

The broad spectrum of clinical manifestations in toxocariasis varies from asymptomatic to non-specific clinical signs which make it difficult to directly identify clinical cases of toxocariasis. The level of serum IgG can remain elevated for years which precludes the discrimination between active and persistent infections; the diagnosis of toxocariasis/*Toxocara* spp. infection can be achieved by histopathological examination, morphometric assessment of larvae (if detected) and/or the specific detection of larval DNA in/from tissues or body fluid samples by molecular means but it is difficult and rarely attempted [11].

In terms of treatment, to date, there are few clinical trials evaluating the effectiveness of the drug in humans. This limits the clinical choice of drugs. Benzimidazole derivatives are effective in the treatment of toxocariasis in humans, in which albendazole is the preferred choice [12]. However, the optimal course of albendazole therapy has not been agreed, and treatment outcomes have varied widely across studies [13].

Thiabendazole is also an option in the treatment of human toxocariasis, which is recognized by the US FDA [14] and included in the Guidelines for Diagnosis and Treatment of the Ministry of Health in 2020 [15]. However, studies evaluating the treatment results and safety of thiabendazole in our country are still limited in number.

All the difficulties and problems in terms of diagnosis and treatment of toxocariasis in humans mentioned above make it necessary to conduct in-depth studies. We conducted the topic: "Researching clinical, laboratory findings and treatment outcome of patients with toxocariasis by thiabendazole in Medic medical center, Ho Chi Minh city, Vietnam in 2017-2019", for the following goals:

*1. Describing the clinical and laboratory findings among patients with toxocariasis in Medic medical center, Ho Chi Minh city, Vietnam in 2017-2019.*

*2. Evaluation of the treatment outcome and safety of thiabendazole for human toxocariasis.*

## STRUCTURE OF THESIS

The thesis covers 145 pages, including: Introduction with 2 pages; Overview with 34 pages; Researching object and methods with 23 pages; Researching findings with 42 pages; Discussion with 41 pages; Conclusion with 2 pages; Petition with 1 page. The thesis has 10 figures, 55 tables. There are 194 references, in which 55/194 documents have been published for 5 recent years.

## Chapter 1: OVERVIEW

Human toxocariasis, caused by *T. canis* or *T. cati*, is currently a health concern of the scientific community around the world, reflected in the number of publications. There is an increasing number of publications in the literature from countries in Asia, Africa, Oceania, Europe and the Americas [3].

Most experts divide into 4 main clinical types: visceral larva migrans; ocular larva migrans, neurotoxocariasis and common/covert toxocariasis [11].

In 2001, Pawlowski proposed five criteria including epidemiological factors, clinical features and paraclinical indicators to diagnose a case of toxocariasis in humans [58].

In 2016, the Ministry of Health issued the document "Infectious Disease Case Definition" referring to a confirmed case including clinical and test criteria for anti-Toxocara spp. IgG ELISA was positive [16].

For many years, the treatment of toxocariasis in humans was considered unnecessary or ineffective. However, the results of randomized controlled clinical trials indicate that an indication for treatment is necessary to prevent larval migration to the brain, eyes, and internal organs [58], [71].

Currently, the Guidelines of the World Health Organization and the Ministry of Health have made a number of recommendations for drugs that can be used to effectively treat human toxocariasis [15], [72].

Treatment of specific drugs in combination with symptomatic treatment. Guidelines for diagnosis, treatment and prevention of human toxocariasis of the Ministry of Health (2020) include regimens of albendazole, thiabendazole or ivermectin [15].

Worldwide, Stürchler *et al*. (1989) treated 34 patients with visceral larva migrans for 5 days with thiabendazole 25 mg/kg/day divided into 2 (19 patients) and albendazole 15 mg/kg/day divided into 2 (15 patients). Treatment outcomes were assessed after 30 weeks. In the thiabendazole group, 27.0% were clinically cured. In the albendazole group, 32.0% were clinically cured. The authors recommend that albendazole be used for the treatment of visceral and ophthalmic patients at a minimum dose of 10 mg/kg/day for a 5-day course [74].

Magnaval *et al*. (1995) evaluated the outcomes of diethylcarbamazine and mebendazole in 39 and 41 patients, respectively. The clinical parameters used to monitor after treatment were the number of eosinophils, the quantification of the total IgE concentration and the Western blot test. The time of assessment was 1 month after the end of treatment. Results analysis showed similar results for diethylcarbamazine and mebendazole on clinical scores and eosinophil count reduction rates. Mebendazole therapy was more effective in terms of the kinetics of IgE concentrations. Patients from the diethylcarbamazine group reported a significantly higher incidence of adverse events. Since then, the authors suggest to treat toxocariasis in humans with mebendazole [76].

For ocular larva migrans, Barisani-Asenbauer *et al*. (2001) reported that oral albendazole 800 mg twice daily for adults and 400 mg twice daily in children in combination with steroids improved visual acuity and did not recur in uveitis in 5

patients during the follow-up period of 13.8 months [79]. In study Ahn *et al*. (2014), combination therapy with albendazole and corticosteroids significantly reduced recurrence at 6 months (17.4%), compared with relapse rates in the corticosteroid-only group (54, 5%). Regarding the dosage of albendazole therapy to date, there is no consensus among clinicians [80]. However, according to Despommier, albendazole is still the drug of first choice in the treatment of toxocariasis in humans [81]. According to a study by Ozimek *et al*. (2015) on the therapeutic efficacy of diethylcarbamazine and thiabendazole in the treatment of toxocariasis in humans, the cure rate of diethylcarbamazine was 75.0% for visceral form and 85.0% for covert toxocariasis and the cure rate for thiabendazole was 70.0% lower for visceral form and 80.0% for covert toxocariasis [82]. Recently published by Hombu (2017) long-term albendazole therapy showed a curative efficacy in 78.0%, adverse events occurring in 15.0% [13].

The evaluation of treatment outcome is based on clinical and laboratory response. Stürchler saw significant clinical improvement at 2 and 6 weeks post-treatment [74]. If the follow-up lasts for more than 6 months, the improvement in clinical signs is difficult to distinguish due to the effects of specific drugs or to the self-limiting course of the disease [75]. According to the experience of Magnaval (2001) it is advisable to evaluate the outcome of treatment between the 4th and 6th weeks after the end of treatment [41]. In general, according to many authors, it is difficult to evaluate treatment results.

In terms of subclinical, the index of eosinophil count has good value for monitoring after treatment. In a trial comparing diethylcarbamazine with mebendazole, Magnaval (1995) showed that both significantly reduced mean eosinophil counts within 1 month of treatment, while total serum IgE levels remained unchanged change [76]. Hombu (2017) studied a prolonged course in Japanese patients who were treated with albendazole at a dose of 10-15 mg/kg/day for 4 weeks, then stopped for 2 weeks and repeated the course for another 4 weeks, using only the test criteria are eosinophils and IgG antibody ELISA to evaluate the treatment results after 3 - 4 months [13]. In a study by Song *et al*. (2020) monitoring the kinetics of eosinophils under the influence of specific treatment showed that there were 12/14 cases of eosinophils returning to normal levels or decreasing in number with the median duration was 3 months and the recommended period of eosinophil follow-up after treatment should be 3-4 months [61]. For IgG antibodies against *Toxocara* spp. by ELISA test, many authors consider it not useful in monitoring treatment due to persistent positive IgG. When comparing IgG between treated and untreated children, the kinetics of IgG antibodies to *Toxocara* spp. decreased very slowly [71] or remained unchanged [75]. In the study of Wiśniewska *et al*. (2012) analyzing the results after treatment in children showed that the kinetics of IgG antibodies changed to a decrease [71]. Meanwhile, imaging lesions such as hypoechoic liver lesions on ultrasound or low-density areas on CT scan of the liver [77] or brain lesions on MRI [78] often change and improve within 1 to 2 months after treatment.

## Chapter 2: RESEARCHING METHODS

**2.1. Researching method of target 1:** *Describing the clinical and laboratory findings among patients with toxocariasis in Medic medical center, Ho Chi Minh city, Vietnam in 2017-2019.*

### 2.1.1. Researching objects, places and time

***- Research subjects:*** Patients who come to the clinic meet the criteria to determine the case of toxocariasis according to the case definition of the Ministry of Health issued under Decision No. 4283/QD-BYT dated August 8, 2016 [16].

+ Clinical: There are signs of toxocariasis, such as itching, rash, headache, abdominal pain, dyspepsia, aches, numbness, fever, wheezing. May be accompanied by one or more symptoms of hepatomegaly, pneumonia, chronic abdominal pain, focal neurological disorders, eye lesions (visual disturbances, eye inflammation, retinal damage);

+ Subclinical: anti-*Toxocara* spp. IgG positive by ELISA test;

+ Additional 2 criteria to define Pawlowski's disease (2001): increased peripheral blood eosinophils and increased total IgE concentration [58].

***- Research location:*** Collecting medical records and examining and describing clinical characteristics at the Infection - Parasites clinic, Medic medical center Ho Chi Minh city (new name is Hoa Hao General Clinic of Hoa Hao Medical Company Limited).

***- Research period:*** From October 2017 to June 2019.

### 2.1.2. Researching methods

#### *2.1.2.1. Study designing*

The study was a cross-sectional descriptive study, analyzing all cases that met the sampling criteria.

***- Research sample size:*** Based on the formula for calculating sample size, a ratio is estimated:

$$n = \left( \frac{Z_{1-\frac{\alpha}{2}}}{m} \right)^2 p(1-p) \text{ [87]}$$

In which: n: minimal sample size; p: the proportion of patients who meet the criteria for disease selection, choose p = 18.7% (according to the results of the author's trial study in 2014 on a similar patient population) [88]; $Z_{1-\alpha/2}$: the confidence coefficient, with 95% confidence, then $Z_{1-\alpha/2} = 1.96$; m: desired relative error, selecting m = 0.07. With the selected values, the calculated sample size is 120 patients. In fact, the project has performed 120 patients.

***- Research content:***

+ Clinical features: Clinical assessment was performed on all subjects and asked for medical history, medical history, and physical examination at the time of study initiation according to case record forms (CRF).

• Skin and mucous membranes: pruritus, urticaria; red rash, streaks or streaks of skin; erythema in each area, each episode; subcutaneous larva migratory syndrome or crawling rash.

• Digestive: epigastric pain; digestive disorders; loss of appetite, nausea.

• Respiratory: persistent dry cough; chest pain; shortness of breath; wheeze.

• Vision: visual disturbances; muscle pain around the eyelids; bilingual.

• Nervous: headache; dizzy; sleep disorders.

+ Laboratory findings:

• Complete blood count: white blood cell count; number of eosinophils.

• Liver enzymes: AST, ALT, GGT.

• ELISA test for antibodies to *Toxocara* spp. IgG:

According to the kit manufacturer's recommendations, optical density OD > 0.35: positive. When OD ≤ 0.35: negative.

• Quantification of total IgE concentration in serum: total IgE concentration increases when ≥ 130 IU/mL as recommended by the company.

**2.2. Researching method of target 2:** *Evaluation of the treatment outcome and safety of thiabendazole for human toxocariasis*

**2.2.1. Researching objects, places and time**

***- Research subjects:*** The patient met the criteria for determining toxocariasis cases according to the definition issued by the Ministry of Health under Decision No. 4283/QD-BYT dated August 8, 2016 [16] with clinical features , subclinical and additional 2 criteria for case definition of Pawlowski (2001) in objective 1.

***- Research location:*** The Infection - Parasites clinic, Medic medical center Ho Chi Minh city.

***- Research period:*** From October 2017 to June 2019.

**2.2.2. Researching method**

***2.2.2.1. Study designing:*** Non-controlled clinical intervention study of thiabendazole (self-control before and after treatment).

***- Research sample size:***

According to the study of Ozimek *et al* (2015), the results of thiabendazole in the treatment of human toxocariasis showed a cure rate of 70.0% for visceral form and 80.0% for covert toxocariasis [82]. Therefore, in this study, we chose the estimated rate of treatment failure of thiabendazole as p = 25.0%, confidence level 95.0%, accuracy d = 10.0% to estimate size. Minimum sample according to the following table:

**Table 2.3. Minimum sample size based on treatment failure rate of thiabendazole**

| d | Estimated rate (p), 95.0% confidence level | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0.05 | 0.10 | 0.15 | 0.20 | **0.25** | 0.30 | 0.35 | 0.40 | 0.45 | 0.50 |
| 0.05 | 73 | 138 | 196 | 246 | 288 | 323 | 350 | 369 | 380 | 384 |
| **0.10** | 18 | 35 | 49 | 61 | **72** | 81 | 87 | 92 | 95 | 96 |

*(Source: Scientific research methods, Scientific links, 2015)*

Therefore, the minimum sample size that needs to be studied to evaluate the results of treatment with thiabendazole is n = 72 patients. To overcome the loss of samples and follow-up during the study, we added 10.0% of the cases, then the sample size needed for the study was 80 patients.

***- Research content:*** Treatment of human toxocariasis with thiabendazole, dose according to patient's weight and regimen according to FDA guidelines.

**Table 2.4. Dosage of thiabendazole used in the study** [14]

| Weight (kg) | Day 1 - 2 (or day 1 - 7) | | Notes |
|---|---|---|---|
| | Hour 0 | Hour 12 | |
| 13.6 - < 22.6 | 250mg | 250mg | - With cutaneous larva migrans is 2 days and visceral larva migrans is 7 days;<br>- If after 2 or 7 days of the end of the course, the assessment of the damage is still severe, an additional dose of 2 may be indicated;<br>- Do not use more than 3,000 mg/day. |
| 22.6 - < 34.0 | 500mg | 500mg | |
| 34.0 - < 45.0 | 750mg | 750mg | |
| 45.0 - < 56.7 | 1,000mg | 1,000mg | |
| 56.7 - < 68.0 | 1,250mg | 1,250mg | |
| ≥ 68.0 | 1,500mg | 1,500mg | |

+ Treatment results of the drug are evaluated based on clinical examination and tests at the time before and after treatment. In the thesis, clinical and subclinical evaluation at 3 time points after treatment is 1 month, 3 months and 6 months. All 3 follow-up visits include clinical examination and blood tests or imaging (depending on lesions). In addition, patients may be invited to return for a follow-up visit any day when symptoms are severe or a serious adverse drug event occurs.

+ In the case of adverse drug effects with mild to moderate severity, the patient is treated with antihistamines, if severe, the patient should be hospitalized.

+ At the time of re-examination for ocular, visceral (liver, lung, spleen) or neurological forms, repeat imaging (ultrasound, CT scan or MRI) is indicated to evaluate the response results. treatment response.

+ If the patient does not come for the follow-up appointment, the investigator must contact him by phone. In case of late re-examination, clinical and laboratory results are still assessed, still considered valid for up to 6 months. Conversely, within 6 months after treatment, patients who do not come to the clinic for follow-up are considered lost to follow-up.

+ Evaluate some possible undesirable effects after taking the drug in clinical terms: dizziness, headache, abdominal pain, nausea, digestive disorders, muscle pain, fever, itching, skin erythema,...

+ Evaluation of some possible undesirable effects after taking the drug on subclinical: white blood cells, red blood cells, haemoglobin, liver enzymes.

**2.3. Statistical methods and data analysis**

According to the biomedical statistical method, using the software SPSS 16.0. The results are presented in the form of tables and graphs.

Test the normal distribution of quantitative variables by Skewness index (deviation) and Kurtosis (hunchback). The proportions were compared using the $\chi^2$ test. Compare the mean values between two independent groups using the t-test. Comparison of rates between the two groups before and after treatment by McNemar test. Compare the mean values between the two paired groups using the paired t-test. Test the degree of reduction of eosinophils, total IgE concentration and optical density at the time points before and after treatment with Kaplan-Meier, log-rank test.

A value of $p < 0.05$ was considered to be statistically significant.

**2.4. Ethics in research**

- The research outline of the topic was approved by the ethics committee in biomedical research of the National Institute of Malaria - Parasites - Entomology.

- Subject's consent is obtained. Describe the rights and obligations of research participants, and responsibilities of researchers.

## Chapter 3: RESEARCHING RESULTS

**3.1. Describing the clinical and laboratory findings among patients with toxocariasis in Medic medical center, Ho Chi Minh city, Vietnam in 2017-2019.**

**3.1.1. Study patient characteristics**

During the study period from 2017 - 2019, we received 120 patients who met the selection criteria.

**Table 3.2. Mean age and distribution by age group (n = 120)**

| Age characteristics | | Number | Ratio (%) |
|---|---|---|---|
| Age group | < 20 | 13 | 10.8 |
| | 20 - 39 | 42 | 35.0 |
| | 40 - 59 | 49 | 40.9 |
| | ≥ 60 | 16 | 13.3 |

| | |
|---|---|
| Average age ($\bar{X}$ ± SD)<br>(min - max) | 41 ± 15<br>(14 - 70) |

**Remarks:** The age distribution was from 14 to 70 years old, the mean age was 41 ± 15 years old, of which the age group from 40 - 59 accounts for the highest proportion (40.9%), the age group under 20 accounts for the highest percentage. lowest (10.8%).

**Table 3.3. Proportion of patients by age and sex (n = 120)**

| Age group | Male (n, %) | Female (n, %) | p ($\chi^2$) |
|---|---|---|---|
| < 20 | 6 (46.2) | 7 (53.8) | 0.782 |
| 20 - 39 | 12 (28.6) | 30 (71.4) | 0.005 |
| 40 - 59 | 20 (40.8) | 29 (59.2) | 0.199 |
| ≥ 60 | 7 (43.8) | 9 (56.2) | 0.617 |
| **Total** | **45 (37.5)** | **75 (62.5)** | 0.006 |

**Remarks:** In the age group from 20 - 39, the rate of toxocariasis was higher in female than in male (71.4% versus 28.6%). The difference in disease prevalence by sex in this age group was significant (p = 0.005). Meanwhile, the difference in disease prevalence by sex in age groups < 20; 40 - 59 and ≥ 60 were not significant. Overall for all age groups, the distribution among females was higher than that of males (62.5% vs 37.5%, respectively female/male ratio 1.67), the difference was significant (p = 0.006).

**3.1.2. Clinical characteristics of the study population**

**Bảng 3.10. Phân bố lý do khám bệnh ở bệnh nhân nghiên cứu (n = 120)**

| Organisation involved | Number | Ratio (%) |
|---|---|---|
| Cutaneous manifestation | 93 | 77.5 |
| Neurologic disorders | 42 | 35.0 |
| Digestive disorders | 38 | 31.7 |
| Respiratory disorders | 26 | 21.7 |

**Remarks:** The highest rate of disease was manifested in the skin and mucous membranes (77.5%), followed by the nervous system (35.0%), the digestive system (31.7%) and the respiratory system (21.7%).

**Table 3.11. Symptoms on skin and mucous membranes (n = 120)**

| Symptoms/signs | Number | Ratio (%) |
|---|---|---|
| *Characteristics* | | |
| Chronic urticaria | 69 | 57.5 |
| Pruritus | 30 | 25.0 |
| Erythematous rash | 22 | 18.3 |
| Cutaneous larva migrans | 12 | 10.0 |

| *Nature of mucosal skin damage* | | |
|---|---|---|
| Often | 50 | 41.7 |
| Sometimes | 43 | 35.8 |

**Remarks:** Symptoms of urticaria accounted for the highest rate (57.5%), pruritus (25.0%), erythema in each area (18.3%) and signs of cutaneous larva migrans (10.0%). The rate of frequent occurrence is 41.7%, the rate of intermittent occurrence is 35.8%.

**Table 3.12. Nervous system symptoms (n = 120)**

| Symptoms/signs | Number | Ratio (%) |
|---|---|---|
| Headache | 32 | 26.7 |
| Dizziness | 20 | 16.7 |
| Sleep disorder | 11 | 9.2 |

**Remarks:** The most common symptom on the nervous system is headache (26.7%).

**Table 3.13. Symptoms on the digestive system (n = 120)**

| Symptoms/signs | Number | Ratio (%) |
|---|---|---|
| Abdominal pain | 28 | 23.3 |
| Loss of appetite | 20 | 16.7 |
| Diarrhoea | 18 | 15.0 |
| Liver involvement | 10 | 8.3 |

**Remarks:** The most common chronic abdominal pain accounted for 23.3%, anorexia, nausea 16.7%, digestive disorders 15.0% and liver damage 8.3%.

**Table 3.14. Symptoms on the respiratory system (n = 120)**

| Symptoms/signs | Number | Ratio (%) |
|---|---|---|
| Dry cough | 18 | 15.0 |
| Chest pain | 7 | 5.8 |
| Difficult breathing | 4 | 3.3 |
| Wheezing | 3 | 2.5 |

**Remarks:** The rate of dry cough accounted for 15.0%, chest pain 5.8%, shortness of breath 3.3% and wheezing 2.5%.

**3.1.3. Laboratory characteristics of the study population**

**Table 3.16. Peripheral blood eosinophil count (n = 120)**

| Eosinophils (cells/mm$^3$) | Number | Ratio (%) |
|---|---|---|
| Normal (< 500) | 0 | 0.0 |
| Slight increase (500 - < 1.500) | 110 | 91.7 |
| Average increase (1.500 - < 5.000) | 10 | 8.3 |

| | | |
|---|---|---|
| Marked increase (≥ 5.000) | 0 | 0.0 |
| Mean ($X$ ± SD) | 919 ± 491 | |
| Nhỏ nhất - lớn nhất | 518 - 3,350 | |

**Remarks:** All patients have elevated peripheral blood eosinophils. The percentage of mildly elevated eosinophils (500 - < 1,500 cells/mm$^3$) was 91.7%. The average rate of eosinophils (1,500 - < 5,000 cells/mm$^3$) was 8.3%. The mean peripheral blood eosinophil count was 919 ± 491 cells/mm$^3$.

**Table 3.17. Serum total IgE concentration (n = 120)**

| **Characteristics** | | **Number** | **Ratio (%)** |
|---|---|---|---|
| **Total IgE concentration (IU/mL)** | Normal (< 130) | 0 | 0.0 |
| | Increase < 4 times (130 - < 520) | 52 | 43.3 |
| | Increase ≥ 4 times (≥ 520) | 68 | 56.7 |
| Mean ($X$ ± SD) | | 764.7 ± 630.6 | |
| Min - Max | | 135 - 3,000 | |

**Remarks:** Total IgE concentrations were increased above the normal limit, in that IgE increased to less than 4 times the normal limit of 43.3%, IgE increased above 4 times the normal limit of 56.7%. The average IgE concentration was 764.7 ± 630.6 IU/mL, the distribution range of values was from 135 - 3,000 IU/mL.

**Table 3.18. Optical density of anti-*Toxocara* spp. IgG (n = 120)**

| **Anti-*Toxocara* spp. IgG (OD)** | **Number** | **Ratio (%)** |
|---|---|---|
| 0,35 - < 1,0 | 41 | 34.2 |
| 1,0 - < 2,0 | 48 | 40.0 |
| ≥ 2,0 | 31 | 25.8 |
| Mean ($X$ ± SD) | 1.51 ± 0.85 | |
| Min - Max | 0.36 - 3.50 | |

**Remarks:** The average optical density (OD) of IgG by ELISA test was 1.51 ± 0.85, the distribution of IgG values was from 0.36 to 3.50. The optical density of the 3 groups were respectively: OD group from 0.35 - < 1.0 accounted for 34.2%, OD group from 1.0 - < 2.0 accounted for 40.0% and OD group ≥ 2.0 accounted for 25.8%.

**3.2. Evaluation of the treatment outcome and safety of thiabendazole for human toxocariasis**

**Table 3.22. Demographic and clinical characteristics of the patients (n = 80)**

| Symptoms/signs | | Number | Ratio (%) |
|---|---|---|---|
| Age (year) | Mean ± SD | 41.6 ± 15.2 | |
| Gender | Male | 33 | 41.2 |
| | Female | 47 | 58.8 |
| BMI (kg/m$^2$) | Mean ± SD | 22.2 ± 3.0 | |
| *Cutaneous manifestation* | | *65* | *81.3* |
| | Chronic urticaria | 47 | 58.8 |
| | Pruritus | 21 | 26.3 |
| | Erythematous rash | 15 | 18.8 |
| | Cutaneous larva migrans | 11 | 13.8 |
| *Neurologic disorders* | | *24* | *30.0* |
| | Headache | 18 | 22.5 |
| | Dizziness | 11 | 13.8 |
| | Sleep disorders | 8 | 10.0 |
| *Digestive disorders* | | *24* | *30.0* |
| | Abdominal pain | 20 | 25.0 |
| | Loss of appetite | 14 | 17.5 |
| | Diarrhoea | 10 | 12.5 |
| | Liver involvement | 7 | 8.8 |
| *Respiratory disorders* | | *17* | *21.3* |
| | Dry cough | 13 | 16.3 |
| | Chest pain | 6 | 7.5 |
| | Difficult breathing | 4 | 5.0 |
| | Wheezing | 3 | 3.8 |
| *Clinical form* | | | |
| | Common toxocariasis | 73 | 91.3 |
| | Visceral larva migrans | 7 | 8.7 |
| *Thiabendazole regimen* | | | |
| | 2 days | 73 | 91.3 |
| | 7 days | 7 | 8.7 |

**Remarks:** The mean age of the intervention group was 41.6 ± 15.2 years old. The female sex ratio is higher (female/male = 1.4). Common symptoms were

in the skin and mucous membranes, accounting for 81.3%, followed by the nervous system 30.0%, the digestive system 30.0% and the respiratory system 21.3%. The clinical form included the common toxocariasis in 73 patients (91.3%) and the visceral larva migrans in 7 patients (8.7%). The treatment regimen with thiabendazole according to clinical form, respectively, included a 2-day regimen (91.3%) and a 7-day regimen (8.7%).

### 3.2.1. Treatment outcome of chemotherapy with thiabendazole

**Table 3.32. Results of clinical and subclinical treatment after 1 month (n = 80)**

| Clinical and subclinical symptoms | Criteria | Number | Ratio (%) |
|---|---|---|---|
| Cutaneous manifestation | Cured | 23 | 35.4 |
| | Improved | 42 | 64.6 |
| Digestive disorders | Cured | 6 | 25.0 |
| | Improved | 18 | 75.0 |
| Neurologic disorders | Cured | 6 | 25.0 |
| | Improved | 18 | 75.0 |
| Respiratory disorders | Cured | 9 | 52.9 |
| | Improved | 8 | 47.1 |
| Eosinophil count | Normalisation | 43 | 53.8 |
| | Raised | 37 | 46.2 |
| Total IgE concentration | Normalisation | 9 | 11.2 |
| | Raised | 71 | 88.8 |
| Anti-*Toxocara* spp. IgG (OD) | Negative | 5 | 6.3 |
| | Positive and ≥ 30% off | 16 | 20.0 |
| | Positive and < 30% off | 30 | 37.5 |
| | No decrease or increase | 29 | 36.2 |

**Remarks:** After 1 month of treatment, clinically, symptoms on skin and mucosal lesions disappeared from 35.4%, remaining 64.6%. Gastrointestinal and neurological symptoms disappeared from 25.0% to 75.0%. The symptoms on the respiratory tract improved by 52.9%, remaining 47.1%. On clinical examination, normal eosinophils (< 500 cells/$mm^3$) were 53.8%, eosinophils increased 46.2%. Total IgE concentration in serum was normalized at 11.2%, IgE increased by 88.8%. The optical density of IgG after 1 month of treatment, the negative rate was 6.3%, it was still positive but 30% OD reduction compared to before treatment was 20.0%, the optical density decreased < 30% OD compared to before treatment was 37.5% and optical density did not decrease or increase compared to before treatment was 36.2%.

**Table 3.42. Results of clinical and subclinical treatment after 3 months (n = 80)**

| Clinical and subclinical symptoms | Criteria | Number | Ratio (%) |
|---|---|---|---|
| Cutaneous manifestation | Cured | 49 | 75.4 |
| | Improved | 16 | 24.6 |
| Digestive disorders | Cured | 18 | 75.0 |
| | Improved | 6 | 25.0 |
| Neurologic disorders | Cured | 15 | 62.5 |
| | Improved | 9 | 37.5 |
| Respiratory disorders | Cured | 15 | 88.2 |
| | Improved | 2 | 11.8 |
| Eosinophil count | Normalisation | 64 | 80.0 |
| | Raised | 16 | 20.0 |
| Total IgE concentration | Normalisation | 23 | 28.8 |
| | Raised | 57 | 71.2 |
| Anti-*Toxocara* spp. IgG (OD) | Negative | 7 | 8.8 |
| | Positive and ≥ 30% off | 35 | 43.7 |
| | Positive and < 30% off | 22 | 27.5 |
| | No decrease or increase | 16 | 20.0 |

**Remarks:** After 3 months of treatment, the symptoms on skin and mucosal lesions disappeared from 75.4%, remaining 24.6%. Gastrointestinal symptoms disappeared from 75.0%, remaining 25.0%. Neurological symptoms recovered from 62.5%, remaining 37.5%. Respiratory symptoms have recovered from 88.2%, remaining 11.8%. On clinical examination, the rate of eosinophils returned to normal (< 500 cells/$mm^3$) was 80.0%, the rate of eosinophils increased by 20.0%. Total IgE concentration was 28.8% normal, IgE increased by 71.2%. The optical density of IgG by ELISA test after 3 months of treatment was negative, the rate was 8.8%, it was still positive but decreased ≥ 30% OD compared to before treatment was 43.7%, optical density decreased < 30 % OD compared to before treatment was 27.5% and optical density did not decrease or increase compared to before treatment was 20.0%.

**Table 3.51. Results of clinical and subclinical treatment after 6 months (n = 80)**

| Clinical and subclinical symptoms | Criteria | Number | Ratio (%) |
|---|---|---|---|
| Cutaneous manifestation | Cured | 60 | 92.3 |
| | Improved | 5 | 7.7 |

| | | | |
|---|---|---|---|
| Digestive disorders | Cured | 21 | 87.5 |
| | Improved | 3 | 12.5 |
| Neurologic disorders | Cured | 22 | 91.7 |
| | Improved | 2 | 8.3 |
| Respiratory disorders | Cured | 16 | 94.1 |
| | Improved | 1 | 5.9 |
| Eosinophil count | Normalisation | 75 | 93.8 |
| | Raised | 5 | 6.2 |
| Total IgE concentration | Normalisation | 52 | 65.0 |
| | Raised | 28 | 35.0 |
| Anti-*Toxocara* spp. IgG (OD) | Negative | 9 | 11.3 |
| | Positive and ≥ 30% off | 46 | 57.5 |
| | Positive and < 30% off | 22 | 27.5 |
| | No decrease or increase | 3 | 3.7 |

**Remarks:** After 6 months of treatment, the symptoms on skin and mucosal lesions disappeared from 92.3%, remaining 7.7%. Gastrointestinal symptoms recovered from 87.5%, remaining 12.5%. Neurological symptoms recovered 91.7%, remaining 9.3%. Respiratory symptoms were cured in 94.1%, remaining 5.9%. On subclinical, eosinophils were 93.8% normal, eosinophils increased 6.2%. Total IgE concentration was 65.0% to normal, IgE increased by 35.0%. The optical density of 6 months after treatment is negative rate is 11.3%, still positive but 30% OD reduction compared to before treatment is 57.5%, optical density decreases < 30% OD compared to before treatment was 27.5% and optical density did not decrease or increase compared to before treatment was 3.7%.

**Table 3.52. Overall results of treatment (n = 80)**

| **Results** | **1 month after therapy** | | **3 months after therapy** | | **6 months after Therapy** | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Cured | 25 | 31.2 | 63 | 78.8 | 69 | 86.3 |
| Improved | 53 | 66.3 | 16 | 20.0 | 8 | 10.0 |
| Unchanged | 2 | 2.5 | 1 | 1.2 | 3 | 3.7 |
| p | < 0.001*, 0.139† | | | | | |

*: Significant (p < 0.05) between 1 and 3 months, 1 and 6 months; †: Comparison between 3 and 6 months.

**Remarks:** The final treatment results at 6 months showed that the cure rate was 86.3%, the disease reduction was 10.0% and no cure rate was 3.7%.

**3.2.2. Evaluation of the safety of thiabendazole treatment in human toxocariasis**

**Table 3.53. Liver enzyme index before and after 6 months of treatment (n = 80)**

| AST (U/L) | Initial diagnosis | 1 month after therapy | 3 months after therapy | 6 months after therapy |
|---|---|---|---|---|
| Normal | 54 (67.5%) | 52 (65%) | 62 (77.5%) | 62 (77.5%)aaa, bb |
| Increase | 26 (32.5%) | 28 (35.0) | 18 (22.5%) | 18 (22.5%) |
| Mean | 27.6 ± 9.1 | 28.5 ± 11.2 | 26.6 ± 7.4 | 26.0 ± 8.0[b] |
| **ALT (U/L)** | **Initial diagnosis** | **1 month after therapy** | **3 months after therapy** | **6 months after therapy** |
| Normal | 53 (66.2%) | 50 (62.5%) | 55 (68.8%) | 65 (81.3%)aaa, bbb, ccc |
| Increase | 27 (33.8%) | 30 (37.5%) | 25 (31.2%) | 15 (18.7%) |
| Mean | 27.7 ± 16.0 | 31.6 ± 26.0 | 28.2 ± 16.7 | 22.0 ± 11.2aaa, bbb, ccc |
| **GGT (U/L)** | **Initial diagnosis** | **1 month after therapy** | **3 month after therapy** | **6 months after therapy** |
| Normal | 50 (62.5%) | 46 (57.5%) | 51 (63.7%) | 54 (67.5%)bbb |
| Increase | 30 (37.5%) | 34 (42.5%) | 29 (36.3%) | 26 (32.5%) |
| Mean | 50.4 ± 54.2 | 50.5 ± 46.2 | 48.3 ± 51.0 | 42.7 ± 44.9[a, b, c] |

a: compared with initiation of treatment, b: compared with 1 month after treatment, c: compared with 3 months after treatment. Number of characters representing significance level: a: < 0,05; aa: < 0,01, aaa: <0,001.

**Remarks:** The rate of AST within the normal range after 6 months of treatment was 77.5%, the rate of AST increased was 22.5%, the difference in rates was significant compared to before treatment ($p < 0.001$). The mean value of AST after 6 months of treatment was 26.0 ± 8.0 U/L, not significantly different from before treatment. The rate of ALT within the normal range after 6 months of treatment was 81.3%, the rate of ALT increase after 6 months of treatment was 18.7%, the difference in rates was significant compared to before treatment ( $p < 0.001$). Average value of ALT after 6 months of treatment was 22.0 ± 11.2 U/L, significantly different from the mean value of ALT before treatment ($p < 0.001$). The rate of GGT within the normal range after 6 months of treatment was 67.5%, the rate of GGT increase after 6 months of treatment was 32.5%, the difference in rates was not significant compared to before treatment . The mean value of GGT

after 6 months of treatment was 42.7 ± 44.9 U/L, significantly different from before treatment ($p < 0.05$).

**Table 3.54. Haematological index before and after 6 months of treatment (n = 80)**

| **White blood cells (cells/mm$^3$)** | **Initial diagnosis** | **1 month after therapy** | **3 months after therapy** | **6 months after therapy** |
|---|---|---|---|---|
| Normal (n, %) | 63 (78.8) | 72 (90.0) | 74 (92.5) | 77 (96.2)$^{a,}$ $^{bb}$ |
| Increase (n, %) | 17 (21.2) | 8 (10.0) | 6 (7.5) | 3 (3.8) |
| Mean | 8,297 ± 2,117 | 7,993 ± 1,587 | 7,655 ± 1,406 | 7,738 ± 1,267$^{a}$ |
| **Red blood cells (x 10$^6$ cells/mm$^3$)** | **Initial diagnosis** | **1 month after therapy** | **3 months after therapy** | **6 months after therapy** |
| Normal (n, %) | 80 (100) | 80 (100) | 80 (100) | 80 (100) |
| Reduction (n, %) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Mean | 4.88 ± 0.53 | 4.77 ± 0.67 | 4.69 ± 0.82 | 4.83 ± 0.48 |
| **Haemoglobin (g/dL)** | **Initial diagnosis** | **1 month after therapy** | **3 months after therapy** | **6 months after therapy** |
| Normal (n, %) | 78 (97.5) | 76 (95.0) | 76 (95.0) | 79 (98.8) |
| Reduction (n, %) | 2 (2.5) | 4 (5.0) | 4 (5.0) | 1 (1.2) |
| Mean | 14.2 ± 1.4 | 14.2 ± 1.5 | 14.1 ± 1.3 | 14.2 ± 1.3 |

a: compared with initiation of treatment, b: compared with 1 month after treatment, c: compared with 3 months after treatment. Number of characters representing significance level: a: < 0,05; aa: < 0,01, aaa: <0,001.

**Remarks:** The rate of white blood cell count within the normal range after 6 months of treatment was 96.2%, significantly different from before treatment and 1 month after treatment ($p < 0.05$). The average white blood cell count after 6 months of treatment was 7,738 ± 1,267 cells/mm$^3$, significantly different from before treatment, but not significant compared with the time after treatment 1 month and 3 months. All 80 treated patients had red blood cell counts within normal limits and did not decrease during treatment. The average number of red blood cells after 6 months of treatment was 4.83 ± 0.48 x 10$^6$ cells/mm$^3$, not significantly different from the time before treatment, after 1 and 3 months of treatment. The percentage of normal haemoglobin after 6 months of treatment was 98.8%, not significantly different from the time of previous treatment. The average haemoglobin concentration 6 months after treatment was 14.2 ± 1.3 g/dL, not different from before treatment and 1.3 months after treatment.

**Table 3.55. Symptoms due to possible side effects of thiabendazole (n = 80)**

| Symptoms | Number | Ratio (%) | Duration of symptoms |
|---|---|---|---|
| Dizziness/headache | 15 | 18.8 | D1 - D7 |
| Abdominal pain, nausea | 5 | 6.3 | D1 - D2 |
| Diarrhoea | 4 | 5.0 | D1 - D2 |
| Itching, rash | 3 | 3.7 | D1 - D2 |
| No side effect | 53 | 66.2 | |

**Remarks:** Regarding the possible undesirable effects of thiabendazole on the study sample, the rate of unwanted effects may be 33.8%, in which dizziness and/or headache 18.8%, abdominal pain, nausea 6.3%, diarhoea 5.0% and itching, rash when using the drug was 3.7%. The rate of no unwanted effects could be 66.2%.

## Chapter 4: DISCUSSION

### 4.1. Describing the clinical and laboratory findings among patients with toxocariasis in Medic medical center, Ho Chi Minh city, Vietnam in 2017 - 2019.

**- Some clinical features**

The most common symptoms in patients with toxocariasis were cutaneous manifestations (77.5%), followed by neurological manifestations (35.0%), gastrointestinal (35.0%) and gastrointestinal symptoms (31.7%) and respiratory (21.7%) (table 3.10). Manifestations of the disease are quite diverse, but the most common symptoms are damage to the digestive organs (especially the liver), respiratory, nerve, eye, allergic or systemic manifestations (fever, fatigue,…). It was because of the diverse and non-specific manifestations of the disease that studies have shown very different rates of clinical manifestations. Nguyen Van De et al (2014) studied on 108 patients infected with *Toxocara* spp. had clinical manifestations at some hospitals in Hanoi, experiencing symptoms of pruritus, urticaria (57.4%), fever for more than 1 week (56.5%), headache (53.7%). pneumonia - bronchiolitis (50.0%), fatigue (47.2%), anorexia (38.9%), convulsions - epilepsy (32.4%), digestive disorders (20.4%), enlarged liver (13.9%), eye symptoms (10.2%), splenomegaly (7.4%), in addition to bleeding, thrombocytopenia, edema [113]. Nguyen Van Chuong et al (2014) studied in the central - central highlands on 102 patients who experienced symptoms of itching, rash, erythema with the highest rate (66.67%), followed by abdominal pain (epigastric, liver, pain around umbilicus) accounted for 50.98%, headache, dizziness, blurred vision accounted for 40.2%, generalized muscle pain (36.3%), asthenia, fatigue accounted for 35, 3%, signs of larvae moving/scraping under the skin 12.7%, digestive disorders 11.76%, fever with muscle pain 11.76%, sleep

disturbances 6.86%, some symptoms uncommon symptoms such as unexplained fever, muscle cramps, sensory disturbances... [8]. A study by Le Thi Cam Ly et al (2015) on 190 patients examined at the Hospital for Tropical Diseases in Ho Chi Minh City found that the rate of symptoms of itching was 83.11%, headache 38.0%, fatigue, anorexia, abdominal pain 30.0%, urticaria 9.0%, subcutaneous inflammation 5.19% [101].

**- Some paraclinical features**

***+ Characteristics of the number and percentage of eosinophils in the peripheral blood***

Most patients (91.7%) had a mildly elevated eosinophils count (500 - < 1,500 cells/$mm^3$). The average rate of increased eosinophils count (1,500 - < 5,000 cells/$mm^3$) was 8.3%. The average number of eosinophils in peripheral blood was 919 ± 491 cells/$mm^3$, the distribution range was from 518 to 3,350 cells/$mm^3$ (table 3.16). The research results in the thesis are consistent with a number of studies in Vietnam and around the world. The level of eosinophils elevation in some patients with toxocariasis can be very high, up to 15,000 - 100,000 cells/$mm^3$ [139]. However, the majority of studies showed a moderate elevation of eosinophils in patients with toxocariasis, possibly because the majority of patients in these studies were mild infections while the number of severe infections is rare.

***+ Characterization of total IgE serum concentration***

In the study sample, the total serum IgE concentration increased, the average IgE concentration was 764.7 ± 630.6 IU/mL, distributed from 135 - 3,000 IU/mL, in which, IgE increased less than 4 times the limit of normal (130 - < 520 IU/mL) was 43.3%, which is more than 4 times the limit of normal (≥ 520 IU/mL) was 56.7% (table 3.17). This result was consistent with a number of other studies in Vietnam showing an increase in IgE in patients infected with *Toxocara* spp. Nguyen Tan Vinh et al. found that children infected with *Toxocara* spp. had an increased rate of total IgE concentration 2.45 times higher than that of uninfected children (with p = 0.001) [91]. Research by Do Nhu Binh et al on 17 patients with *Toxocara* spp. found that 14/17 patients had elevated total IgE [136]. Glickman et al. found that the average IgE concentration of 37 patients with "common toxocariasis" was 851 IU/mL, with 81.1% increase in total IgE, and 67.6% increase in specific IgE [45].

***+ Characterization of IgG optical density by ELISA test***

In the study sample, the average optical density (OD) was 1.51 ± 0.85, the value distribution was from 0.36 to 3.50. The optical density of the group from 0.35 - < 1.0 accounted for 34.2%, the group from 1.0 - < 2.0 accounted for 40.0% and the group ≥ 2.0 accounted for 25.8% (table 3.18). The results showed that most of the patients participating in the study had a low increase in antibody titers, and the group with high antibody titres (OD ≥ 2.0) only accounted for 25.8%. This result was slightly different from the study of Do Thi Phuong Linh et al. (2013), found most patients have high antibody titres [135]. The study of Phan Thi Nha Truc et al (2020) in Dak Lak found that the most common rate (70.1%) was in patients with high IgG titres (OD ≥ 2.0), optical density values had significant differences related to the number of symptoms, the higher the optical density (p = 0.021), optical

density was also related to the occurrence of some symptoms such as pruritus, chronic urticaria, cough anhydrous [98]. Some other studies in Vietnam showed that the titer of IgG antibodies against *Toxocara* spp. at a relatively low level. Nguyen Van Chuong et al (2014) studied in the central - central highlands showed that most (60.78%) had a low optical density ratio (patient OD/threshold OD) (1 - 1.2). [8]. Research by Do Nhu Binh et al. found that the average optical density was 1.2; 75.7% have optical density from 0.3 - 1.5, similar to the results of this thesis [136].

**4.2. Evaluation of the treatment outcome and safety of thiabendazole for human toxocariasis**

**- Evaluation of the treatment outcome of thiabendazole for human toxocariasis**

***+ Evaluation results after 1 month***

After 1 month of treatment, the rate of some symptoms decreased significantly compared to the time before treatment such as itching, urticaria (58.8%, reduced to 26.3%, $p < 0.001$), signs and symptoms appeared frequently (42.5% before treatment, reduced to 22.5%, $p < 0.001$), gastrointestinal symptoms such as abdominal pain (25.0% before treatment, reduced to 13.8%, $p = 0.004$), anorexia, nausea (before treatment 17.5%, after treatment reduced to 7.5%, $p = 0.008$), digestive disorders (before treatment 15.0%, reduced to 5.0%, $p = 0.008$), headache (before treatment 22.5%, reduced to 15.0%, $p = 0.031$), persistent dry cough (before treatment 16.2%, after treatment 1 month to 6.3%, significant difference with $p = 0.008$).

Regarding clinical examination, after 1 month of treatment, the average number of eosinophils decreased significantly compared to before treatment. In 53.8% of patients, the eosinophil rate returned to the normal limit, there were no more cases of moderate eosinophil increase. The average IgE concentration after 1 month of treatment decreased significantly compared to before treatment. There are 11.3% of IgE patients within the normal limit. The mean OD value of the IgG ELISA test after 1 month of treatment was $1.19 \pm 0.85$, significantly reduced compared to before treatment ($1.35 \pm 0.89$, $p = 0.039$). Only 6.3% of patients had a negative IgG ELISA test. The results of the thesis show that the paraclinical parameters have improved after treatment. The mean values of eosinophils, total IgE and IgG all decreased significantly at 1 month after treatment. However, in terms of normalization rates, there was a clear difference. The rate of eosinophil returning to normal (53.8%) was the highest, followed by the rate of IgE to normal level (11.3%), the rate of IgG negative was very low (6.3%). The results of the thesis are consistent with some other studies. Huynh Hong Quang et al (2019) studied to evaluate the efficacy and safety of thiabendazole in the treatment of parasitic larva migratory syndrome in humans. After 2 months, the rate of normal eosinophil was 93.9%, the rate of negative IgG test is 19.85% [174]. Nguyen Van Chuong et al (2014) found that the rate of increase in eosinophil after 1 month was 51.72% [8]. Magnaval (1995) found that at 1 month after specific treatment, the number of eosinophil decreased markedly while total IgE and specific IgE levels

decreased significantly compared to before treatment, Western blot test (detection of specific IgG) found that 6/80 (7.5%) patients were negative [76].

***+ Evaluation results after 3 months***

After 3 months of treatment, most symptoms were significantly reduced, except for sleep disorders. Some symptoms go away completely, such as chest pain, shortness of breath, and wheezing. The research results of the thesis were consistent with the research of some other authors showing that most of the clinical symptoms were significantly reduced 3 months after specific treatment. The study by Wiśniewska-Ligier et al (2012) found that after 3 months of treatment, the rate of abdominal pain decreased significantly (23.9% to 8.7%), enlarged lymph nodes (28.3% to 8.7%) [71].

Regarding clinical examination, the parameters continued to decrease compared to before treatment. Normal eosinophil rate was 80.0%, eosinophil rate also increased by 20.0%. The average number of eosinophils after 3 months of treatment was 372 ± 245 cells/$mm^3$. Total serum IgE concentration was 28.7% normal, IgE still increased 71.3%, the value of serum IgE concentration distributed in the range of 55.0 - 2,560 IU/mL, average 416.0 ± 469.7 IU/mL. IgG ELISA test after 3 months of treatment, the negative rate was 8.8%, still positive but decreased by 30.0% OD compared to before treatment was 43.7%, optical density decreased < 30.0% OD compared to before treatment was 27.5% and optical density did not decrease or increase compared to before treatment was 20.0%. The research results of the thesis showed that eosinophils decreased faster than total IgE concentration. Most patients had eosinophil values in the normal range (80.0%), while this rate for IgE was 28.7%, for IgG was 8.8%.

***+ Evaluate results after 6 months***

After 6 months of treatment, all symptoms decreased significantly compared to before treatment. The results of the thesis are consistent with some other studies, after 6 months most of the clinical symptoms have decreased in frequency or gone. Huynh Hong Quang et al (2019) evaluated the efficacy and safety of thiabendazole in the treatment of parasitic larva migratory syndrome and found a clinical improvement after 6 months of 93.0% [174]. Nguyen Van Chuong et al (2014) treated in the central - central highlands with albendazole, the rate of remaining symptoms after 6 months was 17.07% [8].

Regarding clinical examination, 93.8% had normal eosinophils, only 6.2% increased. Total IgE concentration to normal is 65.0%, IgE increased by 35.0%. There were 11.3% negative IgG ELISA tests but most of the optical density was reduced. The study results showed that eosinophils returned to normal in most patients 6 months after treatment. Total IgE levels also returned to normal in most cases, but only a small percentage had anti-*Toxocara* spp. IgG ELISA negative. The results of some studies also showed a high rate of eosinophils returning to normal 6 months after treatment, such as 87.09% [8], 97.6% [174].

The percentage of patients who tested positive for IgG ELISA remained high (87.8%) although most of the optical density values had decreased. The rate of negative IgG ELISA tests in the thesis was lower than the results of some studies in

Vietnam. However, the post-treatment test results in the thesis are consistent with a number of studies around the world showing that in the test indicators including BCAT, the fastest rate of decrease, then IgE, while IgG decreased slow.

***+ Final treatment results***

The final treatment results at 6 months after treatment showed that the cure rate was 86.3%, the disease reduction was 10.0% and no cure rate was 3.7%. Some studies in Vietnam also show high results of thiabendazole in the treatment of human toxocariasis. Nguyen Van Chuong et al (2013) found thiabendazole to be highly effective in typical subcutaneous larval disease with a cure rate of 96.5% [73]. Huynh Hong Quang et al (2019) studied to evaluate the results and safety of thiabendazole in the treatment of parasitic larva migratory syndrome. Clinical improvement after 2 months was 87.2%, after 6 months. is 93.0% [174]. Compared with the efficacy of albendazole, the cure rates for thiabendazole in several studies were similar. Stürchler (1989) compared the efficacy of albendazole and thiabendazole and found the two drugs to be equally effective [74]. Nguyen Thi Hong The et al (2004) used albendazole for children, the good response rate was 94.5% [103]. Nguyen Van Chuong et al (2014) treated in the central - central highlands with albendazole, the rate of clinical symptoms after 1 month was 78.16%, after 3 months was 57.14%, after 6 months was 17.07% [8]. Hombu found that the effectiveness of long-term albendazole was only 78.0% [13].

**- Evaluation of the safety of thiabendazole for human toxocariasis**

***+ Rate of occurrence of unwanted effects***

Research results showed that 33.8% of patients had unwanted effects. This rate was quite high and consistent with the comments of some authors, the side effects after taking thiabendazole are often high [177]. Thiabendazole is considered a drug with a high rate of undesirable effects, but this rate is very different in the publications. There are studies that show this rate to be quite high, but there are also studies that show it to be low. Stürchler (1987) studied thiabendazole in the treatment of toxocariasis in dogs and cats and found the rate of undesirable effects was 60.0% [74]. Bisoffi et al (2011) studied that the rate of undesirable effects of thiabendazole for strongyloidiasis treatment was 73.1% [178]. Rafael Igual-Adell et al. (2004) reported that the rate of undesirable effects of thiabendazole was quite low (16.0%) [179]. In Vietnam, there is a study showing that the rate of unwanted effects of thiabendazole is also quite low [174].

***+ Manifestations of undesirable effects***

The most common undesirable effects detected in patients were dizziness and/or headache 18.8%, in addition, abdominal pain, nausea 6.3%, diarrhoea 5.0% and itching, rash when taking the drug was 3.7%. No serious adverse events were reported during treatment and all patients completed the treatment regimen. This result is consistent with some other studies showing that the undesirable effects are usually related to the nervous, digestive, and skin. In the study of Huynh Hong Quang et al (2019), undesirable effects when taking thiabendazole were headache (2.3%), nausea (2.3%), loss of appetite, mild abdominal pain (1,2%), pruritus, urticaria (1.2%); 1 patient vomited after taking the drug [174]. Adenusi et al (2003)

found that the common undesirable effects of thiabendazole were dizziness (53.21%), fatigue (49.54%), nausea (44.95%), loss of appetite (34.78%), disorientation (14.68%), headache (6.42%), abdominal pain (5.5%) [181].

***+ Changes in liver enzymes***

The results of evaluating liver enzyme changes over time in the thesis showed that at the time of evaluation (1, 3 and 6 months after treatment), the rate of increase in AST, ALT and average values did not change, except at 6 months post-treatment. The rate of ALT within the normal range after 6 months of treatment was 82.4% (increased compared to before treatment, 66.2%, $p = 0.002$); The mean value of ALT after 6 months of treatment was 22.04 ± 11.22 U/L, significantly different from the mean value of ALT before treatment. The increased prevalence of ALT within the normal range may be related to the recovery of liver damage. This result is consistent with Huynh Hong Quang et al. (2019) found that haemoglobin, haematocrit, white blood cell, ALT, AST did not differ between before and 2 months, 6 months after treatment [174].

***+ Changes in hematological indices***

The results of the thesis showed that the rate of white blood cell count within the normal range after 6 months of treatment was 96.2%, significantly different from before treatment and 1 month after treatment ($p < 0.05$). This result suggests that the leukocyte is responsive to thiabendazole regimen, however, this response is not as strong as that observed in eosinophils. In the manufacturer's recommendations, thiabendazole mentioned transient leukopenia (transient leukopenia) after treatment, however, in our study, we did not encounter any patient with this undesirable effect. Meanwhile, Zubair et al (2013) observed that people infected with *Toxocara* spp. in India had lower average haemoglobin than those who were not infected, from which the author hypothesized that the disease was related to the condition anemia [194]. The results of the thesis showed that all 80 treated patients had red blood cell counts within normal limits and did not decrease during the course of treatment. The average number of red blood cells after 6 months of treatment was $4.83 \pm 0.48 \times 10^6$ cells/mm$^3$, not significantly different from the time before treatment, after 1 and 3 months of treatment. The percentage of haemoglobin in the normal range after 6 months of treatment was 98.8%, not significantly different from the previous treatment time. The average haemoglobin concentration at 6 months after treatment was 14.2 ± 1.3 g/dL, not different from before treatment and at 1; 3 months after treatment. These results show that thiabendazole does not cause undesirable effects of anemia in patients.

## CONCLUSION

**1. Describing the clinical and laboratory findings among patients with toxocariasis in Medic medical center, Ho Chi Minh city, Vietnam in 2017 - 2019.**

***1.1. Clinical features (n = 120)***

- The mean age was 41 ± 15 years old, the age group 20 - 59 years old accounts for 75.9%. The female/male distribution ratio was 1.67.

- The most common symptoms were in the cutaneous manifestations (77.5%), followed by neurological manifestations (35.0%), digestive (31.7%) and respiratory (21.7%).
- The cutaneous include urticaria (57.5%), pruritus (25.0%), erythema in each area (18.3%), cutaneous larva migrans (10.0 %).
- Manifestations on the nervous system included headache 26.7%, dizziness 16.7% and sleep disorders 9.2%.
- Chronic abdominal pain was the most common symptom in the group of gastrointestinal manifestations (23.3%), in addition to anorexia, nausea 16.7%, digestive disorders 15.0%, lesions liver on imaging 8.3%.
- Respiratory manifestations included dry cough 15.0%, chest pain 5.8%, dyspnea 3.3% and wheezing 2.5%.

***1.2. Laboratory characteristics (n = 120)***

- All patients had an increase in the number of eosinophils in the peripheral blood, but 91.7% had a mild increase (from 500 - < 1,500 cells/$mm^3$).
- The mean total serum IgE concentration was 764.7 ± 630.6 IU/mL, 43.3% of patients had IgE increase less than 4 times the normal limit.
- The mean optical density of anti-*Toxocara* spp. IgG was 1.51 ± 0.85, value distribution from 0.36 to 3.50.

**2. Evaluation of the treatment outcome and safety of thiabendazole for human toxocariasis**

***2.1. Results of thiabendazole in treatment (n = 80)***

- After 1 month of treatment, the cure rate was 31.2%, disease reduction was 66.3% and no cure rate was 2.5%.
- After 3 months of treatment, the cure rate was 78.8%, the disease reduction was 20.0% and the cure rate was 1.2%.
- After 6 months of treatment, the cure rate was 86.3%, the disease reduction was 10.0% and the cure rate was 3.7%.

***2.2. Safety of thiabendazole in treatment (n = 80)***

- Manifestations of undesirable effects of thiabendazole drug appeared in 33.8% of patients, including dizziness and/or headache 18.8%, abdominal pain, nausea 6.3%, diarrhoea 5.0% and pruritus, rash 3.7%. There were no serious adverse events, in no case stopping the study.
- Liver enzyme values did not increase at time 1; 3 and 6 months after treatment. - Thiabendazole treatment regimen did not cause undesirable effects of general leukopenia or anemia in this group of patients.

## SCIENTIFICNESS AND NOVELTY OF TOPIC

The study has a scientific theoretical basis and empirical evidence on patients who come to the Medic center, a medical facility in the south of Vietnam with a large number of patients infected with *Toxocara* spp. visit and receive treatment every day. The staff is professionally trained and the facilities are modern, fully satisfying in the implementation of the project;

The topic was reviewed, edited, supplemented by the National Institute of Malaria, Parasitology and Entomology by the Science and Biomedical Ethics Committee of the National Institute of Malaria, Parasitology, and Entomology. Under the guidance of the teachers, scientists inside and outside the Institute have experience and reputation as a reliable basis for feasibility in implementation;

Study on results of thiabendazole regimen in the treatment of patients infected with *Toxocara* spp. and evaluate the unwanted effects, the safety of the drug. The new point of the study is to find an effective, short-term regimen with few unwanted effects in the treatment of toxocariasis in dogs and cats, increasing the choice of drugs for clinical treatment.