STRONGYLOIDIASIS TREATMENT

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Ivermectin (200 µg/kg daily) is the cornerstone of treatment; a 2-day dose has been shown to cure 93% of patients

For disseminated strongyloidiasis, daily ivermectin for 14 (or more) days is the standard treatment. In those unable to take oral medication, there are rectal and injectable routes of administration, including subcutaneous routes, that have been used successfully.

Albendazole 400 mg twice a day for 10 to 14 days is an alternative; shorter courses of albendazole are not as effective as ivermectin.

Treated patients are still at risk for reinfection, because immunity to *S. stercoralis* infection has not been formally demonstrated.

For infected pregnant patients, clinicians may prefer to defer treatment for strongyloidiasis until after the first trimester. All of the anthelmintic medications discussed in this article are US Food and Drug Administration (FDA) category C agents.

All persons found to harbor Strongyloides organisms should be treated, even if they are asymptomatic, because of the risk of hyperinfection and with the aim of eradicating the infection.

A positive serologic test is an indication for treatment, even if multiple stool examinations are negative. Empirical treatment of high-risk persons should be considered if there will be a delay in receiving results of serology.

As for other parasitic infections, there is active research to develop vaccines and prevent reinfection,91 and for *S. stercoralis,* there have been some vaccine candidates that have undergone preclinical testing

Management of hyperinfection and disseminated strongyloidiasis includes prompt administration of anthelmintics and broad-spectrum antibiotics with activity against enteric organisms and, when possible, discontinuation or reduction of immunosuppression.

The drug of choice for severe, complicated strongyloidiasis is ivermectin, which should be given daily and continued until larvae are no longer detected in the stool, sputum, and urine for 2 weeks.

Immunocompromised hosts may require hospitalization and intensive care in disseminated infection. Consider contact isolation in these patients, because sputum, stool, vomitus, and other bodily excreta may contain infective (filariform) larvae.

Follow-up examinations are indicated, and treatment should be repeated if:
- **larvae are identified in feces examined for up to a year after completion of therapy**

Serologic examination for 1 to 2 years after treatment is more reliable for monitoring response to treatment.
Following successful treatment, IgG antibodies to Strongyloides have been shown to decline or disappear as soon as 6 to 12 months

Eosinophilia, if present, should resolve as well.

- **Ivermectin is a semisynthetic antibiotic derived from *Streptomyces avermitilis*. The organism was isolated from a soil sample taken from a golf course in Japan.**
- **Ivermectin is marketed under the brand names Stromectol (Merck, Whitehouse Station, NJ) in the United States, Mectizan (Merck) in Canada, and Ivexterm (Valeant Pharmaceuticals, Montreal, Canada) in Mexico.**
- **It is an option for treatment of cutaneous larva migrans, head lice, and scabies.**

Ivermectin activates neuromuscular membrane-associated chloride channels. The subsequent influx of chloride results in membrane hyperpolarization and muscle spasm particularly affecting the nematode pharynx, thus halting nutrient ingestion.

- **Although ivermectin binding sites are present in the CNS of mammals, its affinity for nematode ligands is about 100 times greater than for mammals, explaining its selectivity.**

FASCIOLIASIS TREATMENT

Unlike infections with other flukes, fascioliasis responds poorly to praziquantel

First-line treatment is with a single oral dose of TRICLABENDAZOLE, a well-tolerated benzimidazole used in veterinary practice that is highly effective against mature and immature flukes.
Rates of cure of 78% to 99% have been reported, and persons not cured with a single dose usually respond to a second dose.

Treatment should be repeated if radiographic findings or eosinophilia fail to resolve or the titers of serologic tests do not decrease.
Resistance of *F. hepatica* to triclabendazole is widespread in cattle and has been observed in human fascioliasis.

Rates of cure with an alternative regimen, nitazoxanide, 500 mg twice daily for 6 to 7 days, have been as high as 95% in several small trials but lower in others.
Another alternative, bithionol, requires 10 to 15 doses, causes frequent side effects.
Artesunate has activity against *F. hepatica,* but cure rates are less than those with triclabendazole, and artemether had little effect in a trial in Egypt.

- Triclabendazole is a benzimidazole compound used routinely **since 1983** in veterinary practice for the treatment of fascioliasis. It was first used for the treatment of human infection in 1986; however, its use in humans ***expanded in 1989 during an outbreak of fascioliasis near the Caspian Sea***, when Iranian authorities approved the use of the veterinary formulation to treat human infections.
- In 1997 after the remarkable success of clinical trials using triclabendazole for the treatment of fascioliasis and paragonimiasis, WHO recommended that the drug be placed on the Essential Drugs List.

Triclabendazole appears to be remarkably safe.

Adverse events, when they have occurred, have been mild:

-Abdominal pain

-Headache

-Nausea

-Fatigue

Abdominal pain

21.5% of patients who received triclabendazole in a dose of 5 mg/kg daily for 3 days

6.7% receiving 10 mg/kg twice daily for 1 day

31.3% receiving a single dose of 10 mg/kg

The abdominal pain is transient lasting less than 5 days, is typically located in the right upper quadrant, is relieved by oral spasmolytics, and has been attributed to the expulsion of dead or dying worms from the hepatobiliary system into the intestinal tract. The contention that nearly all the adverse reactions in human clinical studies can be attributed to the death of adult worms is supported by ultrasound studies that have demonstrated dilated intrahepatic bile ducts caused by transient biliary obstruction associated with expulsion of dying worms.

.. No evidence of dose-related
toxicity or carcinogenicity has been observed in animals

in pregnancy
Where possible, it seems prudent to avoid use in the first trimester. Triclabendazole is known to pass into breast milk, but there are no reports of adverse events in nursing infants.
No data exist regarding drug-drug interactions.

دوز پیشنهادی شامل یک رژیم درمانی به میزان ۱۰ میلی گرم به ازای هر کیلوگرم وزن بدن می‌باشد. اگرچه بروز حملات گذرای تب همراه با تغییراتی در تست های کبدی گزارش شده است؛ ولی تحمل کلینیکی دارو عالی می‌باشد. در صورتی که دارو بعد از غذا به مصرف برسد، جذب بهتری خواهد داشت. میزان موفقیت درمان با تک دوز 10mg/kg بین ۷۹/۴ تا ۸۳ درصد است در حالی که مصرف دو دوز 10 mg/kg از دارو در یک روز (با فاصله ۱۲-۶ ساعت) بعد از صرف غذا، با درمان صد درصد همراه بوده است

جدول تجویز تریکلابندازول بر حسب وزن (۳۲)

Number of Triclabendazole Tablets(250 mg)	Dosage (mg)	Weight (kg)
1/2	125	≤ 12.5
1	250	> 12.5 - ≤ 25
1+ 1/2	375	> 25 - ≤ 37.5
2	500	> 37.5 - ≤ 50
2 +1/2	625	> 50 - ≤ 62.5
3	750	> 62.5 - ≤ 75
3 +1/2	875	> 75 - ≤ 87.5
4	1000	> 87.5 - ≤ 100

عوارض تریکلابنداز ول خفیف بوده وشایع‌ترین آن درد شکم ، درد اپیگاستر و تعریق می‌باشد. عوارض کمتر شایع عبارتند از: خستگی، تهوع، استفراغ، سرگیجه، سرفه، تب، خارش و کهیر. (راش جلدی چندان شایع نمی‌باشد).

پیگیری و مراقبت پس از درمان

باتوجه به اینکه پس از شروع درمان ممکن است برخی علائم بالینی در بیمار ظاهر شود که با عوارض جانبی دارو اشتباه شود، بهتر است بیماران از نظر بروز علائم و نتایج درمانی در روزهای صفر (روز درمان)، روزاول (۲۴ساعت پس ازشروع درمان)، روزچهارم پس از درمان و یک هفته پس از آن پیگیری شوند. همچنین حدود یک ماه پس از درمان بایستی اقدامات تشخیصی مناسب برای اطمینان از حصول درمان کامل بیمار به عمل آید.

معیارها و ملاک‌های مهم درمانی در بیماران مبتلا به فاسیولا

در فاز حاد ملاک‌های درمان بیماران عبارتند از (۳۸):

۱- تشدید موقت علائم بالینی که به دنبال آن بهبودی حاصل می‌شود.

۲- تست‌های آزمایشگاهی: کاهش تعداد ائوزینوفیل ها و سطح سرمی IgE که پس از آن کاهش سطح آنتی بادی‌های ضد فاسیولا و ناپدید شدن آنتی ژن‌های دفعی-ترشحی فاسیولا درسرم اتفاق خواهد افتاد.

۳- رادیوگرافی: هیچ مطالعه سیستماتیک در این زمینه انجام نشده است. نتایج التراسوند که به صورت تجربی تشریح شده اند عبارتند از: ناپدید شدن کانون‌های مهاجر هیپواکوئیک (در سونوگرافی مناطقی از کبد که دچار آسیب شده‌اند در مقایسه با بافت سالم اطراف دارای اکوی ضعیف و یا فاقد آن می باشد) در کبد و پسرفت اسپلنومگالی. همچنین ناپدید شدن عوارض بیماری (خونریزی، آسیت وریزش جنب) پس از درمان مشاهده شده است.

سایر ملاک‌های درمان عبارتنداز:

۴- کولیک صفراوی همراه با اتساع مجاری صفراوی و افزایش گذرای گاماگلوتامیل ترانس پپتیداز وآلکالن فسفاتاز در روز ۷-۱ پس از درمان

۵- کاهش آنتی بادی‌های ضد فاسیولا

۶- ناپدید شدن ائوزینوفیلی

۶- ناپدید شدن IgE

ملاک‌ها و معیارهای مهم شکست درمان (۳۸):

محقق شدن هر یک از ملاک‌های زیر تا روز ۶۰ به‌عنوان شکست درمان تلقی می‌شود:

۱- اثبات وجود تخم انگل در مدفوع

۲- پایدار ماندن آنتی ژن‌های دفعی- ترشحی فاسیولا در مدفوع

۳- مشاهده هلال در بررسی سونوگرافی

سایر ملاک‌های شکست درمان عبارتند از:

- برطرف نشدن تهوع، خارش و درد شکمی
- افزایش تیتر آنتی بادی‌های ضد فاسیولا
- باقیماندن ائوزینوفیلی
- پایدار ماندن IgE