1 more than 3 nails for adults, or

Science, Statistics

1Onychomycosis and TerbinafineAshton, R., Leppard, B., Cooper, H.

(2014). Differential Diagnosis in Dermatology. (4th ed.). Florida: CRC Press.

According to Ashton, Leppard, and Cooper (2014) onychomycosis, also known as tinea unguium or fungal nail infection, is caused by dermatophyte (Greek for ‘ skin-plant’) fungi which multiply on the nail plate while living off the keratin within the nail itself causing it to become brittle, discoloured and thickened. Usually seen in toenails due to their slower growth rate and thus enabling the infection to take hold, Ashton, R.

Leppard, B and Cooper, H. (2014) point out that they can be challenging to diagnose, despite their commonality, due to its similar appearance to other nail thickening conditions such as onycholysis (separation of the nail at the nail bed) and subungual hyperkeratosis (thickened skin underneath the nail) within psoriasis sufferers. Both typically cause yellowing and distortion of the nail, however as neither are compromised by a rate of growth they’re often simultaneously visible on the fingernails as well, in contrast to onychomycosis which is primarily restricted to the toenails. Regarding distribution, they state that fungal nail infections do not affect every single nail, instead sporadically infecting one or two nails on one foot before moving onto the other. It can also be helpful to check between the toes or on the instep for signs of fungal skin infection. If there is any remaining doubt microscopy or a fungal culture will confirm the cause.

They go on to discuss the various treatments for onychomycosis, the most common being either a topical treatment applied to the nail itself or systemic therapy of anti-fungal medication. Recommended for mild cases with less

than 50% of the distal nail plate affected and spread to no more than 3 nails for adults, or for all cases seen in children over 12 – currently no treatments are recommended for young children – is the topical treatment of 5% amorolfine (Loceryl) varnish a couple of times a week after the cleansing and filing of the affected nail over a period of 9-12 months. It has relatively few side effects compared to systemic options, the most common being a burning and itching sensation on the nail post application, but has a low success rate of around 15-30%. For more severe cases in adults a course of Terbinafine may be recommended at a dosage of 250mg orally every day for 3 to 4 months, though it is worth noting that due to the nature of the drug the liver function should be assessed at a minimum of every 4 to 6 weeks throughout the treatment as it can cause liver toxicity – however, the frequency of this is currently unknown. Common side effects of the medication include nausea, diarrhoea and myalgia (B. N. F.) and it typically has a success rate of approximately 55%.

Itraconazole can be a useful alternative despite being shown to be less efficient as it does not require liver checks if taken pulsed at 400mg daily, though it is not recommended for patients with a history of heart failure or liver disease. Topical and systematic treatment can be combined and is shown to improve the cure rate, however, if neither has worked after 12 months the complete removal of the infected nails followed by a course of Terbinafine may be necessary. This textbook was a practical source with easy to follow information but with a lack of treatment options for patients, instead rigidly sticking to the choice that they consider best (Terbinafine) with little explanation as to why.

They don’t reference or site statistics or specific papers which can prove inconvenient at times, which could prove difficult if a practitioner came across an atypical patient or a more complex case. Van Duyn Graham, L., & Elewski, B. (2011). Recent updates in oral terbinafine: its use in onychomycosis and tinea capitis in the US.

Mycoses: Diagnosis, Therapy and Prophylaxis of Fungal Diseases, 54(6), e679 – e685. doi: 10. 1111/j. 1439-0507. 2011.

02038. xIn this article Van Duyn Graham and Elewski (2011), two American dermatologists based in Alabama, arguing that the use of terbinafine is still the best treatment option for onychomycosis over 20 years after it was first approved for use. They explain how Terbinafine works, being a fungicidal agent which helps prevent the synthesis of ergosterol, a key component of fungal cell membranes, which in turn cause the cells to die and comparing it to how ‘ azole’ drugs (e. g. Itraconazole) function. Acting later on in fungal ergosterol biosynthesis in comparison to Terbinafine, it works by blocking several enzymes required to create fungus.

However, they end up metabolised by the liver which means that they are contraindicated with several drugs and removes their ability to treat patients with co-morbidities or who take other medications – a sizable proportion of onychomycosis suffers, particularly the elderly and those who have diabetes. Compared to other systemic treatments such as the ‘ azoles’ they claim that Terbinafine is the safest option owing to the low rate of severe side effects (0. 04%), stating that its apparent suitability for prescription during pregnancy is proof of its safety – though it is worth noting that tests

presuming its harmlessness to expectant mothers were undertaken on animals which bring into question how safe it really is, with several drugs of the past that had proven safe on creatures such as chimpanzees having devastating effects on unborn children, e. g. Thalidomide. Most side effects are gastrointestinal with 4.

9% experiencing diarrhoea or nausea and dermatological such as rashes or eczema, however, a small proportion of patients may experience severe side effects such as liver failure, acute generalised exanthematous pustulosis (aka pustular drug eruption) and erythema multiforme. According to Van Duyn Graham and Elewski (2011) oral Terbinafine is delivered to the stratum corneum, nails and hair with the ability to penetrate both the nail bed and the nail matrix, a key factor in why it’s more efficient than fungal nail paints which only sit on the surface because the matrix produces the cells which become the nail plate. This is known from several studies that tested nail clippings both during and after treatment and found strong levels of Terbinafine up to seven weeks post-treatment, a contributing factor to this being the drug’s half-life of 200-400 h which enables it to continue to treat the fungus several weeks after completion. Though they state that numerous studies show a better cure rate with Terbinafine compared to Itraconazole, the other most common drug for systemic fungal treatment, in onychomycosis caused by dermatophyte fungi (approximately 90% of all cases) they also admit that Itraconazole is more efficient when it comes to the treatment of cases triggered by non-dermatophyte moulds and candida, citing a 2005 study which showed a 92% cure rate with Itraconazole in onychomycosis cases caused by Candida species compared to just 40% with

Terbinafine. Noting that a critical flaw in many onychomycosis studies is the lack of real follow up to determine whether the patient relapsed, they cited a study by Piraccini et al. (2010) which showed that after 12 months only 11. 9% of patients who had been treated with Terbinafine relapsed compared to 35. 7% of those who had been treated with Itraconazole.

Although a small study (73) patients, it does reinforce the case for Terbinafine over other antifungal drugs. Van Duyn Graham and Elewski are well respected in their field and put forward an adequate article on the benefits of Terbinafine over other options with several interesting and well thought out points, demonstrating its numerous advantages. However, it does have its flaws, particularly regarding the studies cited as many are either based on tiny groups or are dated with one going back as far as 1980. Another issue is the way that they gloss over the small but not insignificant chance of liver failure and the risks of use in pregnancy when guidelines have been based on animal trials. Heikkilä, H.

, & Stubb, S. (2002). Long-term results in patients with onychomycosis treated with terbinafine or Itraconazole. British Journal of Dermatology, 146(2), p250-p253.

doi: 10. 1046/j. 1365-2133. 2002.

04639. xFollowing up from a previous double-blind, double-dummy, randomised, multicentre study four years later the authors, who appear to be Finnish doctors, aimed to find out if Terbinafine was still more efficient than Itraconazole in the long-term. Aware that relatively few onychomycosis

studies focus on how patients do years after treatment, a majority instead opting to centre on short-term results, Heikkilä and Stubb (2002) decided to document and compare both the clinical and mycological cure rates of Finnish patients who had been treated by either Terbinafine or Itraconazole 4 years post-treatment. The original study was designed to compare not only the differences in effectiveness between the two drugs but also the impact it had taking either medication for three months instead of the recommended 4. Taking place across 6 European countries including Finland and lasting 72 weeks, it involved 496 participants both male and female between the ages of 18 and 75 years with a clinical diagnosis of onychomycosis of the toenail confirmed with positive results on mycological culture and microscopy. Only patients who had onychomycosis caused by dermatophytes were allowed to take part, so those with fungal infections due to candida or yeast were not permitted.

Another requirement was that they had to have an affected big toenail capable of regrowth. At the end of the study, four months of Terbinafine proved the most effective treatment. Interested in the long-term results of the various treatments, Heikkilä and Stubb tracked down the 91 patients from Finland who participated and invited them to take part in a re-examination study. 3 of them didn’t respond, and another two could not be located, so the total number of people examined was 86. Between the end of the first study (72 weeks) and the follow up (4 years), 10 of the patients had received additional systemic treatment for onychomycosis so hence were excluded. The remaining 76 participants were made up of 38 men and 38 women, ranging from 25-72 years.

At the examination, they looked at each patient’s treatment history and took a nail cutting from them. These samples were taken to Helsinki University Hospital where they assessed the original treatment’s success in three areas: mycological cure, clinical cure and complete cure. The results were that 78% of those who had taken four months of Terbinafine in the original study had remained wholly cured compared to just 24% of the patients who had been treated with four months of Itraconazole. It appears that participants on Terbinafine continued to be clear, but the group on Itraconazole saw fungal regrowth. Heikkilä and Stubb did an interesting study which helped to combat the lack of studies on the long-term effects of systemic treatments for onychomycosis and showed how it remains to be the best option for fungal nails regarding success rate compared to the alternatives.

There were a few difficulties with this study. Firstly, there is relatively little information available about either of the study’s authors which leaves the reader unable to be 100% certain about their credentials. Secondly, they did the follow-up study on the Finnish patients, vastly reducing the number of participants which in turn reduces the accuracy of the figures. Thirdly, they had to rely on the original study being entirely accurate for the follow-up results to be correct.

Overall, I feel that the article was interesting and further showed the high success rate of Terbinafine – especially in the long-term – though I wouldn’t advise anyone to form a complete opinion on the drug’s healing abilities based on this piece alone. Valkova, S. (2012). Treatment of dermatophyte

onychomycosis with terbinafine (Lamisil) pulse therapy. Journal of IMAB, 10(2004), p45-46. doi: 10. 5272/jimab. 2004101.

45In this piece for the journal of the International Medical Association of Bulgaria, Valkova – a Bulgarian dermatologist – describes the success of his recent study into the efficiency of Terbinafine pulse therapy in the treatment of dermatophyte nail infections. Valkova treated seven patients, made up of four males and three females, aged between 33-65 years – 4 of whom had onychomycosis of the toenails, 2 had an infection of the fingernails, and one had both fingernails and toenails affected. The diagnosis had been confirmed by both clinical and mycological examinations. The volunteers had been infected for between 1-8 years, and the degree of involvement in the nail palate varied from 75% to 100%.

Those with liver, renal of cardiovascular problems were excluded. Participants were given 500mg of Terbinafine daily for one week a month over a duration of 4 months for those with toenail infections and three months for those with affected fingernails. All patients were examined both monthly and six months post-treatment. After six months, the subjects were split into one of three categories based on mycological evaluation: mycologically cured with residual malformation, mycologically cured without residual malformation and not mycologically cured. Of the patients with onychomycosis of the fingernails three were mycologically cured without residual malformation, one was mycologically cured with residual malformation – a “ small band of onycholysis and residual subungual

hyperkeratosis," according to Valkova (2012) – and one was not mycologically cured.

All cases of onychomycosis of the fingernails were mycologically cured without residual malformation. It is worth noting that one participant experienced itchiness due to the drug but this was successfully combated with antihistamines, and they were able to continue with the study. Valkova goes on to point out that their results coincide with the many other studies demonstrating the superiority of Terbinafine compared to other systemic options and that it remains to be the best course of choice for the treatment of fungal nail infections. Mentioning the consistent 20-30% failure rate in Terbinafine studies, they discuss how the 14. 3% rate in their study correlates with this. The patient with uncured onychomycosis continued to have " long narrow linear streaks" on their toes according to Valkova. They then go on to cite unpublished data by Baran who claims that the streaks on the nail occur because the nail plate has not adhered to the nail bed within these areas so hence the terbinafine does not reach it, preventing treatment.

The data provided by this study corresponds with the overall consensus that despite its faults Terbinafine remains to be the most effective treatment for onychomycosis. This study was concise, well explained and was well referenced. However, it was not without fault – the most obvious of which is the incredibly small size of the study (7 participants) that in turn severely impacts its reliability, as well as an instance of citing unpublished data which automatically decreases the study's overall trustworthiness. All four studies mentioned demonstrate the effectiveness of Terbinafine as the most reliable

treatment for onychomycosis due to its high success rates and low rate of severe adverse effects. Based on the research available a podiatrist with a patient suffering from fungal toenails could confidently suggest Terbinafine as a dependable treatment option providing the patient was old enough and possessed a robust liver and immune system, though they would have to have ensured that they took a comprehensive medical history first as well as schedule follow-ups in order to avoid complications.