

## **Doxycycline and (photo-)onycholysis**

### **Introduction**

Doxycycline is a tetracycline antibiotic with a broad spectrum of activity. It is produced by several manufacturers and has been on the international market since 1966 [1]. It is indicated *for infections caused by doxycycline sensitive bacteria: infections of the respiratory tract (including ear nose and throat infections), infections of the urogenital tract (including uncomplicated gonorrhoea, non-gonococcal-urethritis, syphilis), infections of skin and connective tissue, infections of the gastro-intestinal tract, infections with borrelia burgdorferi and eye infections (especially trachoma)* [2].

Adverse drug reactions mentioned in the SPC with respect to skin and allergic reactions are: maculopapular and erythematous rash, exfoliative dermatitis, urticaria, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus and photodermatitis. The SPC does not mention (photo-)onycholysis [2].

Photo-onycholysis refers to separation of the nail plate from the nail bed after exposure to ultraviolet light. Although the complication is not dangerous, it is painful in the early stages of the process [3].

### **Reports**

Up to March 2003, the Lareb database contains a total of 8 reports of onycholysis as a suspected adverse drug reaction. Three reports refer to (photo-)onycholysis associated with the use of doxycyclin.

- The first case concerns a 12-year old boy. Twelve days after starting doxycyclin, he developed a photosensitivity reaction in his face upon sunbathing: swelling and redness of his face, ears, lips and nose. Also white spots arose on his cheeks, ears, nose and upper lip. The doxycyclin course was finished 2 days later. The patient developed onycholysis 3 weeks afterwards (5 weeks after starting doxycyclin).
- The second case describes a 38-year-old woman who developed onycholysis 3 days after starting a doxycyclin course. At first, one nail came off; 2 weeks later two other nails followed. The patient was on holidays and had been sunbathing. She did not develop any other adverse skin reactions. As concomitant medication she used citalopram. Two months later (one month after finishing the doxycyclin course), she was recovering.
- A third patient, also a 38-year-old female, developed severe pain in the nails several hours after starting doxycyclin for Lyme disease. She was on holidays and was exposed to sunlight. During the continued doxycyclin course (14 days) her nails became less painful, but the middle parts of the nails became disconnected from the skin. All finger nails were involved, plus 4 of the toe-nails. Onycholysis occurred in this patient as single adverse skin reaction. It took 5 months for her nails to recover.

### **Other sources of information**

#### *Literature*

Several case reports of onycholysis upon use of doxycyclin are described in literature. In all cases the combination with sunlight exposure is described as an important condition, pointing to a phototoxic reaction[3-7].

#### *Databases*

The database of the WHO Monitoring Centre contains 6973 possible ADRs during the use of doxycycline, and 141 reports of onycholysis as an adverse drug reaction to drugs in general. An association between doxycyclin and onycholysis was suggested in 15 reports. The Reporting Odds Ratio of this combination is 48.3 (95% CI 28.7-82.6). Associations between onycholysis, minocycline, tetracycline were not statistically significant disproportionately present in the WHO database.

### *Mechanism*

Tetracycline induced phototoxic skin reactions, including onycholysis, are well known ADRs. Due to the fact that the nailbed is relatively unprotected from sunlight, onycholysis may be the sole expression of a phototoxic reaction [8]. The nail contains less melanin, therefore offering less ultraviolet protection to the nailbeds. This is supported by the observation that local application of chemical sunscreen may be protective [3,6].

The phototoxic reaction may be mediated by excited-state singlet oxygen and free radicals, which arise upon irradiation with UV-A and cause selective injury to mitochondria, within which doxycyclin is localised [3].

### **Conclusion**

Three cases in the database of the Netherlands Pharmacovigilance Centre Lareb show an association between doxycyclin and photo-onycholysis. Due to the absence of melatonin in the nail, onycholysis may occur even without other phototoxic skin reactions. These findings are supported by data from the WHO-database. In addition, the WHO-database suggests that this association is limited to doxycyclin. Literature supports this association as well.

### References

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