In vitro evaluation of phototoxic properties of systemic antipsoritics

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Introduction

Systemic antipsoritics agents such as fumaric acid esters, apremilast, methotrexate, anti-TNF-α agents, ustekinumab and secukinumab induce an amelioration of psoriasis within several weeks, but PASI 100 is not always reached. Phototherapy is superior to certain biologic and induces remission in a shorter time period. Therefore a combination therapy with phototherapy at the beginning of a systemic therapy or in case of only a partial remission can be reasonable. In order to be aware of photosensitive properties of these substances we assessed the in vitro phototoxic potential of these substances using a photohaemolysis test.

Material and Methods

Test substances

Tests were performed with the following compounds:

- Apremilast (Otsuka, Calgane, Summit, USA)
- Adalimumab (Humira®, AbbVie, Wiesbaden, Germany)
- Etanercept (Esbriet®, Pfizer, Kent, United Kingdom)
- Fumaric acid esters (Fumaderm®, Bogen Idex, Ieming, Germany)
- Infliximab (Remicade®, Janssen Biologics, Leiden, The Netherlands)
- Methotrexate (Mextrel®, Medac, Wedel, Germany)
- Secukinumab (Cosentyx®, Novartis, Basel, Switzerland)
- Ustekinumab (Stelara®, Janssen-Cilag, Beerse, Belgium)

Benzophenone (Merck, Dernstadt, Germany) was used as positive control.

UV sources

- Waldmann UV-A 700 (Waldmann, Schwaningen, Germany), emitting in the region of 340 to 440 nm (maximum approximately 365 nm).
- TL 20W/12 light bulb (Philips, Hamburg, Germany) with a main emission range of 275 to 365 nm (maximum approximately 315 nm).

Photohaemolysis test

Washed fresh human erythrocytes from healthy donors were suspended at a dilution of 1:200 in TCM buffer containing 0.03% human albumin. A 0.4 ml of the test sample – blank – erythrocyte-free sample were incubated with 0.1 ml of the test substance preparations at three concentrations (orientated to the plasma concentrations) for one hour at 37°C. Both substance-free erythrocyte samples (blank) as well as samples containing the test substances were exposed to 0, 25, 50, 75 J/cm² UVA or to 0 (0), 800 (0.36), 1600 (0.72) or 2400 (1.08) mJ/cm² UVA. To obtain total haemolysis (100%) erythrocytes were exposed to distilled water. After an incubation period of 20 min in the dark, supernatants were recovered by centrifugation. The released haemoglobin in the supernatants was determined as cyanmethaemoglobin.

Results

Adalimumab induced photohaemolysis up to 8.0% with UVB-rich irradiation. Fumaric acid ester and infliximab induced photohaemolysis up to 13.8 % with UVB-rich and UVA-rich irradiation and ustekinumab up to 11.6 % with UVA-rich irradiation alone (Tab. 1). Single photohaemolysis values of these substances after the highest UV-doses used are shown in Fig. 1 and 2. Apremilast, etanercept, methotrexate and secukinumab did not induce significant haemolysis with UVA or UVB irradiation with values < 5% (Tab. 1).

Discussion

Our in vitro photohaemolysis test demonstrated minor phototoxic properties (< 15% photohemolysis) of some of the used systemic antipsoritics (adalimumab, fumaric acid ester, infliximab, ustekinumab). Because we did not see increased phototoxicity with either UVA-rich or UVB-rich irradiation the combination of these substances is probably safe with regard to the absence of severe phototoxic properties. Nevertheless acute photosensitizing effects in humans or long-term side effects of such combination therapies cannot be excluded by this test.

References


