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Colour Doppler ultrasound of the nailbed: an objective tool for monitoring responses to vasodilatory treatment of connective tissue disorders?

Sir, Connective tissue disorders (CTD), such as systemic sclerosis (SSc) and systemic lupus erythematosus (SLE), often present with secondary Raynaud’s phenomenon (sRP) and painful digital skin lesions like scarring or ulcerations at the fingertip [1–5]. They are caused by a progressive reduction of microvascular lumina [3, 5]. Treatment with vasodilatory drugs aims to stop or even reverse this process [6].

Intravenous iloprost is a powerful vasodilatory drug which has been shown to improve symptoms in severe cases. However, based on clinical parameters, it is often quite difficult to define the time period of treatment which individually will give the best results or to select the patients and time for re-treatment [6–8]. Available methods, such as nailfold microscopy or laser Doppler flow measurements, are less suitable for reliable drug monitoring because it is difficult to define reproducible vessels [9]. Here, we used colour Doppler ultrasound (CDU) [10] to visualize and quantify changes in nailbed vascularity in response to vasodilatory treatment.

Thirteen patients [11 females and two males; median (range) age 42 (13–78) yr; SSc = 10, SLE = 3] were examined prospectively. All patients suffered from painful sRP and presented with digital skin lesions such as scarring and/or ulcerations. Only non-smokers and individuals without evidence of concomitant vascular disease were admitted. No other vasodilatory medication was allowed during the study.

The aim was to monitor quantitative changes in peripheral vascularity in CTD patients after termination of vasodilatory therapy with iloprost. Iloprost (Ilomedi, Schering, Germany) was administered intravenously (1.5–2.0 mg/kg/min over 6 h) for a 5–21-day period. Before and 7 days after the end of treatment, the patients were examined to evaluate digital skin changes. Clinical improvement of digital skin lesions (physician’s assessment) after therapy was classified as none (0), slight (1), or substantial (2). Pain relief (patient’s assessment) was expressed as a percentage comprising the reduction in chronic pain and the reduction in both severity and frequency of RP (visual analogue scale).

For ultrasound examinations we used a Sonoline Elegra equipped with a Multi-D linear array transducer (VFX13-5/12 MHz; Siemens, Issaquah, USA) which is particularly suited for imaging structures close to the skin surface. CDU was performed on the second finger of the clinically leading hand, according to the previously established protocol, at ambient temperature (19–21°C) and after a warm (40°C) and cold (10°C) challenge [10]. Vascularity was defined by quantifying colour signals (Quarticon, EchoTech, Germany) in standardized regions of the nailbed [10]. Vascularity was measured before and 7 days after the termination of iloprost therapy. The Wilcoxon test was used to determine the significance of pain relief, the improvement of
digital skin lesions, and the increase in vascularities after iloprost therapy. For a correlation of clinical parameters with the increase in vascularities the Spearman correlation was used.

CDU revealed a significant increase in mean vascularities 7 days after the end of iloprost therapy (Fig. 1). The results were statistically significant for all three conditions used (ambient temperature, after cold and warm challenge). After therapy, mean pain relief was 38 ± 22% (P < 0.01) and mean improvement in microscopically determined digital skin lesions was ‘1.0’ (slight improvement; P < 0.01). Pain relief correlated well with the increase in vascularities after therapy at ambient temperature (r = 0.87, P < 0.01), after a warm challenge (r = 0.82, P < 0.01), and after a cold challenge (r = 0.69, P < 0.05). Correlations between the improvement in digital skin changes and the increase in vascularities after therapy were r = 0.76 (P < 0.01) at ambient temperature, r = 0.82 (P < 0.01) after a warm challenge, and r = 0.61 (P < 0.05) after a cold challenge.

Previously, we have shown that CDU of the nailbed is easy to perform with a high observer reproducibility yielding a good classification of the patient’s disease status; vascularities at ambient temperature and after dynamic challenges were significantly lower in CTD patients compared with healthy controls [10]. The CDU results presented here reveal an increase in mean vascularities after iloprost treatment. It is important to note that the vascularities were determined 7 days after iloprost treatment was stopped; this allows comparison of patients treated for different lengths of time with iloprost and documents a prolonged therapeutic effect after the end of vasodilatory therapy. CDU correlated well with the individual clinical responses to vasodilatory therapy. In single cases the therapeutic effect could be better demonstrated when applying temperature challenges rather than at ambient temperature, a fact that underlines the importance of the dynamic challenges for monitoring drug effects. The individual effects of iloprost might reflect distinct accumulated microvascular damage within individuals. Here, a direct comparison of CDU and nailfold microscopy might be useful to predict the individual response.

In conclusion, CDU of the nailbed provides the opportunity to monitor the therapeutic effect of vasodilatory treatment in CTD patients in an objective manner. Further studies will address the question of whether CDU can also determine progression or regression of the underlying disease over time.

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Fig. 1. Bar graph showing means ± standard deviation of the vascularities (colour signals/region of interest) at ambient temperature (open bars), after warm challenge (light grey bars), and after cold challenge (dark grey bars) before and 7 days after the end of iloprost therapy (•).