Research article

Evaluation of systemic oxidant/antioxidant status and paraoxonase 1 enzyme activities in psoriatic patients treated by narrow band ultraviolet B phototherapy

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Objectives: Ultraviolet B is a potent oxidative stress (OS) inducer in the skin; however, there are no data about the systemic oxidative effect of narrow band ultraviolet B (NB-UVB) phototherapy. In this study, we aimed to investigate the change in the OS status of psoriatic patients who were treated by NB-UVB phototherapy and to determine the relationships between OS, psoriasis severity, and systemic inflammatory condition.
Methods: Twenty-four psoriatic patients were treated with a total of 30 sessions of NB-UVB irradiation. Psoriasis area and severity index (PASI), serum levels of high sensitive C-reactive protein (hsCRP), total antioxidant status (TAS), total oxidant status (TOS), the oxidative stress index (OSI), serum paraoxonase (PON), and arylesterase (ARE) activities before and after NB-UVB therapy were determined.
Results: PASI scores significantly decreased after NB-UVB therapy ($P = 0.001$). The pre- and post-treatment hsCRP and TAS levels were similar ($P = 0.253$ and 0.301, respectively). TOS and OSI values significantly increased after phototherapy (both $P < 0.001$). PON and ARE activities did not change after treatment (both $P > 0.05$). There was no correlation between PASI and hsCRP, TAS, TOS, OSI, PON, and ARE values ($P > 0.05$).
Conclusion: A systemic OS may emerge in psoriatic patients treated by NB-UVB phototherapy.

Keywords: Erel's method, Narrow band ultraviolet B phototherapy, Psoriasis, Oxidative stress

Introduction

Psoriasis is a chronic immune-mediated inflammatory skin disease. Oxidative stress (OS), represented by increased oxidant products and decreased antioxidant system, was suggested to play an important role in the pathogenesis of psoriasis.[1] OS has harmful effects on the organism via excess cytotoxic effects and oxidative damage. Endogenous oxidation and reduction mechanisms of normal cellular metabolism, ultraviolet rays, air pollution, smoking, and microorganisms may cause OS.[2,3]

Till now, concentrations of molecules involved in OS such as reactive oxygen species (ROS) and nitric oxide, lipid peroxidation products including oxidized low-density lipoprotein (ox-LDL), malondialdehyde, and thiobarbituric acid reactive substance (TBARS), and vitamins that act as antioxidants have been investigated in psoriasis.[4–7] However, measurements of these molecules are time consuming, expensive, and individual values do not reflect global oxidative status of the organism. The methods established by Erel measure the total oxidant status (TOS) and total antioxidant status (TAS) which reflect the global effects of various oxidants and provide an evaluation of the efficiency of all antioxidants in the organism in a practical way.[8,9]

The PON1 enzyme has paraoxonase (PON) and arylesterase (ARE) activities, which are located in the high-density lipoprotein (HDL) structure and reflect the antioxidant activity of PON1 in the absence of an acknowledged biological substrate of PON1. These enzymes have anti-inflammatory and antioxidant defence activities against lipid oxidation. They protect LDL and HDL from OS-related peroxidation.[10] The PON/ARE activities were reported to be higher or lower in psoriatic patients than healthy individuals in different studies.[5,6,10,11] Higher levels

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of lipid peroxidation products and lower PON1 activity suggested that psoriasis is associated with OS.[11]

Narrow band ultraviolet B (NB-UVB) phototherapy is an effective treatment for psoriasis, which suppresses Th17 and interferon signalling pathways that play critical roles in the pathogenesis of the disease.[12] On the other hand, UVB has been shown to be a potent OS inducer in the skin by *in vitro* studies.[13–16] In this study, we aimed to investigate (i) the change in the OS status of the patients with psoriasis who were treated by NB-UVB phototherapy; and (ii) to determine the relationships between OS, psoriasis severity, and systemic inflammatory condition.

Methods

Subjects

This was a single centre, prospective longitudinal study. The study included 15 males and 9 females with moderate plaque type psoriasis (psoriasis area and severity index, PASI: 10–20). The age of participants at inclusion ranged from 18 to 60 years (mean ± SD: 37.9 ± 12.3). The disease duration ranged between 1 and 41 years (median: 12.5 years). The median age of onset of psoriasis was 20 years (range: 7–48 years). Patients who were under 18 years old, pregnant, nursing, photosensitive, smokers, or who had other dermatologic, systemic, or autoimmune disorders were not included. Patients did not receive systemic therapy for psoriasis for at least 6 months or topical therapy for at least 2 weeks before participation. Patients did not use any oral supplementation or topical agent including antioxidants or vitamins and any anti-inflammatory drugs. Disease severity was assessed by the PASI[17] before NB-UVB therapy and after the 30th session of treatment by the same dermatologist. The study was approved by the hospital's ethics committee. All participants signed written informed consent.

Phototherapy treatment

All patients were treated with a Dermalight – Medisun 2800 PC-44-AB cabin (Schulze & Bohm GmbH – Bruhl, Germany) with TL100W/01 fluorescent lamps (310–315 nm; Medisun, Germany). The initial dose, dependent on the phototype of the patient, was 0.1–0.3 J/cm^2, and an increasing dose schedule based on an increase of 0.1 J/cm^2 was used at each session (thrice weekly; a total of 30 sessions), until a maximum dose of 2.5 J/cm^2 was reached. Total cumulative mean dose was 37.2 J/cm^2. Eyes and genital areas were shielded during treatment.

Blood sampling and assays

Venous blood samples were collected from all participants in the early morning after an overnight fast of at least 8 hours, before the first session of NB-UVB treatment and after the 30th session of the therapy. None of the collected samples was icteric or haemolyzed. The samples were separated by centrifugation at 2500 × g for 10 minutes, and sera were stored at −80°C until use. All samples were assayed at the same time.

The levels of high sensitive C-reactive protein (CRP) (hsCRP) were measured by nephelometric assay. Serum TAS level was measured using an automated colorimetric measurement method based on the bleaching of the characteristic colour of a more stable ABTS (2,2′-azino-bis[3-ethylbenzothiazoline-6-sulfonic acid]) radical cation by antioxidants. The imprecision of the assay is <3%, and the results were expressed as mmol Trolox equivalent/L.[9] Serum TOS level was measured using an automated colorimetric measurement method, in which oxidants present in the sample oxidize the ferrous ion-*o*-dianisidine complex to ferric ion. The oxidation reaction was enhanced by glycerol molecules, which are abundant in the reaction medium. The ferric ion produced a coloured complex with xylenol orange in an acidic medium. The colour intensity, which was measured spectrophotometrically, correlated with the total number of oxidant molecules present in the sample. The assay was calibrated with hydrogen peroxide and the results were expressed in terms of micromolar hydrogen peroxide equivalent per litre (μmol H_2O_2 Eq/L).[8] The oxidative stress index (OSI), which is an indicator of the degree of OS, was calculated according to the formula: OSI (arbitrary unit) = TOS (mmol H_2O_2 Eq/L)/TAS (mmol Trolox Eq/L) × 100.[1] Serum PON and ARE activities were determined using commercially available kits (Rel Assay Diagnosticss, Mega Tıp, Gaziantep, Turkey). Serum PON activity towards paraoxon was measured following hydrolysis of paraoxon to yield p-nitrophenol and diethyl phosphate in the absence of NaCl (baseline activity). The molar extinction coefficient of *p*-nitrophenol was 17 000/mol/l/cm at pH 8; the results were expressed in U/l. Serum ARE activity was determined by the presence of phenol following the reaction of phenyl acetate. The molar extinction coefficient of phenol was 4000/mol/l/cm; the results were expressed in kU/l.

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, version 11.5 for Windows; SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as median and interquartile ranges 25 and 75 (median (IQR 25–IQR 75)). Categorical variables were reported as number and percentage. The Wilcoxon test was performed to compare the pre- and post-treatment values of TAS, TOS, OSI, hsCRP, PON and ARE. These markers were also compared between females

and males before and after treatment by using *t* test and Mann–Whitney *U* test. Spearman correlation analyses were performed to evaluate relationships between PASI, hsCRP, TAS, TOS, OSI, PON, and ARE values. A *P* value of <0.05 was considered statistically significant.

Results

In Table 1, comparisons of pre- and post-treatment values of PASI scores and OS parameters are summarized. PASI scores significantly decreased after 30 sessions of NB-UVB therapy (16.40 vs. 5.35; $P = 0.001$). The post-treatment values of hsCRP and TAS were similar with pre-treatment levels (3.12 vs. 2.89; $P = 0.253$ and 2.20 vs. 2.27; $P = 0.301$, respectively). TOS levels and OSI values significantly increased after NB-UVB therapy (6.92 vs. 9.80; $P < 0.001$ and 0.30 vs. 0.45; $P < 0.001$, respectively). PON and ARE enzyme activities did not change after phototherapy (both $P > 0.05$). When females and males were compared, the two genders were similar in regard to TAS, TOS, OSI, hsCRP, PON, and ARE values both before treatment and after treatment (all $P > 0.05$). There were no correlations between PASI, hsCRP, TAS, TOS, OSI, PON, and ARE values (all $P > 0.05$) (Table 2). A significant correlation between hsCRP and ARE activity was present at baseline ($r = 0.511$, $P = 0.011$).

Table 2 Correlation analysis of PASI and hsCRP with oxidative stres parameters (PON and ARE activities, TAS, TOS, OSI) before and after 30 sessions of NB UVB therapy*

	Pre-treatment		Post-treatment	
Parameters	*R*	*P*	*r*	*P*
PASI-PON	−0.080	0.710	0.027	0.901
PASI-ARE	0.046	0.830	−0.018	0.935
PASI-TAS	0.075	0.727	0.046	0.833
PASI-TOS	−0.167	0.436	0.175	0.413
PASI-OSI	−0.350	0.094	0.049	0.819
PASI-hsCRP	−0.128	0.552	−0.284	0.179
hsCRP-PON	0.182	0.396	0.172	0.421
hsCRP-ARE	0.511	**0.011**	−0.118	0.584
hsCRP-TAS	0.393	0.057	0.081	0.708
hsCRP-TOS	0.377	0.070	0.265	0.212
hsCRP-OSI	−0.127	0.553	0.103	0.633

ARE, arylesterase; hsCRP, high-sensitive C-reactive protein; OSI, oxidative stress index; PASI, psoriasis area and severity index PON, paraoxonase; TAS, total antioxidant status; TOS, total oxidant status.
r, Spearman's rho.
Significant *P* values are highlighted in bold.

Discussion

The results of our study demonstrated that NB-UVB therapy was an effective treatment for psoriasis; however, the increase in oxidants showed that NB-UVB therapy induced a systemic OS. The NB-UVB phototherapy did not change the levels of TAS, PON, and ARE activities, suggesting that NB-UVB therapy might not modulate total systemic antioxidant mechanisms. To our knowledge, our study is the first clinical study establishing the systemic effect of NB-UVB phototherapy on global oxidant and antioxidant status of psoriatic patients. Till now, oxidative effects of UVB irradiation were demonstrated by many *in vitro* studies.[13–16] UVB radiation was shown to induce an increase in intracellular ROS molecules such as superoxide radical, hydrogen peroxide, and hydroxyl radicals. Hydrogen peroxide was dose dependently produced by UVB irradiated keratinocytes.[13] Activation of the keratinocyte membrane epidermal growth factor receptor and NADPH oxidase were found to be the major sources of ROS. Increased ROS concentration caused the upregulation and activation of transforming growth factor β, which is a potential mediator for the effects of acute and chronic UV irradiation.[14] Anti-inflammatory and antioxidant drugs were suggested to inhibit production of ROS.[15] All this evidence shows that many inflammatory processes are triggered through generating ROS in the epidermal keratinocyte as a skin response to UVB *in vitro*.

In the literature, there is one clinical trial investigating the systemic effects of broad band UVB (BB-UVB) phototherapy in psoriatic patients.[4] In that

Table 1 The PASI scores, levels of high-sensitive C-reactive protein, triglyceride, total oxidant status, total antioxidant status, oxidative stress index, and activities of paraoxonase (PON), and arylesterase of psoriatic patients before and after 30 sessions of NB-UVB therapy*

Variables	Pre-treatment	Post-treatment	*P*
PASI	16.40 (13.33–18.33)	5.35 (4.15–6.30)	**0.001**
hsCRP (mg/l)	3.12 (1.23–4.20)	2.89 (1.10–4.08)	0.253
PON activity (U/l)	163.00 (68.50–228.25)	159.50 (66.00–222.50)	0.797
ARE activity (kU/l)	237.5 (222.20–249.20)	244.00 (215.00–252.00)	0.786
TAS (mmol Trolox Eq/l)	2.20 (2.03–2.50)	2.27 (1.98–2.60)	0.301
TOS (μmol H_2O_2 Eq/l)	6.92 (6.52–7.48)	9.80 (8.11–12.89)	**< 0.001**
OSI (arbitrary unit)	0.30 (0.27–0.38)	0.45 (0.38–0.56)	**< 0.001**

ARE, arylesterase; hsCRP, high sensitive C reactive protein; OSI, oxidative stress index; PASI, psoriasis area and severity index PON, paraoxonase; TAS, total antioxidant status; TOS, total oxidant status.
*Continuous variables were expressed as median and interquartile ranges 25 and 75 (median (IQR 25–IQR 75)).
Significant *P* values are highlighted in bold.

study, Karaarslan *et al.* measured a significant elevation in lipid peroxidation represented by TBARS and nitrite–nitrate levels in the systemic circulation by chronic exposure to BB-UVB radiation. It is known that serum (or plasma) concentrations of the different oxidant species can be measured separately, but the measurements are time-consuming, labour-intensive and costly, and require complicated techniques. The oxidant effects of different oxidant molecules are also additive. Therefore, the TOS of samples were measured instead.[8] In this study, the Erel's method used to determine TOS shows the cumulative oxidative effects of various oxidants that are generated in biological systems, including hydrogen peroxide, lipid hydroperoxide, protein hydroperoxide, peroxynitrite, and other ROS and reactive nitrogen species.[8] In addition, we evaluated the change in TAS of the psoriatic patients treated by NB-UVB therapy. Erel's method used in the present study allowed us to measure the TAS of the whole organism instead of measuring each antioxidant separately. In recent *in vitro* studies, the anti-oxidant drugs were demonstrated to reduce the concentrations of ROS in UVB irradiated keratinocytes.[15,18] To the best of our knowledge, data about the effect of oral or topical antioxidants in psoriatic patients treated by NB-UVB are not available. Since OS could not be balanced with increased total anti-oxidant status and anti-oxidant enzyme activities of psoriatic patients in our study, it remains to be investigated whether anti-oxidant agents may detoxify harmful systemic oxidative effects of NB-UVB therapy.

Although non-specific, CRP is the most sensitive indicator of inflammation and is used to predict and diagnose low-grade inflammatory conditions such as atherosclerosis.[19] Psoriasis is confirmed to be a systemic inflammatory condition with high CRP concentrations.[7,20,21] Moreover, a decline in CRP levels was observed after appropriate treatments that reduce PASI scores.[20] In parallel to those observations, we also expected that hsCRP levels would reduce after NB-UVB therapy as psoriatic lesions regress. However, the concentration of hsCRP was similar to pre-treatment values. Among recent studies, Coimbra *et al.*[20] found a positive significant correlation between CRP and PASI in a large group of patients consisting of mild, moderate, and severe psoriasis. They treated 17 psoriatic patients with NB-UVB therapy thrice weekly for 12 weeks by a similar procedure to our study. They achieved a significant reduction in PASI scores and CRP levels and suggested CRP to be a powerful, sensitive and objective marker to evaluate psoriasis severity. Romani *et al.*[22] treated a group of 50 moderate–severe psoriatic patients with a mean of 26.8 NB-UVB treatments and achieved reduction both in disease severity and CRP concentrations. The CRP levels correlated with PASI at baseline, not after the treatment. In contrast, some previous studies did not report such a correlation between disease severity and CRP levels.[23,24] In our study, CRP levels did not show a significant reduction after NB-UVB therapy. We also could not demonstrate a correlation between CRP and PASI before and after NB-UVB therapy. These results suggested us that both systemic inflammatory condition and OS of the organism may be independent of psoriasis severity. Differences in disease severity and ethnicity of patient groups may be responsible for the contrary results of the studies compared. Inter-personal differences of PASI evaluations may also affect the results of analyses.

Although UV radiation has anti-inflammatory effects on psoriatic plaques,[12] it was demonstrated that UV radiation causes skin inflammation.[25] Laihia *et al.*[25] reported that acute exposure to erythemal UVB-induced skin inflammation resulted in an increase in circulating CRP concentrations. They achieved reduction in CRP levels after suberythemal repeating doses of solar stimulating UV radiation. However, there are no data about the change in CRP levels after chronic UVB exposure of normal skin. In our study, the absence of change in circulatory CRP levels under NB-UVB phototherapy suggested us that NB-UVB therapy might have induced a systemic inflammation although it reduced local inflammation in psoriatic lesions. We think that UVB-mediated additive systemic inflammatory and oxidative effects might have inhibited any reduction in hsCRP levels.

PON1 acts as an anti-oxidant and anti-inflammatory enzyme that inhibits lipid peroxidation.[11,26] Lipid peroxidation products such as ox-LDL are suggested to play role in the immune-inflammatory process in psoriatic skin. Loued *et al.*[26] demonstrated that purified PON1 has a pro-inflammatory effect in the presence of ox-LDL and has an anti-inflammatory effect in the presence of oxidized HDL. Purified PON1 itself has a protective effect against the TNFα-induced expression of ICAM-1, which is less than the protective effect of HDL-associated PON1. These results showed that the anti-inflammatory effect of PON1 against oxidized lipids depends on its association with HDL.

Genotypic and phenotypic differences of PON1 reflect variable enzymatic activities. The PON gene shows two common polymorphisms named Q or R and M or L, which have different PON and ARE activities. The PON allozymes are different for protection against LDL oxidation. When compared, PONQ is more stable and active than PONR during the LDL oxidation process.[27] In a recent study, Asefi *et al.*[10] determined the presence of the PON1 55 M allele, which is associated with lower ARE activity, in psoriatic patients.

Although the increase in inflammation was expected to cause exhaustion of PON activity, interestingly, we

determined a positive correlation between hsCRP levels and ARE activity before phototherapy in our study population. Different genotypic and phenotypic features of our patients or their good capacity of ARE activity for anti-oxidative protection might have led to a positive correlation between hsCRP levels and ARE activity. The disappearance of this correlation after phototherapy suggested to us that NB-UVB therapy-induced additional inflammation might have changed the response of ARE enzyme activity. Inflammatory markers involved in psoriasis pathogenesis other than hsCRP may be more sensitive to changes in NB-UVB therapy and may be more useful for determining the correlation between the inflammation and PON/ARE activities of psoriatic patients.

Conclusion

This study is the first clinical trial that demonstrates the change in TOS of patients with psoriasis treated by NB-UVB phototherapy. NB-UVB therapy is an effective therapy in psoriasis; however, it causes systemic OS. Our results point to the importance of close monitoring of NB-UVB therapy in patients who have OS-related systemic diseases such as atherosclerosis. Future studies investigating the short-term and long-term effects of OS induced by UVB phototherapies are warranted.

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References

1 Emre S, Metin A, Demirseren DD, Kilic S, Isikoglu S, Erel O. The relationship between oxidative stress, smoking and the clinical severity of psoriasis. J Eur Acad Dermatol Venereol 2012 Sep 25. doi: 10.1111/j.1468-3083.2012.04700.x. [Epub ahead of print].
2 Bickers DR, Athar M. Oxidative stress in the pathogenesis of skin disease. J Invest Dermatol 2006;126:2565–75.
3 Pastore S, Korkina L. Redox imbalance in T cell-mediated skin diseases. Mediators Inflamm 2010;2010:861949.
4 Kilinc Karaarslan I, Girgin Sagin F, Ertam I, Alper S, Ozturk G, Yildirim Sozmen E. Broad-band ultraviolet B phototherapy is associated with elevated serum thiobarbituric acid reactive substance and nitrite-nitrate levels in psoriatic patients. J Eur Acad Dermatol Venereol 2006;20:1226–31.
5 Toker A, Kadi M, Yildirim AK, Aksoy H, Alçay F. Serum lipid profile paraoxonase and arylesterase activities in psoriasis. Cell Biochem Funct 2009;27:176–80.
6 Ramadan R, Tawdy A, Abdel Hay R, Rashed L, Tawfik D. The antioxidant role of paraoxonase 1 and vitamin e in three autoimmune diseases. Skin Pharmacol Physiol 2013;26:2–7.
7 Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, *et al.* Psoriasis therapy and cardiovascular risk factors: a 12-week follow-up study. Am J Clin Dermatol 2010;11:423–32.
8 Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem 2005;38:1103–11.
9 Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem 2004;37:277–85.
10 Asefi M, Vaisi-Raygani A, Bahrehmand F, Kiani A, Rahimi Z, Nomani H, *et al.* Paraoxonase 1 (PON1) 55 polymorphism, lipid profiles and psoriasis. Br J Dermatol 2012;167:1279–86.
11 Ferretti G, Bacchetti T, Campanati A, Simonetti O, Liberati G, Offidani A. Correlation between lipoprotein(a) and lipid peroxidation in psoriasis: role of the enzyme paraoxonase-1. Br J Dermatol 2012;166:204–7.
12 Rácz E, Prens EP, Kurek D, Kant M, de Ridder D, Mourits S, *et al.* Effective treatment of psoriasis with narrow-band UVB phototherapy is linked to suppression of the IFN and Th17 pathways. J Invest Dermatol 2011;131:1547–58.
13 Peus D, Vasa RA, Meves A, Pott M, Beyerle A, Squillace K, *et al.* H_2O_2 is an important mediator of UVB-induced EGF-receptor phosphorylation in cultured keratinocytes. J Invest Dermatol 1998;110:966–71.
14 Wang H, Kochevar IE. Involvement of UVB-induced reactive oxygen species in TGF-beta biosynthesis and activation in keratinocytes. Free Radic Biol Med 2005;38:890–7.
15 Murakami M, Taniguchi M, Takama M, Cui JH, Oyanagui Y. UVB-dependent generation of reactive oxygen species by catalase and IgG under UVB light: inhibition by antioxidants and anti-inflammatory drugs. Drug Discov Ther 2008;2:85–93.
16 Travers JB, Berry D, Yao Y, Yi Q, Konger RL, Travers JB. Ultraviolet B radiation of human skin generates platelet-activating factor receptor agonists. Photochem Photobiol 2010;86:949–54.
17 Fredriksson T, Pettersson U. Severe psoriasis – oral therapy with a new retinoid. Dermatologica 1978;157:238–44.
18 Fang Y, Hu XH, Jia ZG, Xu MH, Guo ZY, Gao FH. Tiron protects against UVB-induced senescence-like characteristics in human dermal fibroblasts by the inhibition of superoxide anion production and glutathione depletion. Australas J Dermatol 2012;53:172–80.
19 Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001;103:1813–8.
20 Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, *et al.* C-reactive protein and leucocyte activation in psoriasis vulgaris according to severity and therapy. J Eur Acad Dermatol Venereol 2010;24:789–96.
21 Yiu KH, Yeung CK, Chan HT, Wong RM, Tam S, Lam KF, *et al.* Increased arterial stiffness in patients with psoriasis is associated with active systemic inflammation. Br J Dermatol 2011;164:514–20.
22 Romaní J, Caixàs A, Escoté X, Carrascosa JM, Ribera M, Rigla M, *et al.* Lipopolysaccharide-binding protein is increased in patients with psoriasis with metabolic syndrome, and correlates with C-reactive protein. Clin Exp Dermatol 2013;38:81–4.
23 Vanizor Kural B, Orem A, Cimsit G, Yandi YE, Calapoglu M. Evaluation of the atherogenic tendency of lipids and lipoprotein content and their relationships with oxidant-antioxidant system in patients with psoriasis. Clin Chim Acta 2003;328:71–82.
24 Sergeant A, Makrygeorgou A, Chan WC , Thorrat A, Burden D. C-reactive protein in psoriasis. Br J Dermatol 2008;158:417–9.
25 Laihia JK, Koskinen JO, Waris ME, Jansén CT. Adaptation of the human skin by chronic solar-simulating UV irradiation prevents ultraviolet-B irradiation-induced rise in serum C-reactive protein levels. Photochem Photobiol 2005;81:654–8.
26 Loued S, Isabelle M, Berrougui H, Khalil A. The anti-inflammatory effect of paraoxonase 1 against oxidized lipids depends on its association with high density lipoproteins. Life Sci 2012;90:82–8.
27 Aviram M, Billecke S, Sorenson R, Bisgaier C, Newton R, Rosenblat M, *et al.* Paraoxonase active site required for protection against LDL oxidation involves its free sulfhydryl group and is different from that required for its arylesterase/paraoxonase activities: selective action of human paraoxonase allozymes Q and R. Arterioscler Thromb Vasc Biol 1998;18:1617–24.