

Patch test sensitization caused by para-tertiary-butylcatechol

Results of a prospective study with a dilution series

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Para-tertiary-butylcatechol (PTBC) has been patch tested in Europe at 1% in petrolatum (pet.) and is now suspected of induction of patch test sensitization. A prospective study was initiated to obtain detailed data on this undesirable risk. A dilution series of PTBC (1%, 0.5%, 0.25%, 0.1% pet.) was used. Patch tests were read on days (D) 1–3, 7, 14 and 21 after application. Patients who were unable to return for late readings were telephoned and asked to report any reaction at the patch test sites. 40 out of 46 patients included completed the study. Patch tests were negative in 35 patients. 4 patients showed a positive patch test at later readings only (D7–D21); 2 patients reacted to a concentration as low as 0.1%. Rechallenge was performed in 2 of these patients, revealing a clearly positive reaction as early as D2 after patch test application. PTBC clearly induced patch test sensitization in 10% of the patients. It cannot be excluded that patch testing with 0.25% PTBC or with even lower concentrations might induce patch test sensitization. The optimal patch test concentration still has to be determined but may be within the range of 0.01% to 0.25% PTBC.

Key words: para-tertiary-butylcatechol; patch testing; patch test sensitization; patch test concentration. © Munksgaard, 2001.

Accepted for publication 18 June 2001

Para-tertiary-butylcatechol (PTBC) has long been patch tested internationally at 1% or 0.5%. In 1960, Gaul (1) regarded 1% PTBC as suitable. In 1990, Yu et al. (2) reported a patient sensitized to PTBC by such patch testing. Recently, Estlander et al. (3) found, in a retrospective analysis of their material, 9 patients sensitized to PTBC, 5 being considered sensitized by patch testing. Generally, patch-test sensitization seems to be rare, though the actual rate is unknown for most sensitizers (4). The rate of patch-test sensitization as such seems not to be as important as the rate of patch-test sensitization that becomes clinically relevant (4), data on which are also lacking. We initiated a study with the aim of obtaining more precise data on the patch-test sensitization rate of PTBC on routine patch testing. For this, patch-test readings were not completed at day (D) 3 but performed weekly during D7–D21.

Patients and Methods

Only patients in whom patch testing with PTBC was indicated in investigation of their dermatitis (known or possible exposure to PTBC) were included in the study. Patch tests were performed with PTBC 1% pet., such as used for patch testing in Germany when the study was initiated. Additionally, a dilution series of lower concentrations (0.5%, 0.25% and 0.1% PTBC in pet.) was tested. The patch-test substances were supplied by Hermal (Reinbek, Germany). 1% PTBC and the PTBC dilution series were applied to the left side of the upper back for 24 h; additionally 1% PTBC was tested on the volar side of the left upper arm to allow patients to carry out daily self-examination. Patch tests were read on D1–3, D7, D14 and D21 after patch test application. Patients who were not able to return for all scheduled late readings were

Table 1. Patch-test results of patients sensitized by patch testing with para-tertiary-butylcatechol

Patient	Test concentration	Test site	Results					
			D1	D2	D3	D7	D14	D21
Patient no. 1 44-year-old bus driver, formerly plumber	1.0%	upper back	–	–	–	+	+	+
	0.5%	upper back	–	–	–	?a	?a	?a
	0.25%	upper back	–	–	–	?a	?a	?a
	0.1%	upper back	–	–	–	?a	?a	–
	1.0%	left arm	–	–	–	+	+	+
Patient no. 2 43-year-old polytechnic teacher and hobbyist	1.0%	upper back	–	–	–	–	++	++
	0.5%	upper back	–	–	–	–	?a	++
	0.25%	upper back	–	–	–	–	?a	+
	0.1%	upper back	–	–	–	–	?a	+
	1.0%	left arm	–	–	–	–	++	++
Patient no. 3 43-year-old metal cutter ^{a)}	0.5%	upper back	–	–	–	+++	nd	nd
	0.25%	upper back	–	–	–	+++	nd	nd
	0.1%	upper back	–	–	–	+++	nd	nd
	0.25%	left arm	–	–	–	+++	nd	nd
Patient no. 4 44-year-old electrician, working in a plastics manufacturing plant ^{b)}	1.0%	upper back	–	–	nd	nd	++	++

Nd: not done. Patch-test score: see *Methods*.

^{a)} 1% test concentration omitted. ^{b)} Only 1% test concentration applied, readings performed on D9 and D21.

instructed to carry out self-examination and to return to the clinic if a test reaction occurred. Additionally, they were telephoned on D7, D14 and D21, and asked about reactions at the patch-test sites. Patch-test reactions were scored according to the criteria of the German Contact Dermatitis Research Group (allergic reactions +, ++ or +++, questionable allergic reactions ?a, no reaction –, (5)). Patients who developed, for the 1st time, positive patch-test reactions during the later readings (D7 to D21) were considered as having been sensitized by the patch-test procedure. If depigmentation at patch-test sites occurred, it was additionally recorded. Informed consent was obtained from all patients.

Results

Altogether, 46 patients were enrolled in the study, data of 6 patients being discarded from evaluation because of protocol violation. In 1 patient, only a 1% concentration of PTBC was applied. 36 out of the 40 patients who completed the investigation were male and 4 female. 11/40 patients returned for all late readings.

Negative patch-test results were noted in 35 patients. 1 patient showed a positive patch-test reaction during D1 to D3. All concentrations of PTBC were positive. The patient was a 60-year-old zinc plater who had had a positive patch test to PTBC in 1998 and to p-tertiary-butylphenol-formaldehyde resin in 1996. Because of the known sensitization, late readings were omitted.

4 patients had a positive patch test during late readings only, indicating patch-test sensitization (Table 1). Patient no. 1 was a 44-year-old bus driver who had previously been employed as a plumber. His history elicited no definite exposure to PTBC. Patch tests showed a + reaction to 1% PTBC from day D7 onwards to D21, and a questionable allergic reaction at D7, D14 and D21, respectively, to the lower concentrations. The patient did not consent to rechallenge testing.

Patient no. 2 was a 43-year-old polytechnic teacher and hobbyist who was exposed to various materials, probably including PTBC. Patch-test readings were negative up to D7. Between D14 and D21, he showed positive reactions to PTBC down to a concentration of 0.1%.

Patient no. 3 was a 43-year-old metal cutter who had no known exposure to PTBC. Patch-test read-

Table 2. Rechallenge patch testing in patients sensitized by patch testing with para-tertiary-butylcatechol

Patient	Test concentration	Test site	Results		
			D1	D2	D3
no. 3	0.5%	upper back	–	+	++
	0.25%	upper back	–	+	++
	0.1%	upper back	–	?a	+
	0.01%	upper back	–	–	?a
	0.001%	upper back	–	–	–
no. 4	1.0%	upper back	nd	+++	+++

Patients: see Table 1. Nd: not done. Patch test score: see *Methods*.

ings were negative until D7, when he showed a +++ reaction to 0.5%, 0.25% and 0.1% PTBC. 1% PTBC was not tested in this case, and the patient did not return for readings on D14 and D21, but patch-test reactions were still visible after 3 weeks according to the patient. Rechallenge was performed 3 months later with a dilution series of 0.5%, 0.25%, 0.1%, 0.01%, and 0.001% PTBC, and showed a + reaction to 0.5% and 0.25% and a questionable allergic reaction to 0.1% PTBC on D2; on D3, a ++ reaction to 0.5% and 0.25%, a + reaction to 0.1% and a questionable allergic reaction to 0.01% PTBC, were seen (Table 2).

Patient no. 4 was a 44-year-old electrician, in whom exposure to PTBC could not be confirmed. Patch testing was performed only with 1% PTBC. On D9, he showed a ++ reaction, which remained until D21. Rechallenging 1 month later showed a +++ reaction to 1% PTBC at D2 and D4 (Table 2).

None of the 40 patients developed vitiligo at the patch-test sites.

Discussion

Generally, patch-test sensitization is considered to be an infrequent adverse effect of patch testing though one of the most serious (4). In practice, it may be difficult to differentiate between induction of sensitization due to the patch test and a delayed patch-test elicitation reaction. Delayed patch-test elicitation reactions, developing 7 to 9 days after patch-test application or even later, have been described for several allergens, e.g., metals/metal salts (6). Traditionally, a reaction that develops at least 10 days after patch-test application is regarded as a patch-test sensitization (4), but it has to be suspected even when the positive reaction appears after only 7 to 10 days (7). In our study, 10% (4/40 patients) were clearly sensitized to PTBC from the patch-test procedure. In 3/4 patients, the positive reaction appeared quite early (7 and 9 days after patch-test application, respectively). Nevertheless, we believe that this was a result of a patch-test sensitization rather than a delayed elicitation reaction because: (i) in 2 patients (nos. 3 and 4) rechallenge gave a positive reaction as early as 2 days after patch-test application; (ii) PTBC is not an allergen known to cause delayed patch-test reactions in sensitized subjects; (iii) the results are in accordance with the literature (3). Although only a few patients had been investigated, we decided to stop the study along with routine patch testing with 1% PTBC, because the rate of patch-test sensitization was so surprisingly high.

1% and 0.5% PTBC, respectively, had already been in clinical use for at least 3 decades when Yu

et al. (2) in 1990 first published a case of patch-test sensitization, and more recently the study of Estlander et al. (3) drew further attention to the problem. Usually, patch-test readings are completed 3 to 4 days after patch-test application and the back is the common test site. If the patient does not notice a reaction developing after 10 or 14 days or neglects it, it is impossible to become aware of the problem. Therefore, it would be desirable to perform late readings more frequently. Unfortunately in practice, as we experienced repeatedly during our investigation, it is difficult to motivate patients to return for late readings.

PTBC is a potent allergen. Estlander et al. (3) showed in 2 occupationally-sensitized patients that even 0.001% and 0.0005% concentrations of PTBC, respectively, can elicit a positive patch-test reaction.

As early as 1958, Matz & Blank (8) in a patient with contact allergy to Thermo-Fax paper observed positive reactions to 0.01%, 0.1% and 1% PTBC. Freeman (9) emphasized that exposure to polyester resins and oils containing PTBC at a concentration of only 0.005% could cause allergic contact dermatitis. In our study, 2 patients (nos. 2, 3) who were sensitized by patch testing showed a positive reaction to only 0.1% PTBC. One may assume that the 1% (patient no. 2) and the 0.5% (patient no. 3) concentrations of PTBC, respectively, caused the sensitization and that positive reactions to the lower concentrations developed concomitantly. Nevertheless, with respect to the capability of 0.005% PTBC to cause allergic contact dermatitis, it cannot be excluded that patch testing with 0.25% PTBC or even lower concentrations might induce patch-test sensitization. In accordance with Estlander et al. (3), we recommend that 1% or 0.5% PTBC should no longer be used for routine patch testing. In our opinion, the optimal patch-test concentration remains to be determined, for it is not yet clear whether 0.25% PTBC is sufficiently safe for patch-test application. On the other hand, relevant cases of a PTBC allergy may be missed if the patch-test concentration is made too low. The optimal patch-test concentration may be in the range of 0.01% to 0.25% PTBC. We agree with Estlander et al. (3) that 0.25% PTBC may be recommended for routine patch testing until more precise data are available.

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