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Transdermal β-Blocker Therapy in Essential Hypertension

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Transdermal drug delivery has been applied to various agents in an effort to decrease the frequency of drug administration and increase the patients compliance. In our study, we demonstrated that transdermal application of a β-blocker (20 mg mepindolol) in patients with essential hypertension led to effective blood pressure lowering effect within 1 week (160.1 ± 6.1 mm Hg/95.8 ± 8.3 mm Hg vs 136.8 ± 7.2 mm Hg/84.3 ± 5.0 mm Hg; P < 0.05). A controlled study of transdermal versus oral β-blocker administration in hypertensives is necessary before this new therapeutic system is introduced in antihypertensive treatment. Am J Hypertens 1988; 1:199S–200S

KEY WORDS: Hypertension, transdermal drug delivery, β-blocker.

A recent important advance in drug administration has been the controlled delivery of drugs to the systemic circulation through the intact skin. Current technology makes transdermal therapeutic systems of reasonable size practical for any given drug with low molecular weight, high lipid solubility, and good effectiveness at a reasonable daily parenteral dosage. Up to now transdermal therapeutic systems with nitroglycerine or scopolamine and clonidine have been successfully used in the treatment of angina pectoris, motoric sickness, or hypertension.[1–4]

Furthermore, the experience with the usage of transdermal therapeutic systems does suggest the following advantages: *(a)* first-pass metabolism is avoided, *(b)* lower daily dosage because of continuous drug input and reduced liver metabolism, *(c)* fewer adverse effects due to lower dosages, *(d)* an improvement of the patients' compliance. But the incidence of allergic skin reaction is considered to be a disadvantage of the application of transdermal therapeutic systems.

In 1985 Vlasses et al[5] was the first to evaluate the serum concentration and the β-blockade of transdermally applied timolol in normotensives. In our study we tested for the first time the effectiveness of the blood pressure lowering effect of a transdermal β-blockade with mepindolol in essential hypertensives and the effect on 24-hour blood pressure profiles in essential hypertensives.

METHODS AND MATERIALS

Ten patients with essential hypertension from our outpatient department were included in this pilot study. The mean age was 37.7 ± 11.2 years; there were 6 males, and 4 females; the average blood pressure was *P* systolic 160.1 ± 6.1 mm Hg and *P* diastolic 95.8 ± 8.3 mm Hg. All subjects were deemed to be in good health on the basis of medical history, physical examination, and laboratory screening evaluation. The subjects consumed no other medication from 4 weeks prior and throughout the duration of the study.

An ambulatory 24-hour blood pressure registration, an ECG, a complete blood chemistry, and a clinical examination were performed in each patient before therapy and after 1 and 3 weeks of therapy. Before starting the study patient consent was obtained, and they were informed about the new treatment with the transdermal therapeutic system. Furthermore the local Institutional Review Boards were informed. Each patient taking part

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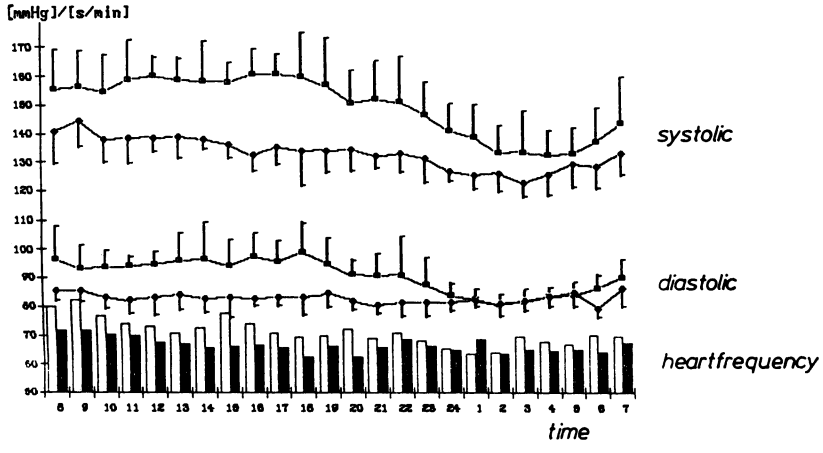

FIGURE 1. *Twenty-four-hour blood pressure profiles and heart rates before therapy* (open figures) *and after 3 weeks of transdermal mepindolol therapy* (closed figures) (bars *represent main value ± SD*).

in the trial received at the same time in a 24-hour-time-course the transdermal therapeutic system, which contained 20 mg mepindolol sulfate, a non-selective β-adreno-receptive blocking agent. In this new therapeutic system, the adhesive area and the effective component of the occlusive matrix-system were separated. All patches were self-adhesive and measured 9.8 cm^2 in size. A microporous control membrane guaranteed a release of 20 mg Mepidolol in 24 hours. Systemic side effects were evaluated at each visit by an analogue scale. Cutaneous compatibility was constantly examined by a dermatologist. Withdrawal from the study was performed because of intolerable side effects or skin incompatibilities. Statistical analysis was performed by Students' t test. Values are given as means ± SD.

RESULTS

The patients of the study group approved this new therapeutic system. One patient had to withdraw because of local skin irritation after 10 days of treatment. After 1 week of therapy, 10 of the patients showed a good blood pressure response, the blood pressure lowering effect even improved after 3 weeks of therapy (Figure 1).

After 1 week, the systolic blood pressure decreased to 136.8 ± 7.2 mm Hg ($P < 0.05$) and diastolic to 84.3 ± 5.0 mm Hg ($P < 0.05$); after 3 weeks the systolic blood pressure was 131.2 ± 2.1 mm Hg and the diastolic blood pressure was 82.1 ± 7.9 mm Hg. The heart rate decreased from 76.7 ± 5.1 beats/min to 72.2 ± 4.1 beats/min after 1 week and after 3 weeks to 69.2 ± 5.2 beats/min (NS). There was no significant change of the evaluated chemistry data.

DISCUSSION

The usage of β-adrenergic blocking agents has increased greatly in the last 10 years. Therefore a long-lasting and well-tolerated transdermal β-blocker could facilitate drug administration and increase the patients' compliance. The results of this first trial with transdermal mepindolol in essential hypertensives document a good blood pressure lowering effect of this new transdermal therapeutic system, which was in the same range as it is expected for oral administration.

Reports of Vlasses et al[5] in a normotensive group showed that measurable serum concentrations of a β-blocking agent in the therapeutic range can be achieved by a transdermal delivery. Furthermore it can be demonstrated that the characteristic blood pressure deviations in the morning and afternoon are significantly reduced after therapy.[6]

The results of this initial study are encouraging. Further studies are warranted to identify the effects associated with longer periods of application and whether or not skin irritation might be a limiting factor in a prolonged exposure. Furthermore a controlled transdermal β-blocker study versus oral β-blocker administration in hypertensive patients is necessary before this new therapeutic system is finally introduced to antihypertensive treatment.

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