

third of the patients resistant to treatment could have been reclassified to treatment responsive after the introduction of compliance monitoring, which improves compliance and thereby blood pressure control.

We also question the validity of the arbitrarily chosen cut-off point for compliance at 80%. This has often been used in the literature but no evidence is available that this number has any clinical relevance.<sup>2</sup> The data presented by Nuesch et al indicate that this percentage has no clinical meaning as some patients could be controlled with less than 80% compliance and others could not. In addition, the investigators did not take into account the dynamic aspect of compliance. Patients' compliance often improves immediately before the consultations (white coat compliance). Thus, it is important to analyse the distribution of the days of non-compliance in relation with the corresponding blood pressure measurements.

To assess the relevance of non-compliance in explaining treatment resistance in hypertensive patients, one should try to improve compliance and evaluate the impact of this intervention on blood pressure control, over an observation period of at least six months. This study was too short and lacked an active intervention.

The inherent message provided by Nuesch et al borders on absurdity—it does not matter whether the patient takes his treatment regularly or not. Do we really question the causal relation that should exist between the ingestion of the antihypertensive medication and blood pressure control?

## References

1. Nuesch R, Schroeder K, Dieterle T, Martina B, Battagay E. Relation between insufficient response to antihypertensive treatment and poor compliance with treatment: a prospective case-control study. *BMJ* 2001; **323**: 142–146. (21 July.)
2. Haynes RB, Sacjett DL, Gibson ES, Taylor DW, Hackett BC, Roberts RS, et al. Improvement of medication compliance in uncontrolled hypertension. *Lancet* 1976; **i**: 1265–1268.

# Pharmacological properties of antihypertensive drugs research need to be acknowledged

**Knut Schroeder, MRC training fellow in health services research ([k.schroeder@bristol.ac.uk](mailto:k.schroeder@bristol.ac.uk)), Alan Montgomery, MRC training fellow in health services research, Shah Ebrahim, professor in the epidemiology of ageing**

*Unité de recherche "Epidémiologie et science de l'information," INSERM U444 Faculté de médecine Saint Antoine, 75571 Paris cedex 12, France*

*Division of Hypertension and Vascular Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland*

*Division of Primary Health Care, University of Bristol, Bristol BS8 2PR*

*Department of Social Medicine, University of Bristol*

*Outpatient Department and Hypertension Clinic of Internal Medicine, University Hospital, CH-4031 Basel, Switzerland*

EDITOR—Nuesch et al suggest that non-compliance with treatment may not be associated with resistance to antihypertensive treatment.<sup>1</sup> Although there is little evidence on this topic, Burnier et al came to the opposite conclusion in a recent publication.<sup>2 3</sup> Their study included 41 hypertensive patients resistant to a regimen including three drugs. Electronic monitoring of compliance alone for two

months led to a significant reduction in mean blood pressure from 156/106 mm Hg (SD 23/11 mm Hg) to 145/97 mm Hg (SD 20/15 mm Hg,  $P < 0.01$ ). But this study was small and did not have a control group.

Nuesch et al could have strengthened their conclusions by providing some additional information. Side effects of treatment may influence compliance but were not considered in the comparisons of compliance and non-compliance or of response and non-response. It is also important to know whether both study groups were similar with regard to the type and number of antihypertensive drugs being used. Non-compliance with long acting medications may affect treatment effect much less than shorter acting agents where the timing of doses may be more important.

The study was too short and too small to come to any firm conclusions about the relation between compliance and blood pressure control. The methods of measuring compliance and blood pressure are not typical of clinical practice and may have induced powerful effects in some patients, thereby removing any relation between compliance and blood pressure control. Future studies should acknowledge the different pharmacological properties of various antihypertensive drugs. Investigators should attempt to define what level of compliance is required to achieve a desired effect of treatment. Electronic monitors can provide valuable additional data that include the exact timing of doses and inter-dose intervals.<sup>4</sup> Although methodologically challenging, analysis of such data might provide more detail on the extent and nature of non-compliance and its relation with blood pressure control.

We are currently recruiting 350 patients with uncontrolled essential hypertension for a primary care based randomised controlled trial on the effectiveness of nurse-led and patient-centred compliance counselling, funded by the Medical Research Council. We will use electronic monitors for 8–12 months after an initial two month run-in period before the intervention. We hope to be able to contribute new data on the relation between medication compliance and blood pressure control.

## References

1. Nuesch R, Schroeder K, Dieterle T, Martina B, Battegay E. Relation between insufficient response to antihypertensive treatment and poor compliance with treatment: a prospective case-control study. *BMJ* 2001; **323**: 142–146. (21 July.)
2. Ebrahim S. Detection, adherence and control of hypertension for the prevention of stroke. A systematic review. *Health Technology Assessment* 1998; **2**(11): i-iv, 1–78.
3. Burnier M, Schneider MP, Chiolerio A, Stubi CLF, Brunner H. Electronic compliance monitoring in resistant hypertension: the basis for rational therapeutic decisions. *J Hypertens* 2001; **19**: 335–341.
4. Metry J-M, Meyer UA. Metry JM. Measuring compliance in clinical trials and ambulatory care. In: Metry J-M, Meyer UA eds. *Drug regimen compliance: issues in clinical trials and patient management*. Chichester: Wiley, 1999: 1–21.

## Author's reply

---

**Edouard Battegay, assistant professor of internal medicine ([ebattegay@uhbs.ch](mailto:ebattegay@uhbs.ch)), Reto Nüesch, senior registrar, Benedict Martina, head of medical emergencies, Thomas Dieterle, senior fellow**

*Unité de recherche "Epidémiologie et science de l'information," INSERM U444 Faculté de médecine Saint Antoine, 75571 Paris cedex 12, France*

*Division of Hypertension and Vascular Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland*