

Influence of oral antidiabetic drugs compliance on metabolic control in type 2 diabetes. A survey in general practice

PJ Guillausseau

SUMMARY

Background: To address compliance with oral antidiabetic agents and its impact on metabolic control in type 2 diabetic patients treated in general practice.

Methods: Prospective assessment of self-reported compliance with a standardized questionnaire in an homogeneous cohort of 11,896 type 2 diabetic patients treated by their general practitioner with one or two oral antidiabetic agents, and analysis of determinants of compliance with treatment (age, diabetes duration, educational level, severity of complications, frequency of antidiabetic oral agents daily dosing).

Results: Optimal compliance (no omission) was reported in only 46% of cases. In multivariate analysis, HbA_{1c} levels were positively correlated with age, daily dosing frequency of oral antidiabetic agents and low educational level, but not with diabetes duration. Low daily dosing was associated with a better metabolic control. HbA_{1c} levels were associated with compliance with treatment, with a 1.4% mean difference between group with optimal and group with worst compliance.

Conclusions: These results suggest the interest of reducing daily dosing frequency of oral antidiabetic agents, in order to improve compliance with treatment and metabolic control.

Key-words: Type 2 Diabetes · Compliance · Antidiabetic Oral Agents · Metabolic Control.

Guillausseau PJ. Influence of oral antidiabetic drugs compliance on metabolic control in type 2 diabetes. A survey in general practice. *Diabetes Metab* 2003,29,79-81

Service de Médecine B, Hôpital Lariboisière, Paris et Université Paris 7 Denis-Diderot.

RÉSUMÉ

Observance thérapeutique et équilibre glycémique. Enquête en médecine générale

Objectif : Evaluer l'observance thérapeutique et son influence éventuelle sur l'équilibre glycémique chez des diabétiques de type 2 suivis en médecine générale.

Méthodes : Evaluation prospective de l'observance avec un questionnaire standardisé dans une cohorte homogène de 11 896 diabétiques de type 2 traités par leur médecin généraliste avec un ou deux antidiabétiques oraux, analyse des déterminants de l'observance (âge, durée du diabète, niveau d'études, complications, fréquence des prises d'antidiabétiques oraux par jour) et étude de l'impact sur l'équilibre métabolique évalué par les taux d'HbA_{1c}.

Résultats : Une observance optimale (aucune omission rapportée) n'a été observée que dans 46 % des cas. En analyse multivariée, les taux d'HbA_{1c} étaient en corrélation avec l'âge, la fréquence des prises quotidiennes d'antidiabétiques oraux et un faible niveau d'études, mais non avec la durée du diabète. Une faible fréquence de prises quotidiennes d'antidiabétiques oraux était associée avec un meilleur équilibre glycémique. Les taux d'HbA_{1c} étaient associés à l'observance thérapeutique, avec une différence moyenne de 1,4 % entre le groupe dont l'observance était optimale et celui dont l'observance était la plus faible.

Conclusions : Ces résultats suggèrent l'intérêt, pour améliorer l'observance thérapeutique et l'équilibre glycémique des diabétiques de type 2, de réduire le nombre de prises quotidiennes d'antidiabétiques oraux.

Mots-clés : Diabète de type 2 · Observance · Antidiabétiques oraux · Contrôle glycémique.

Address correspondence and reprint requests to:

PJ Guillausseau. Service de Médecine B, Hôpital Lariboisière, 2, rue Ambroise Paré, 75010 Paris.
pierre-jean.guillausseau@lrb.ap-hop-paris.fr

Received: September 22th, 2002; accepted: November 10th, 2002

Poor patient compliance with drug treatment has been consistently reported in chronic diseases, such as hypertension [1] and type 2 diabetes mellitus [2-4]. Noncompliance is a major health care concern, as it may reduce effectiveness of the treatment. In type 2 diabetes, several factors have been shown to be associated with a poor level of compliance. Some, as age, number, and severity of complications, low socioeconomic level and low incomes [4] cannot be remedied, but others, as polymedication and multiple daily dose regimens [2, 3] may be corrected. The influence of inadequate compliance on long term metabolic control is controversial. A relationship between low compliance and poor metabolic control has only been evidenced in the particular setting of an indigent population [4], while most studies performed in European and North-American populations have remained inconclusive [5-7]. The goal of the present study was therefore to assess compliance with oral antidiabetic therapy in an homogeneous cohort of patients with type 2 diabetes, in the usual conditions of care provided in Europe, ie, in general practice.

Patients and methods

In a prospective study, we assessed compliance, as well as the factors likely to influence it, in a cohort of 11,896 type 2 diabetic patients. Patients were treated with one or 2 oral antidiabetic agents (sulfonylureas, metformin, α -glucosidase inhibitors) by their general practitioner ($n = 2,687$) in urban or rural setting. Compliance was assessed by self-reporting, using standardized questionnaires. Compliance was graded as no omission, omission 1 to 3 times a month, omission once a week, and omission more than once a week. The cohort comprised 35- to 85-year old patients of both sexes (57% men) with overweight (79.8 ± 14.5 kg) ($m \pm SD$). Known diabetes duration was less than 5 years in 41% of cases, 5 to 10 years in 34%, and in excess of 10 years in 25%. Mean HbA_{1c} was $7.4\% \pm 1.5\%$. Retinal, renal, vascular, coronary, and/or

neurological complications were present in 27% of cases. For statistical evaluation, unpaired *t*-test and multivariate analysis was used.

Results

Optimal compliance with oral antidiabetic agents (no omission) was reported in 5,467 patients (37%), omission 1 to 3 times a month in 4,389 patients (46%), omission once a week in 1,274 patients (11%), and omission more frequent than once a week in 659 patients (6%). Multivariate analysis indicated that HbA_{1c} levels were positively correlated with age ($r=0.73$, $P < 0.0001$), frequency of daily doses of oral antidiabetic agents (once, twice or three times a day) ($r = 0.59$, $P < 0.0001$), and was negatively correlated with educational level ($r = -0.38$, $P < 0.0001$). We did not find any correlation between HbA_{1c} levels and diabetes duration, nor with the number or severity of complications. We observed a favorable influence of a low daily dosing frequency on compliance with an oral antidiabetic therapy, with the best compliance in the case of once-daily dosing (Fig 1). Our results also indicated that a low daily dosing frequency was associated with a better metabolic control (Fig 2), the best metabolic control being achieved with once-daily dosing. HbA_{1c} levels were directly correlated with compliance with treatment (Fig 3).

Discussion

In a cohort of 11,896 type 2 diabetic patients treated in general practice, optimal compliance with oral antidiabetic agents was self-reported in only 46% of cases. This figure is close to findings of previously reported studies [2-4]. As found by others, compliance is affected by the frequency of the doses, the lower the daily dosing frequency the higher the compliance [2, 3], rather than by the number of tablets per dose [8]. A similar favorable result for compliance has been reported in patients treated with antihypertensive

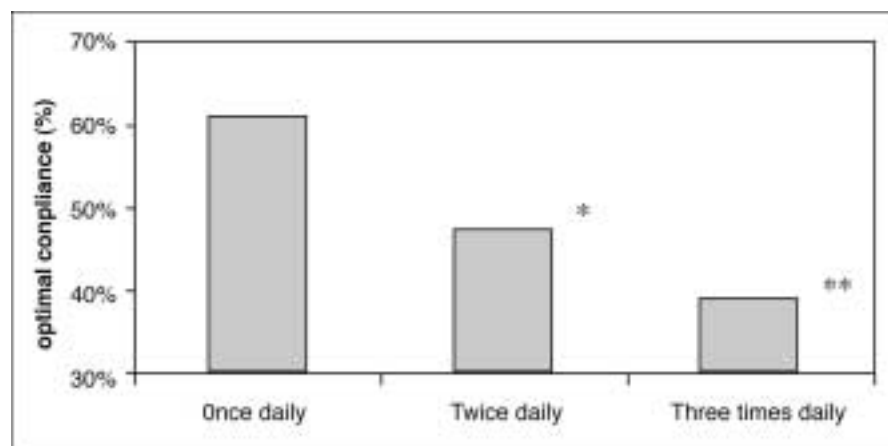


Figure 1

Percentage of type 2 diabetic patients with optimal self-reported compliance with oral antidiabetic agents (no omission) according to the frequency of daily doses (* $P < 0.05$, ** $P < 0.01$ us once daily dosing).

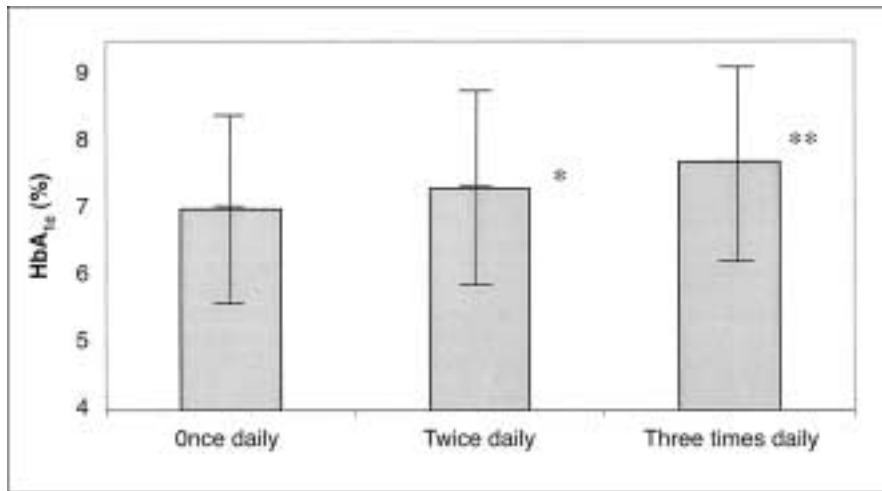


Figure 2

HbA_{1c} levels (%) in type 2 diabetic patients according to the frequency of daily doses of oral antidiabetic agent (* $P < 0.05$, ** $P < 0.01$ vs once daily dosing).

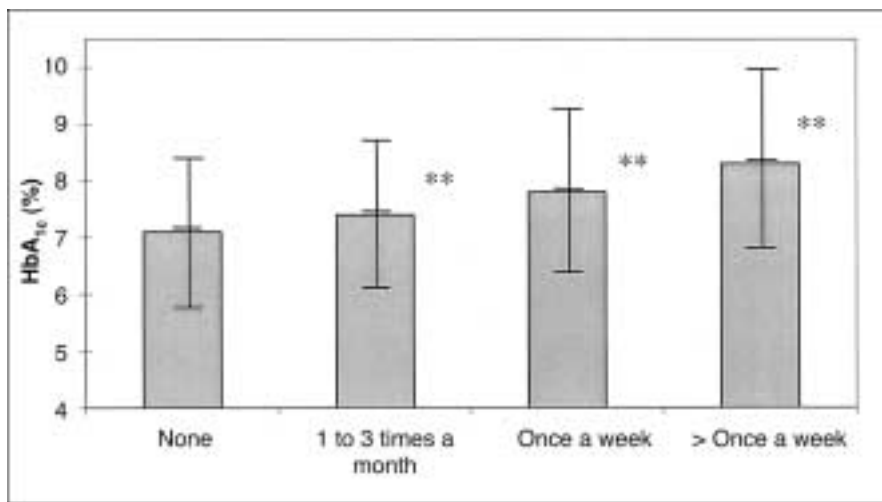


Figure 3

HbA_{1c} levels (%) in type 2 diabetic patients according to their self-reported compliance with oral antidiabetic agent (** $P < 0.01$ vs no omission).

drugs [9-11]. We found a strong influence of compliance on long-term metabolic control, with a mean difference of 1.4% in HbA_{1c} levels ($8.5\% \pm 1.9\%$ vs $7.1\% \pm 1.4\%$) between the group with optimal and the group with worst compliance. An association between compliance and HbA_{1c} levels was not observed in type 2 diabetes [5-7], except in one study performed in a particular setting [4]. These data suggest the utility of reducing daily dosing frequency of oral antidiabetic agents, the only modifiable determinant of compliance, in order to improve compliance with treatment and metabolic control.

References

- Vaur L, Vaisse B, Genes N, Elkik F, Legrand C, Poggi L. Use of electronic pill boxes to assess risk of poor treatment compliance. Results of a large-scale trial. *Am J Hypertens*, 1999, 12, 374-80.
- Paes AHP, Bakker A, Soe-Agnie CJ. Impact of dose frequency on patient compliance. *Diabetes Care*, 1997, 20, 1512-7.
- Donnan PT, Mac Donald TM, Morris AD. Adherence to prescribed oral hypoglycaemic medication in a population of patients with type 2 diabetes: a retrospective cohort study. *Diabetic Med*, 2002, 19, 279-84.
- Schechtman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. *Diabetes Care*, 2002, 25, 1015-21.
- Kravitz RL, Hays RD, Sherbourne CD, *et al*. Recall of recommendations and adherence to advice among patients with chronic medical conditions. *Arch Intern Med*, 1993, 153, 1869-78.
- Wooldridge KL, Wallston KA, Graberc AL, Brown AW, Davidson P. The relationship between health belief, adherence, and metabolic control of diabetes. *Diabetes Educ*, 1992, 18, 495-500.
- Hays RD, Kravitz RL, Mazel RM, *et al*. The impact of patient adherence on health outcomes for patients with chronic disease in the Medical Outcomes Study. *J Behav Med*, 1994, 17, 347-60.
- Dezii CM, Kawabata H, Tran M. Effects of once-daily and twice-daily dosing on adherence with prescribed glipizide oral therapy for type 2 diabetes. *South Med J*, 2002, 95, 68-71.
- Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL. How often is medication taken as prescribed? *JAMA*, 1989, 261, 3273-7.
- Eisen SA, Miller DK, Woodward RS, Spitznagel E, Przybexk TR. The effect of prescribed daily dose frequency on patient medication compliance. *Arch Intern Med*, 1990, 150, 1881-4.
- Waeber B, Erne P, Saxenhofer H, Heynen G. Use of drugs with more than a twenty-four-hour duration of action. *J Hypertens*, 1994, 12, S67-S77.