Availability of Inhaled Insulin Promotes Greater Perceived Acceptance of Insulin Therapy in Patients With Type 2 Diabetes

Nick Freemantle, phd[1]
Lawrence Blonde, md[2]
Didier Duhot, md[3]
Marcus Hompesch, md[4]
Robert Eggertsen, md, phd[5]
F.D. Richard Hobbs, frcgp, frcp, fmedsci[1]
Luc Martinez, md[3]
Stuart Ross, mb, chb, frcp[6]
Björn Bolinder, ba[7]
Elmar Stridde, md[8]

Inhaled insulin (INH, Exubera) is under investigation for preprandial treatment of patients with type 1 and type 2 diabetes (1–3). This dry-powder insulin formulation is delivered by aerosol, permitting the noninvasive administration of rapid-acting insulin (4). Preliminary studies have shown that INH provides reproducible and effective control of glycemia (1,5–7). This randomized controlled trial examined the extent to which the availability of INH affects the perceived acceptability of insulin therapy among patients with type 2 diabetes who failed to achieve target glycemia on current therapy.

RESEARCH DESIGN AND METHODS

— Male or female participants ($n = 779$) aged 35–80 years with at least 3 months duration of type 2 diabetes and a HbA_{1c} >8%, despite current therapy, were recruited from seven countries. Permitted current therapy included dietary measures and/or oral antidiabetic agents (OADs). Patients receiving insulin injections, smokers, or those who had significant pulmonary diseases were excluded. All patients gave informed consent, and local research ethics review boards approved the study.

Participants were randomly assigned to receive either educational information about the potential risks and benefits of all currently licensed treatment options only (OADs and/or subcutaneous insulin, $n = 388$) or information about the potential risks and benefits of licensed treatments and INH ($n = 391$). Patients and physicians independently completed questionnaires describing their treatment preferences. In the following patient-physician consultation, patients were asked to make a theoretical choice about future diabetes therapy. Physicians recorded the patient's theoretical choice of treatment and the actual open-label treatment administered.

The primary outcome was the proportion of patients in each group choosing insulin therapy. It was analyzed using Fisher's exact test and described using the odds ratio (OR) and 95% CIs. The Wilcoxon rank-sum test was used for treatment preferences data.

RESULTS

— Both groups had comparable baseline characteristics. Of patients, 77% in each group had HbA_c values in excess of 10%, and the majority of patients in each group were receiving treatment with one or more OAD in addition to dietary and lifestyle advice.

In the group offered INH as an option, 43.2% (169 of 391) of patients opted for a treatment during the patient-physician consultation that included insulin compared with 15.5% (60 of 388) of patients who were offered standard therapies only (OR 4.16 [95% CI 2.93–5.95], $P < 0.0001$) (Fig. 1*A*). Significantly fewer patients in the group offered INH chose to make no change to their therapy (27.4% [107 of 391]) compared with 43.3% (168 of 388) of patients offered standard treatments (0.49 [0.36–0.67], $P < 0.0001$) (Fig. 1*B*). Similarly, fewer patients who were offered INH chose regimens containing OADs or subcutaneous insulin than those in the standard therapy group (Fig. 1*B*). In total, 35.3% (138 of 391) of patients in the group offered INH chose it as an option.

The proportion of patients choosing insulin in both groups increased with the number of OADs currently being taken. This trend was particularly marked among patients offered INH, with 36.2% of patients taking one OAD opting for insulin therapy, 46.8% of patients taking two OADs, and 65.8% of patients taking three OADs. Equivalent figures for insulin uptake among patients offered standard therapy were 14.1% for patients taking one OAD, 17.9% for patients taking two OADs, and 20.5% for patients taking three OADs.

From the [1]Department of Primary Care & General Practice, University of Birmingham, Birmingham, U.K.; the [2]Ochsner Clinic Foundation, New Orleans, Louisiana; [3]Société Française de Médecine Générale, Issy les Moulineaux, France; the [4]Profil Institute for Clinical Research, Chula Vista, California; the [5]Department of Primary Health Care, Göteborg University, Göteborg, Sweden; the [6]Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada; [7]Aventis Pharma, Bridgewater, New Jersey; and [8]Pfizer, Karlsruhe, Germany.

Address correspondence and reprint requests to Nick Freemantle, PhD, Professor of Clinical Epidemiology & Biostatistics, Department of Primary Care and General Practice, Primary Care Clinical Sciences Building, University of Birmingham Edgbaston, Birmingham B15 2TT U.K. E-mail: n.freemantle@bham.ac.uk.

Received for publication 4 August 2004 and accepted in revised form 6 November 2004.

Abbreviations: INH, inhaled insulin; OAD, oral antidiabetic agent.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

© 2005 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Downloaded from http://diabetesjournals.org/care/article-pdf/28/2/427/666066/zdc00205000427.pdf by guest on 09 October 2024

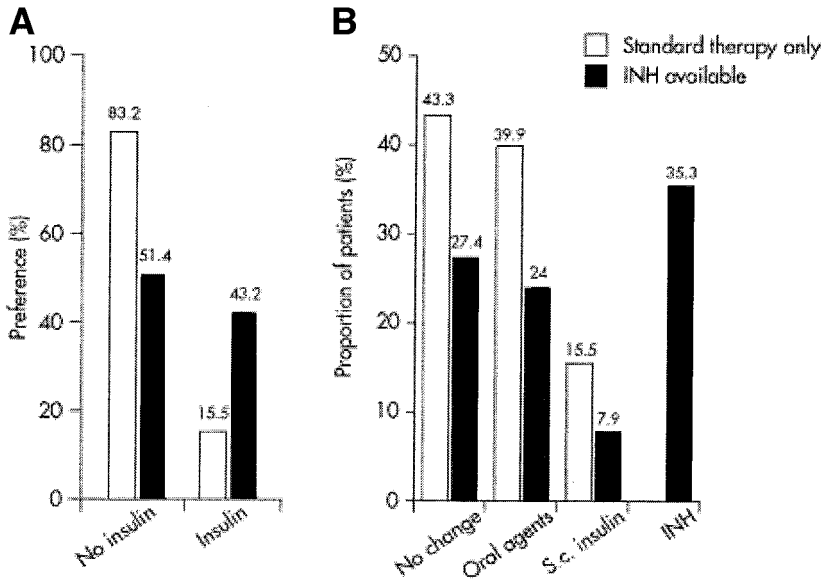

Figure 1—*Proportion of patients choosing insulin therapy (*6A*) and treatment options (*6B*) by group. A: Patient preference for insulin (%). B: Percentage of patients choosing therapy.*

The choice of insulin as a treatment option was influenced by age. Insulin (both INH and subcutaneous) was the most common choice (17.6%) among patients aged 56–65 years. Insulin was the least chosen option in the youngest (35–45 years, 10.7%) and oldest (>75 years, 7.1%) groups of patients. In the 56- to 65-year age category, 52.6% of patients offered INH chose insulin treatment compared with 17.6% of patients offered standard therapies. Similarly, insulin was chosen by 27.0% of the 35- to 45-year age-group and 29.0% of the >75-year age-group.

Before the patient-physician consultation, just under 20% of patients in both groups either agreed or strongly agreed to the addition of injected insulin, contrasted with ~50% of physicians who either agreed or strongly agreed that the patient should consider a course of therapy that included injected insulin. In the actual treatment outcome after the end of the study, ~16% of patients opted for insulin as a treatment option.

CONCLUSIONS — In this study of theoretical treatment choices among patients with type 2 diabetes failing to achieve target glycemic control on diet and/or OAD therapy, the availability of INH as a treatment option significantly increased the proportion of patients who would theoretically choose insulin overall. Patients were three times more likely to choose insulin therapy when INH was available, and INH was the most frequently chosen treatment option. In contrast, the aversion to injectable insulin was strong; despite a mean HbA_{1c} of 9.1%, 4 of every 10 patients who were offered an option of standard therapy only chose to make no change to their treatment. The enhanced willingness of those offered the option of INH treatment to change to a more appropriate therapy increases the potential for achieving improved glycemic control and reduces the risks for microvascular, neuropathic, and macrovascular complications, as well as the associated morbidity, premature mortality, and increased cost.

Before the physician-patient interview, there was a marked contrast between the preferences expressed by patients and physicians for injectable insulin as a treatment option, with around half of the surveyed physicians preferring this option compared with the relatively low enthusiasm for this treatment among patients. Interestingly, patient rather than physician preferences appeared dominant, and low levels of initial preference for injectable insulin translated to low levels of actual choice of injectable insulin at the end of the study. The theoretical preference expressed by patients randomized to the availability of INH in our study may identify a means to overcome patient aversion to insulin therapy, and its availability may thus enable patients to act in accordance with the recommendations of their physicians.

Acknowledgments— This study was funded by Pfizer and Aventis.

The authors thank all the patients and physicians for their time in participating in this study.

References

1. Cefalu W, the Exubera Phase III Study Group: Mealtime rapid-acting inhaled insulin (Exubera) improves glycemic control in patients with type 2 diabetes failing combination oral agents: a 3-month, randomized, comparative trial (Abstract). *Diabetologia* 45:A260, 2002
2. Bélanger A, the Exubera Phase III Study Group: Efficacy and safety of inhaled insulin (Exubera) compared to subcutaneous insulin therapy in patients with type 2 diabetes: results of a 6-month, randomised, comparative trial (Abstract). *Diabetologia* 45:A260, 2002
3. Quattrin T, the Exubera Phase III Study Group: Efficacy and safety of inhaled insulin (Exubera) compared to conventional subcutaneous insulin therapy in patients with type 1 diabetes: results of a 6-month, randomised comparative trial (Abstract). *Diabetologia* 45:A260, 2002
4. Klonoff D: Inhaled insulin (Review). *Diabetes Technol Ther* 1:307–313, 1999
5. Skyler J, Cefalu W, Kourides I, Landschulz W, Balagtas C, Cheng S-L, Gelfand R: Efficacy of inhaled insulin in type 1 diabetes mellitus: a randomised proof-of-concept study. *Lancet* 357:331-335, 2001
6. Cefalu W, Skyler J, Kourides I, Landschulz W, Balagtas C, Cheng S-L, Gelfand R: Inhaled human insulin treatment of patients with type 2 diabetes mellitus. *Ann Intern Med* 134:203–207, 2001
7. Heinemann L, Traut T, Heise T: Time-action profile of inhaled insulin. *Diabet Med* 14:63–72, 1997

Downloaded from http://diabetesjournals.org/care/article-pdf/28/2/427/666066/zdc00205000427.pdf by guest on 09 October 2024