Offering a Randomized Trial of Intensive Therapy for IDDM to Adolescents

Reasons for refusal, patient characteristics, and recruiter effects

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OBJECTIVE — To identify reasons adolescents refuse to participate in a randomized trial of intensive therapy (IT) for IDDM, to describe the patient characteristics of those who consent and those who refuse to participate, and to examine recruiter effects on trial participation rates.

RESEARCH DESIGN AND METHODS — A total of 99 adolescents, age 11–18 years, were provided with the results of the Diabetes Control and Complications Trial and approached for possible study participation by two nurse recruiters. Adolescents refusing the trial were administered a semi-structured interview to describe reasons for study refusal; responses were recorded and later coded into categories. Patient characteristics of consenters and refusers were collected and compared. The differential enrollment rates of the two nurse recruiters were also compared.

RESULTS — A total of 56 patients (~57%) agreed to participate; 43 refused. The four most common reasons for study refusal were *1*) increased clinic visits (42%), 2) increased insulin injections (30%), 3) increased frequency of self-monitoring of blood glucose (SMBG) (28%), and 4) transportation difficulties (19%). Concerns about randomization to an unwanted treatment condition and fears of hypoglycemia or weight gain were rarely cited. Consenters and refusers did not differ in demographic characteristics, disease status, or family composition. Large differences were found between the two nurse recruiters: one experienced a 60% refusal rate, while the other experienced a 27% refusal rate.

CONCLUSIONS — Issues of convenience (increased clinic visits, transportation difficulties) and concerns about the demands of IT (increased injections and SMBG) were the predominant reasons for trial refusal. Patient characteristics did not differentiate consenters from refusers. However, recruiters differed greatly in study refusal rates, suggesting that provider behavior may be an important but understudied aspect of adolescent acceptance of randomized trials in general and IT in particular.

The results of the Diabetes Control and Complications Trial (DCCT) provided evidence that intensive therapy (IT) can improve glycemic control and reduce the risk of retinopathy, nephropathy, and neuropathy (1). Currently, the National Diabetes Information Clearinghouse and the DCCT Research Group recommend IT for patients ≥13 years of age (1,2). However, the DCCT was conducted with a carefully selected group of highly motivated, predominantly adult, IDDM patients. Because DCCT participants were not selected on the basis of their representativeness of the IDDM population at large (3), the suitability of IT for all patients, and for adolescent patients in particular, remains to be seen. IT is labor intensive, consisting of a rigorous regimen of increased insulin injection frequency, increased self-monitoring of blood glucose (SMBG), frequent insulin adjustment, and increased provider contact. In the DCCT, IT was associated with increased weight gain and increased frequency of severe hypoglycemia. Among adolescents, 48% became overweight compared with 28% of those offered conventional care. Further, the rate of severe hypoglycemia was significantly higher in adolescent, compared with adult, treated patients (4).

Recent research has confirmed some of the speculations reported in the lay press (5) that when the DCCT results are presented to patients, many are unwilling to pursue IT either because of the rigors of the regimen or the increased risk of hypoglycemia and weight gain. Thompson et al. (6) provided a leaflet documenting the purpose and results of the DCCT to a large sample of insulin-treated patients, ranging in age from 15 to 60. The patients were then asked to complete a questionnaire ascertaining their interest in pursuing IT. Only 60% stated that the DCCT results would encourage them to improve their diabetes control. Among these patients, only one-third were willing to take three or more injections per day, and only 18% were willing to attend clinic appointments on a monthly basis. Those with a history of severe hypoglycemia were less likely to pursue efforts at improved diabetes control. Female patients were more concerned about weight gain, and younger patients were the least willing to perform more blood glucose tests. Tamborlane, Gatcomb, Held, and Ahern (7) have recognized many of the special considerations in implementing DCCT results with children and adolescents, highlighting the importance of interdisciplinary treatment teams familiar with IT to assist young patients in overcoming such obstacles.

As part of a National Institutes of Health–supported randomized trial, we are comparing IT to conventional treatment (CT) when offered to a nonselect sample of adolescent patients. Described here are the characteristics of the first 99 adolescent patients approached; 56 consented to participate in the trial and 43 refused. Those who refused were interviewed as to their reasons for study refusal. We expected that

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Received for publication 23 June 1997 and accepted in revised form 24 October 1997.

Abbreviations: CDE, certified diabetes educator; CT, conventional treatment; DCCT, Diabetes Control and Complications Trial; IT, intensive therapy; SMBG, self-monitoring of blood glucose.

Table 1—*Reasons given by adolescents for refusing to participate in the trial*

Reason	Frequency	Percentage	Example
Clinic visits	18	42	Too frequent clinic visits Missing school/work because of clinic visits Hassle to come to clinic so often
SMBG	12	28	Must test blood too often Don't want to test during school Increased risk of infection
Shots/injections	13	30	Don't want to take more shots each day Increased risk of bruising
Transportation	8	19	Too far to travel (to clinic) on a regular basis Reliable transportation unavailable
Telephone contact	3	7	Hassle to maintain weekly phone contact with nurse
Randomization	2	5	Risk of randomization into unwanted study condition
Costs	1	2	Financial/material costs (e.g., testing strips, insulin, gas money, transportation fare)
Hypoglycemia	1	2	Fear that blood glucose may go too low if randomized to IT
Weight gain	0	0	Fear of weight gain if randomized to IT

Percentages do not add up to 100 because participants could indicate one or more reasons for refusal.

the prospect of randomization to a nonpreferred condition, the rigors of IT (increased SMBG and insulin injection frequency), issues of convenience (distance from the clinic), and concerns about possible hypoglycemia and/or weight gain might be associated with study refusal. We expected that youngsters from intact better-educated families might be more likely to participate.

RESEARCH DESIGN AND METHODS

Patients and procedures

Patients who met the following eligibility requirements were identified and approached during their regularly scheduled outpatient clinic visit. Those with a minimum age of 11 years, an IDDM duration of at least 1 year, and no evidence of intellectual impairment (normal classroom placement or verbal IQ >85) were considered eligible. In the presence of a parent or guardian, one of two study nurse recruiters took 10–20 min to provide each eligible patient (and his/her parent) with a written and oral description of the results of the DCCT (2) and a description of the requirements of the randomized trial comparing IT to CT. The nurse recruiters then offered to answer any questions. Of the first 99 consecutive patients approached, 56 agreed to participate and 43 refused. (All children and adolescents reported on in this study gave their voluntary assent to participation in accordance with the requirements of the Institutional Review Board of the University of Florida Health Science Center. Parental consent was also obtained.) Of the refusers, 26 stated they might consider entering the trial at a later time, and 17 expressed no interest in the trial at the present time or in the future.

Using a semi-structured interview, all 43 refusers were asked to provide relevant demographic information and to describe their reasons for refusing study participation. Responses were recorded verbatim, and later coded into 10 categories for analysis (Table 1). Category coding was conducted by two raters who exhibited 100% agreement.

All statistical procedures were conducted using SAS software version 6.04 for the personal computer (8).

RESULTS

Reasons for refusal

Reasons for refusal to participate are depicted by category in Table 1. The four most common reasons were *1*) difficulties associated with increased frequency of clinic visits (cited by 42% of the refusers), 2) problems associated with increased injections (30%) or 3) increased SMBG (28%), and *4*) transportation difficulties (19%).

Differences between consenters and refusers

Descriptive characteristics of the consenters and refusers are provided in Table 2. There were no differences between the groups in age, disease duration, sex or race distribution, current GHb levels, distance from clinic, family composition, or socioeco-

Table 2—*Descriptive characteristics of those who consented and those who refused*

	Consented	Refused
n	56	43
Age (years)	14.7 ± 1.7	15.0 ± 2.1
IDDM duration (years)	6.3 ± 3.5	5.3 ± 3.1
Male patients	28 (50)	24 (56)
Caucasian	50 (89)	38 (88)
HbA_{1c} (%)	9.6 ± 1.7	9.2 ± 1.7
One-way drive time to clinic (h)	1.3 ± 0.7	1.2 ± 0.6
One-parent households	18 (32)	9 (21)
Total family income ($1,000s)	47 ± 32	40 ± 20
With state-supported insurance	28 (50)	23 (54)
Parental education (≥ some college)		
Mothers	35 (64)	11 (42)
Fathers	21 (53)	12 (57)

Data are means ± SD or *n* (%). Age range for both groups was 11–18 years. Family income ranges (medians) for the groups of consenters and refusers were 9–155K (40K) and <5–82K (45K).

nomic status. More mothers in the consenter group (64%) than in the refuser group (42%) had at least some college education; this difference approached significance at $\chi^2 = 3.27$, df = 1, $P = 0.07$. Subsequent analyses were conducted in which refusers who indicated they might participate in the trial at a later date and refusers who indicated no interest in the trial at anytime were treated as separate groups; no differences between either refuser group and the consenter group emerged.

Recruiter effect

Both study recruiters were registered nurses. One (recruiter B) was a certified diabetes educator (CDE). Each approached approximately equal numbers of patients (n = 48 for recruiter A, and n = 51 for recruiter B). The refusal rate for recruiter A was 60% compared with 27% for recruiter B, a highly significant difference of $\chi^2 = 10.94$, df = 1, $P = 0.0001$.

CONCLUSIONS — Adolescents in this study were provided with both oral and written descriptions of the results of the DCCT (2). Nevertheless, many of these adolescents subsequently refused to participate in a randomized trial of IT. We expected that concerns about randomization, increased hypoglycemia, and weight gain would be common reasons for refusal; however, concerns of this type were rarely, if ever, reported by the adolescents. Instead, issues of convenience (increased clinic visits, transportation difficulties) and concerns about the intensive nature of the treatment per se (increased injections and SMBG) were the predominant reasons for trial refusal. These data are consistent with that of Thompson et al. (6), who also reported patient unwillingness to increase the frequency of insulin injections and clinic visits.

While increased clinic visits was the most common reason cited for study refusal, there was no difference in drive time to the clinic between those who consented and those who refused. In fact, the groups were comparable in demographic characteristics, disease status, and family composition. Mothers of consenters were more educated, but this effect only approached significance. These data suggest that those likely to consent or refuse a randomized trial of IT cannot be readily predicted by the patient characteristics studied here. In future studies, investigators may wish to collect additional medical history or psychosocial data in an effort to identify better predictors of who consents or refuses to participate in a randomized trial of IT.

In this study, provider characteristics had a strong effect on who consented or refused the trial. Although the recruiters provided the same information to potential trial participants, 60% of adolescents refused when asked by one recruiter. Only 27% refused when asked by the other recruiter. We can only speculate on the cause of this effect. For example, the less successful nurse recruiter was new to the program, while the more successful recruiter was a CDE with a longer established relationship with the adolescents. Communication style and ease with adolescents may also be involved. Although the literature addressing trial participation and IT acceptance has focused almost exclusively on patient characteristics, provider behavior may be an equal, if not more important, area for further study.

Acknowledgments — This study was supported by National Institutes of Health Grant R01-HD13820. We are grateful to the adolescents and families who participated in this research.

References

1. Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977–986, 1993
2. U.S. Department of Health and Human Services: *Diabetes Control and Complications Trial (DCCT)*. Washington, DC, U.S. Govt. Printing Office, 1994 (NIH publ. no. 94-3874)
3. Glasgow RE, Eakin KG, Toobert DJ: How generalizable are the results of diabetes self-management research? The impact of participation and attrition. *Diabetes Educ* 22:573–585, 1996
4. Diabetes Control and Complications Trial Research Group: Effect of intensive treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. *J Pediatr* 125:177–188, 1994
5. Blakeslee S: Program to cut risks of diabetes surprisingly fails to lure patients. *New York Times*, 28 February 1994: Sect. A, p. 1
6. Thompson C, Cummings J, Chalmer J, Gould G, Newton R: How have patients reacted to the implications of the DCCT? *Diabetes Care* 19:876–879, 1996
7. Tamborlane WV, Gatcomb P, Held N, Ahern J: Implications of the DCCT results in treating children and adolescents with diabetes. *Clin Diabetes* 12:115–116, 1994
8. SAS 6.04 software computer program. MS-DOS version. Cary, NC, SAS Inst., 1987