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Effectiveness Of A Diabetic Ketoacidosis Prevention Intervention In Children With Type 1 Diabetes

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Effectiveness of a Diabetic Ketoacidosis Prevention Intervention in Children with Type 1 Diabetes

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EFFECTIVENESS OF A DIABETIC KETOACIDOSIS PREVENTION INTERVENTION IN CHILDREN WITH TYPE 1 DIABETES

Diabetic ketoacidosis (DKA) continues to be common in youth with type 1 diabetes (T1D), with up to 10% of patients reporting at least 1 DKA event annually. Since many of these events should be preventable, we developed a brief educational intervention that was easy to implement in a busy practice setting and tested its effectiveness in reducing emergency department (ED) usage. Subjects aged > 13 years old or the parents of children aged ≤ 13 were given a short pre-test about their knowledge of signs and symptoms of DKA and sick day management practices. They were then instructed on sick day management specific to their treatment modality (pump vs. injection). Finally, they were given a printed tool for sick day management. 244 subjects in our pediatric T1D clinic received the intervention as part of a regular office visit. 76 of these subjects were given a follow-up survey 6-12 months later. Subjects/parents scored higher on the post-test than the pre-test (61.6% vs. 55.0% correct; p=0.007). Subjects/parents also recognized more diabetes sick days (p=0.014) following the intervention and called the emergency line more frequently (p=0.032). Among all subjects, ED use was reduced to 0.13 from 0.22 visits per person-year (p=0.07). ED visits significantly decreased among subjects > 13 years of age (0.10 per person-year after versus 0.21 per person-year prior; p=0.024). A short educational intervention and printed management tool is effective in improving sick-day and DKA knowledge, increasing utilization of diabetes emergency line consultations, and reducing ED visits, especially in teenagers.

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Background

Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in young people with type 1 diabetes (T1D), impacting thousands of Americans each year. DKA is responsible for approximately 50% of the deaths in people with diabetes under 24 years old(1, 2), and over 75% of deaths in women under age 30 (4,5). While the incidence of DKA in patients with undiagnosed diabetes is relatively difficult to influence, the majority of patients with DKA have known diabetes. It is estimated that up to 50% of these cases of DKA may be preventable with appropriate education and regimen adherence(2). Despite the high frequency of DKA admissions among this population, few of the studied interventions have been successfully incorporated into standard practice. With the rising incidence of T1D in the United States(3), it is becoming increasingly important to find innovative approaches to DKA prevention that can be easily integrated into existing practice structures.

Additionally, the burden on the healthcare system is also quite significant. It is estimated that a single episode of DKA costs about $11,000 to treat, and the total cost of all episodes of DKA in the United States in 2004 was more than $1.8 billion(2, 4). This represents over a quarter of the total cost of T1D in America. The cost savings associated with the prevention of DKA are substantial and can justify prevention programs that are relatively expensive(5). Additionally, interventions that allow for the management of mild DKA in the outpatient setting, rather than requiring inpatient admission, can have a large impact on the cost to the healthcare system. With approximately 1.25 milllion individuals with T1D in the United States at this time, the public health implications of a reduction in DKA incidence and hospitalization within the United States are enormous(6).

Given the high contribution of DKA to the overall morbidity and mortality associated with T1D in children and adolescents, prevention programs have long been a focus among researchers. The guidelines for sick day management are an important piece of prevention education, as lapses in blood glucose and ketone monitoring, as well as errors in insulin dosing when endogenous requirements increase – as they do in periods of acute illness – may result in DKA(1, 7). The tenets of these guidelines are consistent throughout the literature: monitor blood glucose and blood or urine ketones frequently, never stop insulin administration completely, watch for dehydration, treat the underlying illness, and follow guidelines for adjusting insulin dosages(1). Despite having such clear and successful guidelines for preventing DKA during sick days, rates of DKA have not decreased over the last few decades(8). It is important to find ways to review these guidelines with patients that can be implemented quickly in a busy practice setting and that can lead to successful reductions in DKA incidence

Methods

This study is a pre-post observational cohort study designed to assess the efficacy of an in-office educational module on sick day management in improving knowledge about DKA and reducing ED and hospital visits among children ages 2-22. Subjects were recruited in a convenience sample from patients in the waiting room at an academic pediatric endocrinology practice (Figure 1). Inclusion criteria included having a diagnosis of T1D and being treated by one of the pediatric providers at the clinic. There were no exclusion criteria. Those subjects who agreed to participate in the study were given a pre-test with multiple choice questions about DKA and sick day management. The questions were divided into “skills” and “understanding” subsets to reflect skills in managing diabetes during sick days and knowledge of the proximal causes of DKA. Two different versions of the pre-test were administered, one reflecting multiple daily injection regimens and one reflecting insulin pump regimens. The surveys were completed by the patient if they were over the age of 13, or the parent if the child was 13 years of age or younger.

Additional information on the number of ED visits, frequency of diabetes sick days, and frequency of calls to the diabetes emergency line were collected from the patient, as well as information on perceived comfort and support in their understanding and management of DKA. Emergency line calls and diabetes sick day frequency were measured via a Likert scale of frequency, where zero was least frequent and five was most frequent. Gender, age, duration of diabetes, age at diagnosis of diabetes, and current hemoglobin A1c (HbA1c) levels were recorded from the electronic medical record. ZIP codes were collected from the medical record as well, and the median income of that ZIP code was recorded as a proxy for socioeconomic status. Diabetes clinicians (physicians, advanced practice nurses, or certified diabetes educators) then reviewed sick-day guidelines with the patients/parents, and patients were sent home with a printed algorithm of sick day management instructions with magnetic backing that could be placed in a convenient location, such as refrigerator door. (Figure 2).

Six months to one year later, subjects were approached at their regularly scheduled office visits to take a post-test, consisting of the same knowledge and skills questions, to assess retention of the information. They again reported use of the emergency line, ED visits, and frequency of diabetes sick days, as well as comfort and support in managing DKA. HbA1c levels were recorded from the medical record. Additionally, subjects were asked about their use of the algorithm.

The primary outcome was ED visit frequency; it was hypothesized that ED visits would decrease following the intervention. Secondary outcomes included frequency of reported sick days and calls to the emergency line, which were hypothesized to increase following the intervention, and HbA1c levels, which were hypothesized to decrease, as better sick day management in patients with frequent sick days would alter average blood glucose levels. Finally, test scores were hypothesized to be higher following the intervention, showing that patients had retained the information that they learned.

Descriptive statistics, univariate analyses, and pre-post comparisons were performed using SAS (version 9.4, SAS Inc. Cary, NC). Baseline sample characteristics were compared between those patients who did follow up and those who did not follow up to ensure that the group that followed up was representative of the study population. Paired t-tests and Wilcoxon signed rank tests were performed for the parametric and non-parametric values, respectively, to see if there was any significant difference before and after the intervention in those subjects who did follow up. The results were dichotomized into those patients who were greater than 13 years of age (who had completed the tests themselves) and those patients who were 13 years of age or younger (whose parents had completed the tests). While this was a post-hoc analysis and the study was not powered to examine sub-groups, such exploratory analyses are important to determine the appropriate next steps in this research.

Results

Of the 244 subjects that completed the intervention, 76 completed the follow-up 6-12 months later. Baseline data between those who followed up and those who did not follow up were compared to ensure that those who did not follow up were not significantly different from those who did follow up (table 1). Gender breakdown, age, duration of diabetes, age at diagnosis of diabetes, income, scores on the pre-test (including understanding and skills sub-scores), and number of ED visits were not significantly different between the two groups. HbA1c, however, was significantly lower in the group that did not follow up than in the group that did follow up (8.05 vs. 8.55, p=0.034).

For subjects who did follow up, test scores, knowledge and skill scores, HbA1c levels, ED visits, and sick day and emergency line call frequency were compared before and after the intervention (table 2). The scores of the post-test were significantly higher than the pre-test, averaging 55.0% correct prior to the intervention compared to 61.6% correct afterwards (p=0.007). The sub-score for understanding increased significantly with the intervention (59.2% after vs. 53.2% prior, p=0.019); the increase in the skills sub-score approached statistical significance (63.3% after vs. 56.4% prior, p=0.059). Similarly, ED visits were also lower (0.13 per person-year following the intervention versus 0.22 per person-year before), though this was not quite statistically significant (p=0.070). Notably, subjects/parents called the emergency line more frequently (1.20 after vs. 0.86 prior, p=0.032), and recognized more diabetes sick days (1.57 after vs. 1.17 prior, p=0.014). HbA1c levels did not change significantly (8.35% after intervention compared with 8.55% prior, p=0.336),

A post-hoc analysis was performed, comparing the 42 subjects over the age of 13, who completed the pre- and post-tests themselves, with the 34 subjects age 13 or younger, whose guardians completed the pre- and post-tests (Table 3). In the older subgroup, scores on the post-test were not significantly higher either overall (60.9% after vs. 55.8% prior, p=0.089), or in either of the sub-scores (understanding: 58.6% after vs. 55.2% prior, p=0.280; skills: 62.6% after vs. 56.1% prior, p=0.209). However, ED visits did decrease significantly following the intervention (0.10 per person-year after vs. 0.21 per person-year prior, p=0.024), and emergency line call frequency increased significantly following the intervention (1.05 after vs. 0.60 prior, p=0.044), while the reported frequency of diabetes sick days was not significantly different (1.62 after vs. 1.26 prior, p=0.122).

In the younger subgroup, subjects' parents had higher overall scores on the post-test following the intervention (62.5% after vs. 54.2% prior, p=0.039) as well as higher understanding sub-scores (60.0% after vs. 50.6% prior, p=0.030), though the skills sub-scores were not significantly higher (64.3% after vs. 56.7% prior, p=0.158). Frequency of diabetes sick days (1.50 after vs. 1.06 prior, p=0.066), ED visit frequency (0.18 per person-year after vs. 0.24 per person-year prior, p=0.535), and calls to the emergency line (1.38 after vs. 1.18 prior, p=0.461) did not change significantly with the intervention. In both subgroups, A1c levels did not change significantly following the intervention.

Discussion

The sick day management intervention successfully improved recognition of diabetes sick days, increased utilization of the emergency line, and improved scores on the post-test compared with the pre-test. ED visits were significantly decreased for subjects > 13 years old. Subjects retained the information that they learned and applied it in recognizing their own diabetes sick days and calling the emergency line first rather than going directly to the ED.

The primary outcome in this study was frequency of visits to the emergency department. The decrease in ED visits must be discussed in the context of the increased calls to the emergency line and increased frequency of reported sick days. The subgroup analyses showed an interesting age dichotomy; there were no statistically significant changes in emergency line calls, sick day frequency, or ED visits among the younger subjects, while older subjects had statistically significant reductions in the number of ED visits and increases in the number of calls to the emergency line. This group of older subjects was the only group in which ED visits were statistically significantly reduced. It seems that the adolescent subjects became more aware of the resources available to them following the intervention, while the parents of younger subjects may have already been using these resources more appropriately prior to the intervention, so that their behavior did not change significantly. It is also noteworthy to consider the possible differences in the etiologies of hyperglycemia and ketosis in the two subgroups: intercurrent illnesses (gastroenteritis, respiratory infections) in the younger groups, compared to insulin omission in the older subjects. This point is purely speculative, however; our study design was unfortunately not able to explore this question.

Prior studies have found reduced incidence of DKA and hospital/ED usage in patients who have received office-based interventions, and this intervention joins those as a successful option for reducing DKA. One study looked at DKA prevention using an office-based education program that focused on recognizing symptoms of DKA and sick day guidelines. The intervention successfully reduced the incidence of DKA from 12 events to 4 events per 100 patient-years(9). Another more extensive intervention involved randomizing families to standard care or the use of Care Ambassadors, who worked with families to remind them about appointments, and documenting the follow-ups as they occurred. Hospital and emergency department (ED) usage was reduced by 50% in the intervention group, including for cases of DKA(10). This study adds to our understanding of this phenomenon by examining the ways in which these outcomes may have been achieved.

The comparison of pre- and post-test scores was an important investigation into the extent to which knowledge was retained. By using a pre- and post-test, we tried to determine if patients were simply following an algorithm or if they internalized a better understanding of the issues at stake in sick day management. Overall, the scores on the post-test were higher than on the pre-test, and the understanding sub-score was significantly higher following the intervention. The significant increase in understanding sub-score suggests that much of the information retained from the intervention related to what DKA is and how dangerous it can be. The fact that the skill sub-score was not significantly different is likely related to the power of the study to detect this difference, as the p-value was borderline at 0.059, though it is possible that subjects simply may not have remembered the specific steps they should take to manage diabetes sick days. This same pattern was seen in the younger subject sub-group. The test scores were not statistically significantly different in the older subject sub-group, however. Perhaps these teenagers were not paying as close attention to the intervention as the parents of younger children did, or maybe they did not retain the information as well or as concretely as the parents. Further studies must be performed to better understand how well teenagers retain information from such educational sessions.

While this intervention is appropriate for implementation among the general clinic populations, there are individuals with recurrent DKA admissions who may require more intensive interventions against DKA. Ellis et al randomized families to standard care or multisystemic psychotherapy (MST), which focuses on alleviating barriers to adherence in all areas of an adolescent’s life, for two years. The program reduced DKA admissions for 24 months following the intervention, and reduced HbA1c during the time that the therapy was taking place. Furthermore, this relatively costly program ended up being cost-effective due to decreased DKA admissions(5). The most extreme intervention program involved removing patients from dysfunctional families and placing them in foster care or residential treatment programs. The incidence of DKA was reduced from 1.14 to 0.29 episodes per patient per year. Obviously, it is important to carefully target such interventions to families that are unable to safely care for their children in the current environment(9).

There are some limitations inherent to the design of this study. It was not specifically designed for subgroup analyses, and the data from the subgroup analysis cannot be considered definitive until the study is repeated with a larger sample size. Additionally, the study may have been under-powered even when conducting analyses of the full data set. For example, with 76 subjects, a power of 0.8, a type I error of 0.05, and a standard deviation of 0.437, the detectable difference for ED visits would be +/- 0.142 per person-year. The statistical non-significance of some results could be because the study was underpowered. This topic will need to be studied further with a larger sample size to determine whether or not the intervention truly impacts ED visits in the overall clinic population, or if it is only statistically significant among the older subjects. Additionally, only about one third of the subjects completed the follow-up survey. While analyses were performed to ensure that those patients who did follow up were a representative population of the subjects in the initial phase of the study, there are many potential confounding factors that were not measured. This was partially ameliorated by the fact that each subject served as his or her own control, comparing the period prior to the intervention to the period following the intervention. Thus, only the subjects who followed up were included in the pre-intervention measures reported here.

There are several future directions in which this research could proceed. A similar study with a larger number of subjects could solve the problems with statistical power that were encountered. The study could even be repeated in the same clinic setting and give new results; the clinic has now switched over to an electronic medical record, and all calls to the emergency line are recorded in each patient's medical record. Historical report was the best option for data collection at the time of the study, but in the future data could be pulled directly from the chart without having to rely on patient report for emergency line usage or ED visit frequency. In addition, a physical, printed algorithm may not be the best way to reach the target population of this intervention. A study could be designed with the algorithm in app form for smartphones so that it is always accessible. Finally, a cost effectiveness analysis should be undertaken to determine if such interventions save money for families and insurance companies. Such sessions are unlikely to be adopted in a widespread fashion unless insurance companies will reimburse for them, and this analysis would be the first step in securing such reimbursements.

In summary, this study was designed to investigate if a brief in-office intervention on sick day management, as well as a take-home algorithm, could help reduce risk of DKA by increasing recognition of diabetic sick days and calls to the emergency line and reducing ED visits. It was found that subjects retained the information they were taught, even up to a year after the intervention, and that they recognized sick days and called the emergency line more regularly. Teenage subjects had significantly fewer ED visits following the intervention, though the decrease in younger subjects did not reach statistical significance, which could imply that such interventions should be targeted to older patients. This intervention was successful in its aims, and could result in improved health outcomes and decreased costs to the healthcare system. It should be examined in other contexts and in a targeted fashion for teenagers with diabetes to see if it is a generalizable intervention that could be routinely delivered to those patients at highest risk for DKA.

References

1. Laffel L. Sick-day management in type 1 diabetes. *Endocrinology and metabolism clinics of North America*. 2000;29(4):707-23.
2. Bismuth E, Laffel L. Can we prevent diabetic ketoacidosis in children? *Pediatric diabetes*. 2007;8 Suppl 6:24-33.
3. Dabelea D, Mayer-Davis EJ, Saydah S, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *JAMA : the journal of the American Medical Association*. 2014;311(17):1778-86.
4. Realsen J, Goettle H, Chase HP. Morbidity and mortality of diabetic ketoacidosis with and without insulin pump care. *Diabetes technology & therapeutics*. 2012;14(12):1149-54.
5. Ellis D, Naar-King S, Templin T, et al. Multisystemic therapy for adolescents with poorly controlled type 1 diabetes: reduced diabetic ketoacidosis admissions and related costs over 24 months. *Diabetes care*. 2008;31(9):1746-7.
6. CfDC. National Diabetes Statistics Report. 2014.
7. Brink S, Joel D, Laffel L, et al. Sick day management in children and adolescents with diabetes. *Pediatric diabetes*. 2014;15 Suppl 20:193-202.
8. Weber C, Kocher S, Neeser K, Joshi SR. Prevention of diabetic ketoacidosis and self-monitoring of ketone bodies: an overview. *Current medical research and opinion*. 2009;25(5):1197-207.
9. Kaufman FR, Halvorson M. The treatment and prevention of diabetic ketoacidosis in children and adolescents with type I diabetes mellitus. *Pediatric annals*. 1999;28(9):576-82.
10. Laffel L, Brackett J, Ho J, Anderson BJ. Changing the process of diabetes care improves metabolic outcomes and reduces hospitalizations. *Quality management in health care*. 1998;6(4):53-62.

Tables

Table 1: Subjects who followed up compared with those who did not follow up

	Followed up (n=76)	Did not follow up (n=168)	p-value*
Gender	55% male	52% male	0.614
Age	13.86	14.01	0.804
Duration of diabetes	5.71	6.34	0.460
Age at diagnosis of diabetes	8.15	7.79	0.547
Income	$83,511	$90,262	0.214
HbA1c	8.55	8.05	**0.034**
% correct	55.0%	56.3%	0.703
Understanding sub-score	53.2%	54.5%	0.730
Skill sub-score	56.4%	57.6%	0.777
ED Visits	0.22	0.22	0.993

*p-values from paired t-test, chi square test

Table 2: Pre-post intervention comparisons (n=76)

	Mean before	Mean after	Difference	p-value*
HbA1c (%)	8.55	8.35	-0.20	0.336
% correct	55.0%	61.6%	6.6%	**0.007**
Understanding sub-score	53.2%	59.2%	6.1%	**0.019**
Skill sub-score	56.4%	63.3%	7.0%	0.059
ED Visits (visits per person-year)	0.22	0.13	-0.09	0.070
Diabetes sick day frequency (Likert)	1.17	1.57	0.39	**0.014**
Emergency line call frequency (Likert)	0.86	1.20	0.34	**0.032**

*p-values from paired t-test, Wilcoxon signed rank test

Table 3: Results Dichotomized by Age				
	Mean before	Mean after	Difference	p-value*
Age > 13 (n=42)				
HbA1c	8.54	8.59	0.06	0.833
% correct	55.8%	60.9%	5.1%	0.089
Understanding sub-score	55.2%	58.6%	3.3%	0.280
Skill sub-score	56.1%	62.6%	6.5%	0.209
ED Visits	0.21	0.10	-0.12	**0.024**
Diabetes sick day frequency	1.26	1.62	0.36	0.122
Emergency line call frequency	0.60	1.05	0.45	**0.044**
Age ≤ 13 (n=34)				
HbA1c	8.57	8.06	-0.51	0.107
% correct	54.2%	62.5%	8.3%	**0.039**
Understanding sub-score	50.6%	60.0%	9.4%	**0.030**
Skill sub-score	56.7%	64.3%	7.6%	0.158
ED Visits	0.24	0.18	-0.06	0.535
Diabetes sick day frequency	1.06	1.50	0.44	0.066
Emergency line call frequency	1.18	1.38	0.21	0.461
*p-values from paired t-test, Wilcoxon signed rank test				

Figure 1: Recruitment

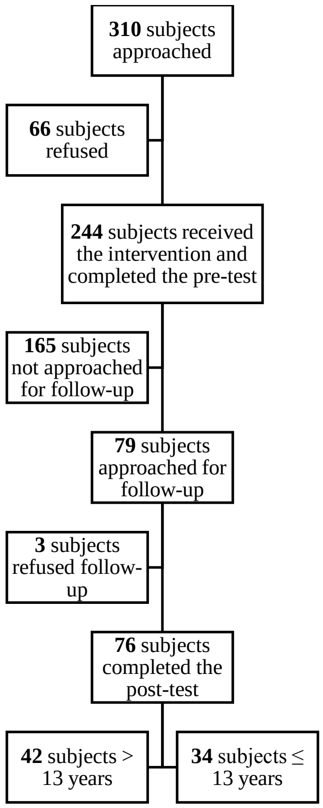

Figure 2: Sick Day Management Algorithms