Letters to the editor

The multinational Conversations and Reactions Around Severe Hypoglycemia (CRASH) study: Impact of health care provider communications and recommendations on people with diabetes

ABSTRACT

The multinational CRASH study found that substantive recommendations from health care providers were predictive of actions taken by people with diabetes during and after a severe hypoglycemic event, which highlights the importance of equipping people with actionable strategies to prevent and treat severe hypoglycemia should a severe hypoglycemic event arise.

Introduction

Hypoglycemia is a major barrier to achieve optimal glycemic control in people with diabetes (PWD) and places significant psychosocial burden on them and their families. We conducted a multinational, cross-sectional observational study, *Conversations and Reactions Around Severe Hypoglycemia (CRASH)*, to understand the preparation for and management of severe hypoglycemia from the perspectives of both PWD and caregivers (CGs). The primary aim of this analysis was to explore the factors, including health care provider (HCP) communications and patient and disease characteristics, that were most predictive of actions taken by PWD during and after severe hypoglycemic events.

Material and methods

This study included CGs and adults with type 1 diabetes (T1DM) or insulin-treated type 2 diabetes (T2DM) who experienced ≥ 1 severe hypoglycemic event in the past 3 years. Severe hypoglycemia was defined as a low blood glucose event that PWD could not treat by themselves. Participants across 6 countries (US, UK, Germany, Canada, Spain, and France) completed a web-based questionnaire around their severe hypoglycemic experiences during July 2018 – February 2020. The survey questions were developed uniquely for this research, but included the Gold score[1], which asks PWD to rate the degree to which they are aware a hypoglycemic episode is commencing on a linear scale (1 = always aware, 7 = never aware). A rating of ≥ 4 indicates the PWD has 'impaired awareness of hypoglycemia'. Study methodology and country-specific findings were reported previously[2–4].

Adjusted multivariable logistic regression models of PWD data were utilized to analyze predictors of actions taken during and after the most recent severe hypoglycemic event. Possible predictive variables were divided into seven variable blocks, ordered temporally as follows: [1] demographics, [2] diabetes and severe hypoglycemia history, [3] HCP communications on severe hypoglycemia and glucagon, [4] locations and symptoms of most recent severe hypoglycemic event, [5] recovery time and actions during most recent severe hypoglycemic event, [6] HCP recommendations made before most recent severe hypoglycemic

event, and [7] HCP recommendations made after most recent severe hypoglycemic event (blocks 1–7, Table 1). Variable selection for the final multivariable model was performed using an iterative, hierarchical process, entering the variables per sets of variables (blocks) sequentially into the process, performing a stepwise selection (entry $p < 0.25$ and stay $p < 0.10$) within each block. Thereby, variables selected in previous blocks are always retained, even with $p > 0.1$ due to addition of the new variables in later blocks[5,6].

Results

Table 1 presents characteristics of study participants (N = 2132 [PWD 1141; CGs 991]) by diabetes types. The mean age of PWD was 48.3 (T1DM) and 55.4 (T2DM) years. Both people with T1DM and T2DM reported a median of 1 (Q1:1, Q3:2) severe hypoglycemic event in the past 12 months. Impaired hypoglycemia awareness, defined as Gold score ≥ 4, was reported in 33.6% and 23.6% of people with T1DM and T2DM, respectively.

With regards to HCP-patient communications, >70% of participants, both PWD and CGs, reported that HCPs did not discuss severe hypoglycemia with them at every visit, and approximately one-third of participants also reported that they did not discuss the most recent severe hypoglycemic event with HCPs. Notably, 25.4% of people with T1DM and 63.6% of people with T2DM reported 'No' to the question, 'Has an HCP ever discussed glucagon with you?'. A significant proportion of all participants reported negative emotional impact while experiencing or witnessing the most recent severe hypoglycemic event ('scared' [62–77%], 'unprepared' [42–58%], 'helpless' [50–61%]).

Modeling data suggested that actions taken during and after the most recent severe hypoglycemic event were most significantly influenced by HCP recommendations compared to other variables examined. Specifically, PWD were significantly more likely to have received a glucagon injection during their recent severe hypoglycemic event (odds ratio [95% confidence interval]: 6.565 [3.533, 12.200]) or use professional health care resources (7.348 [4.965, 10.874]) during the severe hypoglycemic event if their HCPs recommended to do so. Correspondingly, PWD were more likely to change their behavior around glucagon (i.e.

Table 1
Sample Characteristics by Study Subgroup.

Variables by Category	People with Type 1 Diabetes (N=633)	People with Type 2 Diabetes (N=508)	Caregivers Type 1 Diabetes (N=522)	Caregivers Type 2 Diabetes (N=469)	P-values[a]
[1]. Demographics					
Gender, female, n (%)	327 (51.7)	186 (36.6)	359 (68.8)	304 (64.8)	<.0001[d]
Age, years, mean (SD)	48.3 (14.1)	55.4 (12.7)	47.0 (12.6)	49.7 (14.0)	<.0001[b]
College degree, n (%)	461 (72.8)	338 (66.5)	365 (69.9)	320 (68.2)	0.1210[c]
[2]. Diabetes and SH History					
Time since diabetes diagnosis, years, mean (SD)	26.0 (15.5)	13.8 (8.5)	21.3 (16.7)	18.0 (13.3)	<.0001[b]
Impaired awareness hypoglycemia (Gold score ≥4), n (%)[e]	213 (33.6)	120 (23.6)	182 (34.9)	177 (37.7)	<.0001[c]
Number of SH events in the past 12 months, n (%)					0.1471[b]
Mean (SD)	3.3 (8.3)	2.3 (4.9)	3.3 (6.9)	2.5 (5.3)	
Median (Q1, Q3)	1 (1, 2)	1 (1, 2)	1 (1, 3)	1 (1, 2)	
0	103 (16.3)	91 (17.9)	81 (15.5)	83 (17.7)	
1	278 (43.9)	234 (46.1)	222 (42.5)	191 (40.7)	
2	105 (16.6)	80 (15.7)	83 (15.9)	80 (17.1)	
≥3	147 (23.2)	103 (20.3)	136 (26.1)	115 (24.5)	
Number of SH events in the past 3 years					0.0245[b]
Mean (SD)	8.5 (17.1)	5.3 (11.1)	8.3 (17.4)	5.9 (10.8)	
Median (Q1, Q3)	3 (1, 6)	2 (1, 5)	3 (1, 6)	3 (2, 5)	
[3]. HCP Communication on SH and Glucagon					
Discussion of SH with HCP, n (%)					<.0001[d]
At every visit	221 (34.9)	173 (34.1)	140 (26.8)	82 (17.5)	
At some visits	326 (51.5)	251 (49.4)	265 (50.8)	236 (50.3)	
Have not discussed	86 (13.6)	84 (16.5)	117 (22.4)	151 (32.2)	
Ever discussed glucagon with HCP, YES, n (%)	440 (69.5)	126 (24.8)	338 (64.8)	150 (32.0)	<.0001[d]
[4]. Locations and Symptoms of Most Recent SH					
Alone during SH, n (%)	141 (22.3)	186 (36.6)	80 (15.3)	74 (15.8)	<.0001[c]
At home during SH, n (%)	517 (81.7)	409 (80.5)	429 (82.2)	394 (84.0)	0.5513[c]
Number of neuroglycopenic symptoms, mean (SD)	4.9 (3.4)	3.9 (2.9)	5.1 (3.3)	4.7 (3.5)	<.0001[b]
Number of autonomic symptoms, mean (SD)	2.8 (2.0)	2.7 (1.7)	2.3 (1.8)	2.5 (1.9)	<.0001[b]
[5]. Recovery Time and Actions During Most Recent SH					
Time to recovery of SH, n (%)					0.0005[b]
00-15 minutes	100 (16.4)	78 (15.8)	77 (15.1)	38 (8.3)	
15-30 minutes	217 (35.7)	171 (34.7)	196 (38.5)	162 (35.4)	
30-60 minutes	164 (27.0)	135 (27.4)	125 (24.6)	129 (28.2)	
60 minutes or more	127 (20.9)	109 (22.1)	111 (21.8)	128 (28.0)	
Used sugars during SH, n (%)	522 (82.5)	438 (86.2)	421 (80.7)	379 (80.8)	0.0704[c]
Injected Glucagon during SH, n (%)	85 (13.4)	39 (7.7)	77 (14.8)	55 (11.7)	0.0029[c]
Any health care contact during SH (called ambulance, called HCP, went to ER), n (%)	125 (19.7)	91 (17.9)	135 (25.9)	147 (31.3)	<.0001[c]
Scaled sum of acute emotional impact scores (0-100%), mean (SD)	60.2 (26.7)	62.3 (27.8)	59.5 (27.9)	61.7 (26.8)	0.2529[b]
Scaled sum of life domain impacts (0-100%), mean (SD)	13.7 (17.4)	13.0 (16.6)	12.3 (16.2)	12.6 (16.1)	0.9267[b]
[6]. HCP Recommendations Made Before Most Recent SH					
Take sugar, n (%)	488 (77.1)	396 (78.0)	351 (67.2)	294 (62.7)	<.0001[c]
Inject glucagon, n (%)	254 (40.1)	64 (12.6)	206 (39.5)	70 (14.9)	<.0001[c]
Call HCP/ambulance or go to ER, n (%)	136 (21.5)	128 (25.2)	154 (29.5)	150 (32.0)	0.0004[c]
[7]. HCP Recommendations Made After Most Recent SH					
Change insulin regimen (timing/dosing), n (%)	220 (34.8)	208 (40.9)	198 (37.9)	189 (40.3)	0.1276[c]
Change meal plan, n (%)	77 (12.2)	97 (19.1)	76 (14.6)	84 (17.9)	0.0054[c]
Measure BG more often or get CGM, n (%)	195 (30.8)	177 (34.8)	156 (29.9)	128 (27.3)	0.0782[c]
Start carrying sweets/sugar, n (%)	138 (21.8)	212 (41.7)	113 (21.6)	136 (29.0)	<.0001[c]
Obtain glucagon or keep it closer, n (%)	62 (9.8)	42 (8.3)	58 (11.1)	39 (8.3)	0.3460[c]
PWD/CG Actions After Most Recent SH[f]					
Change insulin regimen (timing/dosing), n (%)	235 (37.1)	186 (36.6)	238 (45.6)	193 (41.2)	0.0086[c]
Change meal plan, n (%)	91 (14.4)	119 (23.4)	111 (21.3)	118 (25.2)	<.0001[c]
Measure BG more often or get CGM, n (%)	362 (57.2)	260 (51.2)	289 (55.4)	240 (51.2)	0.1062[c]
Start carrying sweets/sugar, n (%)	291 (46.0)	296 (58.3)	240 (46.0)	264 (56.3)	<.0001[c]
Obtain glucagon or keep it closer, n (%)	57 (9.0)	27 (5.3)	65 (12.5)	41 (8.7)	0.0010[c]

Acute Emotional Impact[g]

Table 1 (*continued*)

Variables by Category	People with Type 1 Diabetes (N=633)	People with Type 2 Diabetes (N=508)	Caregivers Type 1 Diabetes (N=522)	Caregivers Type 2 Diabetes (N=469)	P-values[a]
Scared	393 (62.1)	317 (62.4)	403 (77.2)	341 (72.7)	<.0001[c]
Unprepared	296 (46.8)	293 (57.7)	221 (42.3)	224 (47.8)	<.0001[c]
Helpless	387 (61.1)	295 (58.1)	259 (49.6)	239 (51.0)	0.0001[c]

This analysis included data from the US, UK, Germany, Canada, Spain, and France cohorts of the global CRASH study.

Blocks for the multivariable model are represented by sections 1–7 of the table. Only PWD respondent data (columns 1 and 2) were modelled.

Abbreviations: BG, Blood Glucose; CG, Caregiver; CGM, Continuous Glucose Monitoring; ER, Emergency Room; HCP, Health Care Provider; PWD, People with Diabetes; SD, Standard Deviation; SH, Severe Hypoglycemia, Q1, 1st quartile; Q3, 3rd quartile.

[a] p-values compare the overall difference between the 4 study arms.

[b] Wilcoxon Rank Sum test (non-parametric test for continuous data).

[c] Chi-square test (Binary data).

[d] Cochran-Mantel-Haenszel Test (categorical data with >2 categories).

[e] The Gold score has only been validated for PWD.

[f] Only includes those who took the action.

[g] Data presented are the percentage of participants that 'agreed' or 'strongly agreed' that the most recent severe hypoglycemic event made them feel 'scared', 'unprepared', or 'helpless'.

obtain or keep glucagon closer) (21.272 [10.066, 44.955]) or change their insulin regimen (16.502 [10.500, 25.937]) after the most recent severe hypoglycemic event if recommended by a HCP. Significant predictors were also noted for other actions taken by PWD (i.e. more glucose monitoring, carry snack/food, change meal plan) after the most recent severe hypoglycemic event following HCP recommendations, with no significant differences between type of diabetes, except for the recommendation to 'change meal plan' in which patients with T1DM were less likely to change their meal plans than patients with T2DM (0.574 [0.379, 0.869]).

Discussion

To our knowledge, CRASH is the first multinational observational study providing insights on the preparation for and management of severe hypoglycemia from the perspectives of both PWD and CGs. Clinical guidelines recommend that conversations around hypoglycemia happen at every encounter.[7] Importantly, the results demonstrate that the substance of HCP-patient communications has a significant impact on patient actions. It is reassuring to find that the specific actions taken were those as recommended by HCPs during and after their most recent severe hypoglycemic event. CGs should be made aware of the recommendations from these conversations, as they are often the ones to assist the PWD to recover from severe hypoglycemic events.

Limitations of this study included the possibility of recall bias due to the self-reported nature of data collection. Further, this study was completed before ready-to-use glucagon options were available in respective countries; a future study is warranted to evaluate the impact of ready-to-use glucagon on clinical practice and patient outcomes. Finally, though this was a study of people who had experienced a recent severe hypoglycemic event, conversations were not reported at each encounter, suggesting that conversations and education are presumably even more infrequent for those who have not yet experienced severe hypoglycemia.

This multinational CRASH study highlights the importance of substantive conversations between HCPs and PWD about actionable strategies to prevent and treat severe hypoglycemia in order to ease their fears and prepare them should a severe hypoglycemic event arise.

Author contributions

All authors substantially contributed to in drafting and critical revision of the work. In addition, each author has read and approved the work and assumes responsibility of the content of the work. FS and BDM were involved in the study concept and design. FS, ES, and BDM were involved in formulating the data analysis plan and ES conducted statistical analyses. All authors were involved in the interpretation of study results.

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