Drug therapy and other risk factors for hypoglycemia in patients with type 2 diabetes, hospitalized in Internal Medicine wards. Findings from the FADOI- DIAMOND Study

G. Gussoni[1], S. Frasson[1], V. Borzì[2], A. Fontanella[3], M. Grandi[4], G. Gulli[5], R. Pastorelli[6], B. Solerte[7], A. Ceriello[8], G. Vescovo[9], G. Agnelli[10], M. Campanini[11], for the Research Dept. of FADOI

[1]Research Dept., FADOI Foundation, Milan, Italy
[2]Dept. of Internal Medicine, Hospital 'Policlinico Vittorio Emanuele', Catania, Italy
[3]Dept. of Internal Medicine, Hospital 'Buonconsiglio FBF', Naples, Italy
[4]Internal Medicine, 'Civile' Hospital, Sassuolo, Italy
[5]Internal Medicine, Major Hospital 'SS. Annunziata', ASL CN1, Savigliano, Italy
[6]Internal Medicine, Hospital 'L. Parodi Delfino', Colleferro, Rome, Italy
[7]Internal Medicine, University hospital of Pavia, Pavia, Italy
[8]Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[9]Internal Medicine, Hospital 'S. Antonio', Padua, Italy
[10]Dept. of Internal Medicine, Hospital 'S. Maria della Misericordia', Perugia, Italy
[11]Dept. of Internal Medicine, 'Maggiore' Hospital, Novara, Italy

Objectives: Hypoglycemia is the most common acute adverse effect of glucose-lowering therapy among patients with diabetes mellitus and is associated with poor outcomes and increased mortality. The risk for hypoglycemia may be high also during periods of hospitalization, due to variability in insulin sensitivity related to the underlying diseases, changes in counter-regulatory hormonal responses to procedures or illnesses, modifications of usual nutritional intake and of the glycemic management regimen. Aim of this analysis is to describe the real-world incidence of hypoglycemia, its possible risk factors and the correlations with the therapies in a group of type 2 diabetes patients admitted to Internal Medicine Units, in order to provide a guidance on identification of high-risk patients and administration of the most suitable therapy.

Methods: The analysis comes from the FADOI-DIAMOND study carried out in 53 Italian Internal Medicine Units. The study was designed as a replicate of two cross-sectional surveys interspersed with an educational program: pre-educational survey (PRE phase) and post-educational survey (POST phase). In both phases each center reviewed the charts of the last 30 hospitalized patients with known type 2 diabetes (n=3167 patoents), including information about hypoglycemia during hospital stay. To be qualified, hypoglycemic episodes had to be symptomatic with a blood glucose level < 70 mg/dl and/or specific treatment for hypoglycemia. The association between occurrence of hypoglycemia and potential predictors was evaluated by means of a multivariable logistic regression analysis.

Results: 385 major hypoglycemic events were observed (rate: 12%). According to multivariable logistic regression analysis, advancedage, cognitive dysfunction, high serum creatinine and body mass index lower than 27 kg/m^2 were associated to occurrence of hypoglycemia (Table 1). Patients receiving a combination of rapid and long-acting insulin seemed to be at lower risk of hypoglycemia if compared to those treated with long-acting insulin alone. Hypoglycemia occurred in 19.4% of patients treated according to sliding-scale method vs 11.4% of patients treated with basal-bolus (p < 0.01). A significantly longer length of hospital stay was found in the group with hypoglycemia if compared to no-hypoglycemia patients (12.7±10.9 vs 9.6±6.5 days, respectively, p<0.01). In-hospital mortality rate was significantly higher for patients experiencing hypoglycemia (8.8% vs 4.8% in the group without hypoglycemia, p <0.001).

Conclusion: Hypoglycemia is a not negligible complication in hospitalized diabetic patients, influencing the length of hospitalization. Some categories of diabetic patients hospitalized in general medical wards should be monitored closely for the occurrence of hypoglycemia. Our study showed that at least 1 out of 8 diabetic patients hospitalized in Internal Medicine experiences at least one episode of hypoglycemia, and suggests differential effects of insulin regimens on rates of hypoglycemia. These findings claim for educational efforts addressing this issue and aimed at improving health professional attitudes for hospitalized patients, including more accurate monitoring of blood glucose levels, an optimized carbohydrate supply and appropriate definition of the glucose lowering medications.

Table 1. Predictors for hypoglycemia (multivariable logistic regression analysis)

Parameter	Odds Ratio	95% Lower CL	95% Upper CL	p-Value
Rapid vs Long acting insulin	0.65	0.39	1.06	0.08
Oral antidiabetic drugs vs Long acting insulin	0.99	0.63	1.55	0.95
Rapid + Long vs Long acting insulin	0.46	0.28	0.74	0.01

Age >75 *vs* £ 75 years	1.65	1.30	2.11	< 0.0001
BMI £ 27 *vs* > 27 Kg/m^2	1.43	0.97	2.11	0.07
Comorbidity ≥ 2 *vs* < 2 diseases	0.82	0.64	1.04	0.11
ACE-Inhibitor	0.82	0.66	1.03	0.09
Cognitive dysfunction	1.50	1.17	1.92	0.01
Serum creatinine at admission	1.12	1.02	1.23	0.02
Blood glucose levels at admission	0.99	0.99	0.99	0.01
Glycated hemoglobin at admission	0.96	0.86	1.08	0.49