DOI: 10.7860/JCDR/2022/55130.16401

Short Communication

Internal Medicine Section

Analysis of Burden and Outcomes of Oral Hypoglycaemic Agent Induced Adverse Drug Effects at a Tertiary Care Centre

KAVITA S JOSHI[1], ARNAV H TONGAONKAR[2], ALHAD A MULKALWAR[3]

ABSTRACT

Introduction: Recent studies, both globally as well as in India, have depicted an alarming rise in the prevalence of Diabetes Mellitus (DM). Oral Hypoglycaemic Agents (OHAs) are the most common drugs used in the treatment of type 2 diabetes mellitus. There are numerous established Adverse Drug Reactions (ADR) associated with their use, such as, hypoglycaemia, weight gain, gastrointestinal disturbance, lactic acidosis and fluid retention.

Aim: To assess the incidence of ADRs, clinical profile, severity and causality among the admitted patients, taking OHAs, in a tertiary care hospital.

Materials and Methods: This was a hospital-based, prospective, observational, non interventional cohort study undertaken at the General Medicine Wards of a public teaching hospital, Seth GSMC and KEMH, Mumbai, Maharashtra, India. The present study was conducted in the Department of Medicine from June 2017 to December 2018. The patient's data was recorded using a structured ADR reporting form. The baseline parameters, medical history and underlying diseases, clinical data, characteristics of ADRs and details of medication responsible for ADRs as well as medication for treatment of ADRs were recorded. The data was analysed using descriptive statistics with the Statistical Packages for the Social Sciences (SPSS) version 26.0 software.

Results: Out of 164 patients admitted due to ADRs, within the study period, 48 (29.3%) patients had developed ADRs due to OHAs (sulfonylureas). The severity of ADRs of five patients fell under the moderate category (three males in the age group of 61-80 years and two females in the age group of 21-40 years), all of whom successfully recovered. The remaining 43 (89.6%) were associated with severe ADRs. Four patients had succumbed to the ADR while one reported further sequelae, and the rest of the patients recovered (one was still recovering at the time of data analysis).

Conclusion: Sulfonylurea-induced hypoglycaemia is the most common ADR seen in patients on treatment of type 2 diabetes mellitus. Presence of systemic co-morbidities and polypharmacy are significant risk factors associated with OHA-induced ADRs.

Keywords: Adverse drug reactions, Polypharmacy, Sulfonylurea drugs

INTRODUCTION

The World Health Organisation (WHO) defined an Adverse Drug Reaction (ADR) as "a noxious, unintended, and undesirable effect that occurs as a result of dose normally used in man for diagnosis, prophylaxis, and treatment of disease or modification of physiological function. Response in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility [1]. ADRs are a major public health problem. They are considered a leading cause of morbidity and mortality [2]. Estimated 2.9-5% hospital admissions are due to ADRs and approximately 35% of hospitalised patients experience an ADR during their hospital stay [3]. Adverse drug events can range from mild to life threatening reactions resulting in inconvenience or serious morbidity and mortality besides being a financial burden on the society [4].

Diabetes Mellitus (DM) is a chronic metabolic disorder characterised by hypoglycaemia and associated with a high risk of numerous complications [5]. The prevalence of type 2 DM is rising throughout the world, in developed as well as developing countries [6,7]. At present, a total of 415 million people are affected by diabetes globally and this number is set to rise beyond 642 million by 2040 [8]. In India, over 65.1 million individuals have been diagnosed with the disease and the estimates suggest that roughly 89 million patients may develop by 2030 [9,10]. Patients with type 2 DM require pharmacotherapy throughout life; they also need to have a proper and regular diet along with physical activity so as to maintain the blood sugar levels within normal levels [11]. Diabetes mellitus is affecting India badly leading to increased morbidity with increasing treatment cost. The current pharmacotherapy of diabetes mellitus includes treatment with drugs such as insulin and oral hypoglycaemic agents. With increase in the number of medication, the chances of ADRs also increase, contributing to morbidity and loss of productivity [12].

Oral Hypoglycaemic Agents (OHAs) are the most common drugs used in type 2 DM. There are numerous established ADRs associated with their use such as hypoglycaemia, weight gain, gastrointestinal disturbance, lactic acidosis and fluid retention [13]. Adequate counselling about ADRs and early reporting of the same to physician is essential to avoid such predictable ADRs [12]. Pharmacovigilance of anti-diabetic drugs can play an important role in identifying ADRs and providing valuable feedback to physicians. However, the Pharmacovigilance Programme of India is still in its budding stage [14].

The present study aimed to assess the incidence of ADRs among the admitted patients in a tertiary care hospital taking OHAs. It also assessed the clinical profile of patients with OHA associated ADRs, along with the severity, causality and preventability of these ADRs.

MATERIALS AND METHODS

This was a hospital-based, prospective, observational, non interventional cohort study undertaken at Seth GSMC and KEMH, Mumbai, Maharashtra, India. It was conducted in the General Medicine Wards. The study spanned in the Department of Medicine from June 2017 till December 2018, the study was initiated after obtaining approval from the Departmental Review Board and the Institutional Ethics Committee (IEC/167/2017).

Inclusion criteria: All consenting patients, of age >21 years, either admitted in the Medical Wards of the hospital for ADR following use of OHAs or those who developed OHA-induced ADRs while admitted in the medical wards were included in the study.

Exclusion criteria: Patients on insulin therapy, those with intentional or accidental poisoning, drug abuse (except alcohol) and non compliance to the prescribed medications were excluded from the study.

Study Procedure

The patient's data was recorded using a structured ADR reporting form. The baseline parameters were assessed to obtain relevant data on demographics, clinical condition, co-morbidities, relevant laboratory data and medications used. The medical history and underlying diseases, clinical data, characteristics of ADRs and details of medication responsible for ADRs (suspected drug, dosage, route of administration, indication, date of beginning and stopping therapy, concomitant drugs) as well as medication for treatment of ADRs were obtained from the clinical notes, medication charts, clinical examination, interviews with patient or his/her relatives or caregivers or ward staff, the treatment sheets, drug administration charts, dispensing records and pill/injection count validation. All patients were followed-up till discharge from the hospital or till death. The ADRs were recorded in detail in a descriptive format. The onset, duration and progress as well as the systems affected, the drugs and the class of drugs causing the ADRs, the severity as well as the seriousness of the reactions and the treatment given for the same were recorded. Data pertaining to the adverse event was collected- the likely causative drug/class of drug, causality (WHO-UMC scale) [15], severity (Hartwig and Siegel scale) [16], avoidability (Halla's criteria) [17] and outcome.

STATISTICAL ANALYSIS

The data was analysed using descriptive statistics with the Statistical Packages for the Social Sciences (SPSS) version 26.0 software.

RESULTS

Out of the 164 patients admitted due to ADRs within the study period, 48 (29.3%) developed ADRs due to OHAs (26 males and 22 females). All the patients were on OHAs of the class sulfonylurea-glimepiride (n=38), glibenclamide (n=7), and glicazide (n=3).The age and gender distribution of the subjects is given in [Table/Fig-1].

Variables	Number of patients
Age groups (years) (mean±SD=62.5±13.67 years)	
21-40 years	3
41-60 years	19
61-80 years	24
81-100 years	2
Gender	
Male	26 (54.17%)
Female	22 (45.83%)

[Table/Fig-1]: Age and gender distribution of the subjects with ADRs.

The mean duration of stay was 3.9±2.034 days. Most of the patients (n=43) had co-morbidities. the recovered patients had a mean hospital stay of 2.2 days (extended hospital stay after diagnosis of the ADR). The causality of all subjects (n=48) was found to be probable (WHO-UMC scale). Almost 90% of the patients (n=43) suffered from severe ADRs; 87.5% of the patients (n=42) showed complete recovery as depicted in [Table/Fig-2]. The severity of ADRs of five patients fell under the moderate category (three males in the age group of 61-80 years and two females in the age group of 21-40 years), all of whom successfully recovered. The remaining 43 (89.6%) were associated with severe ADRs.

Outcome	Number of patients
Recovered	42
Recovering	1
Recovered with sequelae	1
Fatal	4

[Table/Fig-2]: Outcome of admitted subjects suffering from OHA induced ADR.

All the subjects who succumbed to the OHA-induced adverse were elderly (age >60 years) males with significant co-morbidities. All oral hypoglycaemic related ADRs in the study were metabolic in nature, manifesting as hypoglycaemia. Of these, 11 patients had missed meals while some had insufficient blood sugar monitoring at the community level. Co-morbidities were seen in 90% of the patients (n=43). Polypharmacy was another frequent risk factor in the study population, seen in 54% of the patients (n=26). Four cases of OHA- induced hypoglycaemia were fatal. As per the Halla criteria, maximum patients (n=43) had developed ADRs which were 'possibly avoidable'. The patient details are presented as a supplement table.

DISCUSSION

Sulfonylureas are the most commonly prescribed class of drugs to treat Type 2 Diabetes Mellitus and hypoglycaemia remains its most common ADR [18]. In accordance with the same, all OHA related ADRs in the present study were found to be due to sulfonylureas, and all of them were metabolic in nature, manifesting as hypoglycaemia. Hypoglycaemia is most likely to occur after a missed meal, [18] which was also reported in 11 of the study patients. In this study, out of 48 ADRs assessed, 45 (93.75%) could have been avoided by more than usual effort by the physician or patient. Studies have reported that only few patients started on OHAs are informed about the adverse effects by their physicians in pre-medication stage and this factor has a significant association with incidence of adverse effects [19]. Physicians should inform patients about the possible ADRs, which might help them cope with unpleasant adverse effects and also enhance adherence to the pharmacotherapy [20]. It is a well-established fact that as the number of medications increase, the chances of developing ADRs also increase [21]. Polypharmacy (higher drug count) and higher co-morbidity scores have been consistently reported as risk factors for ADRs, especially amongst geriatric patients [22]. The present study was no different; with two of the major risk factors in the patients being presence of significant co-morbidities (N=43) and polypharmacy (N=26), both of which were also present in the four elderly males who succumbed to the ADR. It should be noted that in the present study, for those with OHA induced hypoglycaemia, diabetes was not considered a risk factor, since, it was the reason for treatment.

Limitation(s)

The study evaluated the patients admitted to the internal medicine wards only. The study did not calculate the costs based on duration of hospitalisation alone. The patients were brought to the hospital after a prolonged period of uncorrected hypoglycaemia and had sustained hypoglycaemic brain damage. The assessment of whether an ADR has increased the length of stay or caused death, and in particular whether it is due to the underlying disease or due to an ADR, can be extremely difficult.

CONCLUSION(S)

Patients being treated with sulfonylurea drugs are susceptible to hypoglycaemia, especially after missed meals. Presence of systemic co-morbidities and polypharmacy are significant risk factors associated with the same. Polypharmacy is a risk factor that is liable

to increase since life expectancy is increasing, and co-morbidities are likely to increase with age. Thus, with the increasing prevalence of polypharmacy, one should be more watchful for ADR and review all ongoing prescriptions for unnecessary medications, especially in geriatric patients.

REFERENCES

[1] WHO. International Drug Monitoring: The Role of Hospital. (Technical Report Series No. 425). Geneva, Switzerland: World Health Organization; 1969.
[2] Ditto AM. Drug allergy: In:(Grammer, LC and Greenberger, PA) Eds. Patterson's allergic diseases. 8th Edition. Wolter Kluwer. 2018.
[3] Murphy BM and Frigo LC. Development, Implementation and Results of a Successful Multidisciplinary Adverse Drug Reaction Reporting Program in a University Teaching Hospital. Hosp Pharm. 1993;28(12):1199-204.
[4] Raut A, Diwan A, Patel C, Patel P, Pawar A. Incidence, Severity and Financial Burden Associated With Adverse Drug Reactions in Medicine Inpatients: Asian. J Pharm Clin. Res. 2011;4(2):103-11.
[5] International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels,Belgium: 2021. Available at: https://www.diabetesatlas.org.
[6] Misra A, Ramachandran A, Zargar AH. Prediabetes. In: Zargar AH, editor. ECAB clinical update: Diabetology. 1st ed. New Delhi, India: Elsevier; 2008. pp. 2-95.
[7] Magalhães ME, Cavalcanti BA, Cavalcanti S. Could prediabetes be considered a clinical condition? Opinions from an endocrinologist and a cardiologist. Diabetol Metab Syndr. 2010;2:2.
[8] International Diabetes Federation. Belgium. [Accessed on January 11, 2016]. Available from: http://www.diabetesatlas.org/across-the-globe.html.
[9] Ramachandran A. Know the signs and symptoms of diabetes. Indian J Med Res. 2014;140(5):579-81.
[10] Indian Diabetes Market Report and outlook for 2010-2015. Press Release.http://www.mynewsdesk.com/in/pressreleases/indian-diabetes-marketreport-outlook-for2010-2015 bharatbookcom-586410, accessed on November 26, 2015.
[11] Graffigna G, Barello S, Libreri C, Bosio CA. How to engage type-2 diabetic patients in their own health management: Implications for clinical practice. BMC Public Health. 2014;14:648.
[12] Singh S, Nigam N, Gupta S, Kumar S. Adverse drug reactions monitoring of newer oral hypoglycemic drugs in a tertiary care hospital of North India: A prospective study. Int J Basic Clin Pharmacol. 2017;6:2434-40.
[13] Shrestha JTM, Shrestha H, Prajapati M, Karkee A, Maharjan A. Adverse Effects of Oral Hypoglycemic Agents and Adherence to them among Patients with Type 2 Diabetes Mellitus in Nepal. Journal of Lumbini Medical College. 2017;5(1):34-40.
[14] Faich GA. US adverse drug reaction surveillance 1989-1994. Pharmacoepidemiol Drug Saf. 1996;5(6):393-98.
[15] The use of the WHO-UMC system for standardized case causality assessment [Internet]. Uppsala: The Uppsala Monitoring Centre. Available at: http://who-umc.org/pdfs/Graphics/24734.pdf or from http://www.whoumc.org/ pdfs/Causality.pdf.
[16] Hartwig SC, Siegel J and Schneider. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49(9):2229-32.
[17] Hallas J, Harvald B, Gram LF, Grodum E, Brøsen K, Haghfelt T, et al. Drug related hospital admissions: The role of definitions and intensity of data collection, and the possibility of prevention. J Intern Med. 1990;228(2):83-90.
[18] Sola D, Rossi L, Schianca GPC, Maffioli P, Bigliocca M, Mella R, et al. Sulfonylureas and their use in clinical practice. Arch Med Sci. 2015;11(4):840-48. Doi: 10.5114/aoms.2015.53304.
[19] Guillausseau PJ. Impact of compliance with oral antihyperglycemic agents on health outcomes in type 2 diabetes mellitus: A focus on frequency of administration. Treat Endocrinol. 2005;4(3):167-75.
[20] Bezie Y, Molina M, Hernandez N, Batista R, Niang S, Huet D. Therapeutic compliance: A prospective analysis of various factors involved in the adherence rate in type 2 diabetes. Diabetes Metab. 2006;32(6):611-16.
[21] Ahmed B, Nanji K, Mujeeb R, Patel MJ. Effects of polypharmacy on adverse drug reactions among geriatric outpatients at a tertiary care hospital in Karachi: A prospective cohort study. PLoS One. 2014;9(11):e112133. Doi: 10.1371/journal.pone.0112133.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Medicine, Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai, Maharashtra, India.
2. Resident, Department of Medicine, Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai, Maharashtra, India.
3. Intern, Department of Medicine, Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Alhad A Mulkalwar,
Intern, Department of Medicine, Seth Gordhandas Sunderdas Medical College and King Edward Memorial Hospital, Mumbai, Maharashtra, India.
E-mail: alhad.mulkalwar@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 24, 2022
- Manual Googling: Apr 11, 2022
- iThenticate Software: Apr 23, 2022 (17%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 21, 2022**
Date of Peer Review: **Feb 25, 2022**
Date of Acceptance: **Apr 12, 2022**
Date of Publishing: **May 01, 2022**

S. No.	Demography (Age group, Sex, Body weight)	Co-morbidities/Addictions	Other drugs	Manifesting signs and symptoms	Hospital stay (Days)	Outcome	Causality	Severity	Preventability
1	61-80 years Female 50 kg	Renal insufficiency, Tobacco addiction	-	Drowsiness, LOC	2	Recovering	Probable	Severe	Possibly avoidable
2	41-60 years Female 45 kg	HTN, IHD, Polypharmacy	Antihypertensives, Antianginals, Anticoagulants	Drowsiness, LOC, HGT: 52	2	Recovered	Probable	Severe	Possibly avoidable
3	61-80 years Female 42 years	Renal insufficiency, HTN, Tobacco addiction	Antihypertensives, Antianginals	LOC, HGT:60	5	Recovered	Probable	Severe	Definitely avoidable
4	41-60 years Female 50 kg	Renal insufficiency	-	Drowsiness, LOC, HGT: 56	6	Recovered	Probable	Severe	Possibly avoidable
5	41-60 years Female 60 kg	-	-	Giddiness, blackout, palpitation, HGT: 60	3	Recovered	Probable	Moderate	Possibly avoidable
6	21-40 years Female 40 kg	Renal insufficiency, HTN, DM	Antihypertensives, Antianginals	LOC, HGT:50	5	Recovered	Probable	Severe	Unavoidable

7	41-60 years Female 50 kg	Renal insufficiency, HTN, Tobacco addiction	Antihypertensives, Antianginals	Giddiness, Drowsiness, HGT: 60	2	Recovered	Probable	Severe	Possibly avoidable
8	41-60 years Female 60 kg	Renal insufficiency, HTN, Tobacco addiction	Antihypertensives, Antianginals, Antibacterials	LOC, HGT:40	4	Recovered	Probable	Severe	Possibly avoidable
9	61-80 years Female 70 kg	HTN, IHD, Polypharmacy	Antihypertensives, Antianginals, Anticoagulants	LOC, HGT:50	4	Recovered	Probable	Severe	Possibly avoidable
10	41-60 years Male 60 kg	Renal insufficiency, HTN, Polypharmacy	Antihypertensives, Antianginals, Anticoagulants, Anticonvulsants	Decreased verbal output/Right-sided weakness/ HGT 49	5	Recovered	Probable	Severe	Possibly avoidable
11	61-80 years Male 50 kg	-	-	Giddiness, Swaying, Fall, 1 episode of seizure, HGT: 38	5	Recovered	Probable	Severe	Possibly avoidable
12	61-80 years Male 50 kg	Renal insufficiency, HTN, IHD, Polypharmacy, Tobacco addiction	-	Found unconscious after 12 hours, HGT: 36	6	Fatal	Probable	Severe	Possibly avoidable
13	> 80 years Male 55 kg	Renal insufficiency, IHD, Tobacco addiction	Anticoagulants	Found unconscious by relatives, HGT: 40	1	Fatal	Probable	Severe	Possibly avoidable
14	41-60 years Male 60 kg	Renal insufficiency	-	LOC, HGT:50	2	Recovered	Probable	Severe	Unavoidable
15	61-80 years Male 50 kg	Renal insufficiency, Tobacco addiction	-	LOC, HGT:30	2	Recovered	Probable	Severe	Possibly avoidable
16	61-80 years Male 50 kg	Polypharmacy	Antihypertensives, Antianginals, Anticoagulants	Found unconscious by relatives, HGT: 30	2	Fatal	Probable	Severe	Possibly avoidable
17	61-80 years Male 50 kg	Renal insufficiency, HTN, Polypharmacy	Antihypertensives, Antianginals, Anticoagulants, Antibacterials, others	LOC, HGT:38	3	Fatal	Probable	Severe	Possibly avoidable
18	41-60 years Male 52 kg	Alcohol addiction, Tobacco addiction	-	Giddiness, visual blackout, LOC, HGT: 40	6	Recovered	Probable	Severe	Possibly avoidable
19	61-80 years Male 62 kg	Renal insufficiency	-	LOC, HGT:46	4	Recovered	Probable	Severe	Possibly avoidable
20	61-80 years Female 55 kg	Renal insufficiency	-	Sweating, giddiness, LOC, HGT:40	3	Recovered	Probable	Severe	Possibly avoidable
21	41-60 years Male 60 kg	Renal insufficiency, IHD, Polypharmacy	Anticoagulants	LOC, HGT:35	10	Recovered	Probable	Severe	Possibly avoidable
22	41-60 years Male 72 kg	Polypharmacy	Antibacterials	LOC, HGT:52	3	Recovered	Probable	Severe	Unavoidable
23	61-80 years Male 72 kg	HTN, Polypharmacy, smoking addiction	Antihypertensives, Antianginals	LOC, HGT:38	5	Recovered	Probable	Severe	Possibly avoidable
24	41-60 years Female 60 kg	Renal insufficiency, HTN, Polypharmacy	Antihypertensives, Antianginals	LOC, HGT:51	2	Recovered	Probable	Severe	Possibly avoidable

25	61-80 years Female 50 kg	HTN, Polypharmacy	Antihypertensives, Antianginals	Giddiness, palpitation, sweating, drowsiness, HGT:58	2	Recovered	Probable	Severe	Possibly avoidable
26	61-80 years Female 50 kg	HTN, Polypharmacy, Tobacco addiction	Antihypertensives, Antianginals	Found unconscious by relatives, HGT: 30	3	Recovered with sequelae	Probable	Severe	Possibly avoidable
27	61-80 years Male 52 kg	HTN, IHD, Polypharmacy, Tobacco addiction, smoking addiction	Antihypertensives, Antianginals, Anticoagulants	Giddiness, visual blackout, HGT: 56	2	Recovered	Probable	Moderate	Possibly avoidable
28	61-80 years Male 60 kg	Renal insufficiency, HTN, IHD, Polypharmacy, Tobacco addiction	Antihypertensives, Antianginals, Anticoagulants	Drowsiness, irrelevant talk, HGT:43	4	Recovered	Probable	Moderate	Definitely avoidable
29	61-80 years Male 60 kg	Renal insufficiency, Polypharmacy, Tobacco addiction	Antibacterials, others	LOC, HGT:35	3	Recovered	Probable	Severe	Possibly avoidable
30	41-60 years Male 60 kg	Polypharmacy, Smoking addiction	Antihypertensives, Antianginals	Drowsiness, 1 episode of GTCS, HGT: 40	8	Recovered	Probable	Severe	Possibly avoidable
31	61-80 years Female 50 kg	Renal insufficiency, HTN, IHD, Polypharmacy	Antihypertensives, Antianginals, Antiemetics, Anticoagulants, diuretics, others	LOC, HGT:50	3	Recovered	Probable	Severe	Possibly avoidable
32	41-60 years Female 55 kg	HTN, Tobacco addiction	Antihypertensives, Antianginals, Anticoagulants	Giddiness, Drowsiness, HGT: 60	3	Recovered	Probable	Severe	Possibly avoidable
33	61-80 years Female 64 kg	Renal insufficiency, HTN, IHD, Polypharmacy	Antihypertensives, Antianginals, Antiemetics, Anticoagulants, Diuretics, others	Drowsiness, LOC, HGT: 54	4	Recovered	Probable	Severe	Possibly avoidable
34	61-80 years Female 70 kg	Renal insufficiency, HTN, Tobacco addiction	Antihypertensives Antianginals, Antiemetics, Antibacterials	Drowsiness, irrelevant talk, HGT:43	3	Recovered	Probable	Severe	Possibly avoidable
35	61-80 years Female 50 kg	Renal insufficiency, Polypharmacy, Tobacco addiction	Antihypertensives, Antianginals	Drowsiness, 1 episode of GTCS, HGT: 40	6	Recovered	Probable	Severe	Possibly avoidable
36	41-60 years Female 50 kg	-	-	Drowsiness, LOC, HGT: 52	3	Recovered	Probable	Severe	Possibly avoidable
37	61-80 years Female 45 kg	Renal insufficiency, HTN, IHD, Polypharmacy, Tobacco addiction	Antihypertensives, Antianginals, Anticoagulants	Drowsiness, irrelevant talk, HGT:50	3	Recovered	Probable	Severe	Possibly avoidable
38	41-60 years Female 50 kg	-	-	Giddiness, visual blackout, HGT: 60	1	Recovered	Probable	Moderate	Possibly avoidable
39	61-80 years Female 50 kg	Renal insufficiency, HTN, Polypharmacy, Tobacco addiction	Antihypertensives, Antianginals, Anticoagulants	LOC, HGT:30	8	Recovered	Probable	Severe	Possibly avoidable
40	41-60 years Male 50 kg	Renal insufficiency, HTN, Alcohol addiction	Antihypertensives, Antianginals, Anticoagulants	Drowsiness, 1 episode of GTCS, HGT: 45	8	Recovered	Probable	Severe	Possibly avoidable
41	61-80 years Male 45 kg	HTN, IHD, Polypharmacy, Tobacco addiction	Antihypertensives, Antianginals, Anticoagulants	Drowsiness, irrelevant talk, HGT:50	3	Recovered	Probable	Severe	Possibly avoidable
42	> 80 years Male 50	Renal insufficiency, Polypharmacy	Antihypertensives, Antianginals, Antibacterials	Giddiness, palpitation, sweating, drowsiness, HGT:58	5	Recovered	Probable	Severe	Possibly avoidable

43	41-60 years Male 54 kg	HTN	Antihypertensives, Antianginals,	Drowsiness, LOC, HGT: 52	4	Recovered	Probable	Severe	Possibly avoidable
44	61-80 years Male 50 kg	HTN, Polypharmacy	Antihypertensives, Antianginals,	Giddiness, Swaying, Fall	3	Recovered	Probable	Moderate	Possibly avoidable
45	21-40 years Male 54 kg	Renal insufficiency, HTN, IHD, Polypharmacy, Alcohol addiction	Antihypertensives, Antianginals, Anticoagulants, Diuretics	Giddiness, visual blackout, loss of consciousness HGT: 60	8	Recovered	Probable	Severe	Possibly avoidable
46	41-60 years Male 45 kg	Renal insufficiency, HTN, Polypharmacy, Alcohol addiction	Antihypertensives, Antianginals,	LOC, HGT:50	3	Recovered	Probable	Severe	Possibly avoidable
47	41-60 years Male 53 kg	-	-	Drowsiness, Giddiness, HGT: 52	2	Recovered	Probable	Severe	Possibly avoidable
48	21-40 years Male 50 kg	Renal insufficiency	-	Giddiness, visual blackout, HGT: 60	3	Recovered	Probable	Severe	Possibly avoidable

Supplement: Patient information and analysis of outcomes.
HTN: Hypertension; IHD: Ischaemic heart disease; LOC: Loss of consciousness; HGT: Haemo glucose test- mg/dL