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Original Article

Antidiabetics' usage in type 2 diabetes mellitus: Are prescribing guidelines adhered to? A single centre study

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ABSTRACT

Aim: The primary aim of this study was to examine the prescribing patterns of antidiabetic agents (AA) in this hospital according to current prescribing contraindications (PCI). The secondary aims are to assess factors affecting the prescribing of AA and to evaluate the pharmacist impact on their prescribing.
Method: A retrospective cross sectional study was performed to review all prescribed AA over a 3 month period. Data extracted from medical records included: patients' demographics, management and pharmacists' interventions. Appropriateness of prescribing was determined according to the AA prescribing information of the Medical Index of Medical Specialities (MIMS).
Results: A total of 314 AA were examined, of which 74(23%) orders were prescribed despite contraindications. Metformin was the AA to have the most PCI in dosage adjustments in renal impairment (RI). Logistic regression analysis showed patients with severe RI were less likely to be prescribed metformin (OR = 0.115 95%CI(0.048–0.274) $P < 0.01$), instead insulin was preferred (OR = 2.210 95%CI (1.028–4.751) $P < 0.05$). Insulin was also more likely to be prescribed in patients with hypertension and hyperglycaemia (OR=2.005 95%CI(1.005–4.001) $P < 0.05$, OR = 3.535 95%CI (1.756–7.113) $P < 0.01$) respectively. Sulphonylureas were less likely to be prescribed in patients with cardiovascular disease (OR = 0.339 95%CI(0.163–0.708), $P < 0.01$. There was low PCI in the other AA. Pharmacists reviewed 89% of AA. PCI was lower in this group compared to those with no pharmacist input (23% vs 28%).
Conclusion: The audit showed good adherence to PCI. Pharmacist involvement has a positive impact on AP. Prescriber education is required in relation to dosage adjustments of AA in RI.

1. Introduction

Type 2 Diabetes Mellitus is a growing concern of our generation and is now one of the major challenges confronting Australia's health system. Approximately 1.7 million Australians have diabetes, including those who have not yet been diagnosed. In 2008–09, almost $1.5 billion was spent on diabetes, 2.3% of all allocated health-care expenditure in Australia [1]. Of this, $498 million was spent on blood glucose lowering medications [1].

Adverse drug related admissions accounts for about 3% of all hospital admissions [2]. Optimising patients' drug therapy in chronic conditions, such as, diabetes should lead to improving patients clinical outcomes and may contribute to a reduction in hospital admissions due to drug related side effects.

In recent years, pharmacological options for treating type 2 diabetes have expanded substantially [3,4]. The main drug classes utilized in Australia include sulphonylureas, thiazolidinediones, dipeptidyl peptidase-4 inhibitors (DDP4I), glucagon like peptide-1 analogues (GLP1 analogues), sodium glucose co-transporter 2 inhibitors (SGTI), metformin, insulin and acarbose [3].

Metformin is the drug of first choice in Australia with well established cardiovascular benefits and a low risk of hypoglycaemia [5]. Such benefits have led to recent recommendations allowing for a more liberal approach in the prescribing of metformin, specifically in patients with renal impairment [6]. Sulphonylureas are both cost-effective and have decades of associated clinical experience, making them a popular second choice of therapy [7]. However, the place in therapy of many newer agents is yet to be established due to a lack of head to head comparative studies [4]. Choice of medication therapy is currently

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dictated by various patient centred factors such as life expectancy, glycaemic control, and risk of hypoglycaemia, patient preference and co-morbidities such as renal impairment [8].

The management of diabetes is a complex process; inappropriate prescribing of medications may lead to serious complications if not conducted with care. Despite this, medicines such as metformin are still prescribed in the presence of contraindications, potentially leading to life-threatening consequences [9].

Successful diabetes management involve a multidisciplinary team [10]. Pharmacists are becoming increasingly more influential in the management of chronic illnesses as well as in primary care [8]. Pharmacist involvement has already been shown to improve clinical outcomes in patients with type 2 diabetes in the form of case management conducted by pharmacists, disease management programs and the addition of pharmacists to primary care teams [10,11]. However, studies examining the role and influence of hospital based pharmacists in the appropriate prescribing of glucose lowering medications are limited.

The primary aim of this audit was to examine the prescribing patterns of glucose lowering medications in a metropolitan Australian hospital in relationship with absolute contraindications recommended by product manufacturers and current prescribing guidelines. The secondary aims are to study patients' factors that affect the prescribing of antidiabetic agents and to evaluate the pharmacist impact on the appropriate prescribing of glucose lowering medications.

2. Method

A retrospective cross sectional study was performed. The clinical notes of T_2DM patients who were prescribed antidiabetic agents over a three month period in an Australian metropolitan hospital were reviewed. The hospital comprises of 400 beds and provides a range of specialty wards consisting of: stroke ward, gastroenterology, orthopaedics, cardiology, intensive care, geriatrics, mental health, maternity, rehabilitation, emergency unit, general surgery and general medicine.

A predefined list of all commercially available antidiabetic agents was entered in the search engine tool of the electronic prescribing and management system (Cerner®), a system used hospital-wide to prescribe medications for inpatients during admission and on discharge. This is to ensure identification and inclusion of all T_2DM patients prescribed antidiabetic agents admitted during the study period irrespective of their admission diagnosis. The generated list of patients was screened for antidiabetic medications prescribed on discharge, patients demographics, comorbidities, relevant pathology results (e.g. blood glucose, plasma lactate, pH, estimated Glomerular Filtration Rate (eGFR), liver transaminases, and serum creatinine) and the presence of absolute prescribing contraindications according to the prescribing guidelines obtained from the MIMS (Monthly Index of Medical Specialties) drug prescribing guide, and any pharmacist involvement in the patients' medication management.

In this study, inappropriate prescribing of metformin was defined as having a contraindication to its use, identified according to prescribing guidelines in MIMS. These include presence of: severe cardiac failure, diabetic ketoacidosis (DKA), severe hepatic dysfunction, pancreatitis, recent myocardial infarction, severe dehydration, gangrene, lactic acidosis, respiratory failure and renal impairment. Inappropriate prescribing of sulphonylurea was defined as the presence of: DKA, metabolic acidosis, treatment with bosentan, severe renal impairment, or severe hepatic impairment. Inappropriate prescribing of sodium glucose transport inhibitors was defined as the presence of renal impairment. DKA and severe heart failure were identified as contraindications to the prescribing of thiazolidinediones. Severe renal impairment was identified as contraindication to the prescribing of acarbose and glucagon like peptide 1 agonists according to MIMS. The presence of hypoglycaemia with concomitant use of insulin or sulphonylurea and pancreatitis were listed as prescribing contraindications to dipeptyl peptidase-4 inhibitors.

For the purpose of identifying contraindications, in the absence of documented diagnosis: severe cardiac failure was identified as documented symptoms indicating stage 3 or 4 heart failure according to the NYHA classifications in the patients' medical histories [12]. Severe renal impairment was defined as a creatinine clearance (CrCl) less than 30 mL/min or eGFR less than 30 mL/min per 1.73 m^2 [13]. Severe hepatic dysfunction was defined as biochemical evidence of hypoalbuminaemia and abnormal serum levels of at least two of the following: total bilirubin, ALT, ALP or GGT [9]. The presence of hypoglycaemia was defined as an inpatient measurement of Blood sugar level (BSL) less than 3.9 mmol/L, and a documented past history of hypoglycaemic episodes in the patients' medical records [14].

Pharmacists input was determined by checking for a documented pharmacist intervention in the examined patients' medical case notes, a documented pharmacist electronic verification of charted medications or a documented full medication admission and reconciliation form completed by a ward pharmacist. If there was documentation of pharmacist input upon patient's discharge following a pharmacist review as defined above, this was regarded as a pharmacist intervention.

The inclusion criteria consisted of T_2DM patients who were over 18 years of age and prescribed an antidiabetic agent. The exclusion criteria included T_1DM, pregnant patients, patients admitted for less than 24 h, and patients who were palliated or deceased during the examined admission encounter. Patients who had incomplete medical records were also not included, as the medication changes made could not be accurately identified. Patients were also excluded if they had a duplicate order for a particular medication (i.e. the duplicate order was unintentional and had been corrected prior to drug administration).

2.1. Data collection and analysis

Analysis of data involved both descriptive, univariate, and multivariate statistics. Data were analysed using SPSS, version 24.0 (SPSS, Inc, an IBM Company, Chicago, Illinois). Descriptive statistics were used to summarise patients' demographics and management. Chi-squared was used to examine the relationship between 2 categorical variables. A significance level of $P < .05$ or $P < .01$ was considered statistically significant for all tests. Multivariate logistic regression model was used to examine the relationship between the independent variables such as gender, age, presence of comorbidities (such as acute myocardial infarction, kidney disease, hypertension, ischemic heart disease, history of hyperglycaemia, presence of hypoglycaemia, heart failure, presence of stroke, peripheral vascular disease, liver dysfunction, and history of lactic acidosis and the dependent variables on discharge such as treatment with metformin, sulphonylureas, DPP4I and insulin. The results are presented in adjusted odds ratios (OR) with 95% confidence intervals (95% CI).

2.2. Ethical approval

This study gained ethics approval from the metropolitan hospital Human Research and Ethics committee in 2016.

3. Results

A total of 250 admissions were recorded during the study period with a coding of T_2DM. After assessment against the study

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