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Glucose monitoring in new users of second-generation antipsychotics in older people

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ABSTRACT

Objective: Treatment guidelines published world-wide have highlighted concerns of increased metabolic risks associated with second-generation antipsychotics (SGAs).
The aim of the study was to evaluate blood glucose monitoring rates for SGA new users in older people aged 65 years and above during the study period 2006–2012, and investigate the pre-post 2007 Best Practice Advocacy Centre's (bpac^{nz}) glucose monitoring recommendation in New Zealand.
Methods: The study was a population-based retrospective cohort of SGA new users (365 days without pre-exposure to antipsychotics). Pharmaceutical collections data were extracted and used to identify older people dispensed SGAs and linked to the National Minimum Dataset and Laboratory Claims collection. WHO Methodology's Anatomical Therapeutic Chemical method's classification was used to characterise the SGAs dispensed.
Results: Of the 25,603 new users dispensed SGAs, 63.5% received glycaemic control monitoring at least once during the study period. Of these, only 20.1% were monitored at baseline, 38.7% were monitored for glycaemic control within the first 90 days. Glycaemic control monitoring within the first 180 days increased to more than half (57.5%) of the SGA new users. Proportion of individuals monitored were independent ($\chi^2 = 6.1$; $P = 0.4$) of pre-post bpac^{nz} recommendation.
Conclusions: Blood glucose monitoring was underutilized in new SGA users. No significant improvement in glycaemic control monitoring was observed after the 2007 bpac^{nz} consensus statement release at baseline, 90 days and at 180 days. Prescribers must be cautioned about the metabolic risks posed by SGAs and recommend glycaemic control monitoring.

1. Introduction

Antipsychotic users are predisposed to a higher risk of metabolic adverse effects compared to non-users (Birkenhäger-Gillesse et al., 2015; Haupt et al., 2009; Kelbrick & Picchioni, 2013; Morrato, Newcomer, Allen, & Valuck, 2008; Morrato et al., 2009). Antipsychotic use has been associated with reduction in life expectancy, increased risk of glucose intolerance, weight gain, hyperglycaemia, dyslipidaemia, and metabolic syndrome (De Hert, Detraux, van Winkel, Yu, & Correll, 2012; Gonzalez, Ahammed, & Fisher, 2010; Kelbrick & Picchioni, 2013; Newcomer & Haupt, 2006). Specific metabolic side effects (hyperglycaemia, hyperlipidaemia, weight gain) have been reported in randomized trial and cohort studies (Gonzalez et al., 2010; Morrato et al., 2009; Shi et al., 2009). Age-related decline in hepatic enzyme functional capacity may increase the risk of adverse effects associated with antipsychotic medicines in older people (Best Practice Advocacy Centre, 2008; De Hert et al., 2012; Kelbrick and Picchioni, 2013).

The International Diabetic Federation, American Diabetes Association, American Psychological Association, and Best Practice Advocacy Centre (bpac^{nz}) in New Zealand have recommended blood glucose level and lipid profile monitoring for diabetic patients or those with hyperglycaemic symptoms, using any of the threshold measures or a combination that includes, glycosylated haemoglobin (HbA_{1c}) ≥6.5%, fasting blood glucose (≥126 mg/dL), two-hour anhydrous glucose or random glucose screening (≥200 mg/dL), and lipid profile checks (>200 mg/dL total cholesterol, low density lipoprotein > 100 mg/dL, high density lipoprotein levels <40 mg/dL, and triglycerides >150 mg/dL (American Diabetes Association, 2015a, 2015b; American Psychiatric Association, American Association of Clinical Endocrinologist, & North American Association for the Study of Obesity, 2004; Best Practice Advocacy Centre, 2013; International Diabetes Federation (IDF), 2013; Solano and Goldberg, 2006) at baseline, 12 weeks after

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starting SGAs, and then yearly monitoring (Cohn & Sernyak, 2006; Medsafe (New Zealand Medicines and Medical Devices Safety Authority), 2009; Solano & Goldberg, 2006; Zeier, Connell, Resch, & Thomas, 2013). Periodic monitoring of body weight is also recommended, particularly, in those predisposed to diabetes or weight gain (Medsafe (New Zealand Medicines and Medical Devices Safety Authority), 2009). The New Zealand Guidelines Group have recommended that assessment of complex needs for older people must be supported with regular follow-up (New Zealand Guidelines Group (NZGG), 2003).

The SGAs are one of the leading class of psychotropic medicines prescribed in older people in New Zealand (Best Practice Advocacy Centre, 2011; Ndukwe, Tordoff, Wang, & Nishtala, 2014). The SGAs funded in New Zealand through a co-payment health scheme includes; risperidone, olanzapine, quetiapine, clozapine and ziprasidone (New Zealand Formulary (NZF), 2015; Pharmaceutical Schedule, 2015). New users of these SGAs require appropriate and regular blood glucose level monitoring that is consistent with the bpac^{nz} consensus statement (Best Practice Advocacy Centre, 2013). Blood glucose monitoring benefits to control diabetes onset and reduce the risk of metabolic side effects. SGA new users require blood glucose monitoring which has been associated with increased metabolic risks such as diabetes and dyslipidaemia. These metabolic risks vary in individual users depending on the type of antipsychotic used, family history of diabetes, rapid gain in body weight or waist circumference if exposed to antipsychotics within the same period (Best Practice Advocacy Centre, 2007). Specifically, the bpac^{nz} guideline recommends testing of fasting blood glucose for all patients at baseline, at 3 months and then annually. The bpac^{nz} statement also recommended for individuals with high risk of developing diabetes be tested monthly for the first 3 months, once every 3 months in the first year, and then annually. Further, the switch to less diabetogenic antipsychotics (risperidone, quetiapine, haloperidol) was recommended if there has been rapid increase in fasting blood glucose or diabetes develops (Best Practice Advocacy Centre, 2007). Glucose monitoring in SGA new users has not been previously investigated in New Zealand. Therefore, this study sought to evaluate glucose monitoring rates for SGA new users in older people aged 65 years and above, and investigate possible changes in the pre-post 2007 bpac^{nz} recommendation for blood glucose level monitoring in New Zealand.

2. Method

The Human Ethics Committee of the University of Otago, New Zealand approved the study (Approval number H13/001). The study was a population-based retrospective cohort of SGA new users (365 days without pre-exposure to antipsychotics) from 1 January 2006 to 31 December 2012. Firstly, a cohort of SGA new users who had glycaemic control monitoring (fasting blood glucose, glycosylated haemoglobin – HbA_{1c}, or anhydrous glucose screen) followed from index date until they either stopped taking SGAs or were right censored for the duration of study. The second aim of the study investigated possible changes in pre-post bpac^{nz} recommendation on glycaemic control monitoring. Pharmaceutical collections data was used to identify older people, aged 65 years or older, dispensed SGAs. Individual patient data were linked to the National Minimum Dataset (NMDS) for hospital events (to identify diabetes mellitus cases) and Laboratory Claims collection (Labs) (to identify relevant laboratory tests carried out for individuals including the glycosylated haemoglobin, fasting blood glucose test, glucose tolerance test and fasting lipid group test).

With respect to recommended blood glucose level monitoring statements, SGA new users were divided into seven timeframes following the gap period between a dispensing and subsequent laboratory test. For this work, only those in the initial monitoring timeframe (baseline (≤30 days)) of SGA users were followed-up for glycaemic control monitoring in subsequent SGA dispensings, up to the third and fourth dispensings. The Labs database contains claim and payment information for laboratory tests that have been processed for community laboratory tests. World Health Organization Anatomical Therapeutic Chemical (ATC) method's classification was used to characterise the SGAs dispensed risperidone (N05AX08), olanzapine (N05AH02), quetiapine (N05AH03), clozapine (N05AH04) and ziprasidone (N05AE04).

Individuals with an International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) coded-diagnosis for diabetes or those dispensed any antidiabetic medicines (all ATC coded) prior to the index study date were excluded. The dose of SGAs utilized was not considered in this study. However, the proportion of individuals who had glycaemic control monitoring at baseline, 90 days, 180 days and 12 months were calculated.

2.1. Data analyses

Chi-square (χ^2) statistic was used to compare proportions of individuals monitored within specified time frames, pre-post the 2007 bpac^{nz}'s statement release on glycaemic control monitoring in all SGA new users in New Zealand (Best Practice Advocacy Centre, 2007). Wilson's 95% confidence intervals were used to assess change in proportion between monitored subgroups before and after the BPAC monitoring statement was released (Newcombe, 1998; Wilson, 1927). All data analyses were performed using SPSS version 22, 2013 USA (IBM Corp. Released, 2013).

3. Results

Of the 25603 new users dispensed SGAs, 63.5% (16261 new users) had glycaemic control monitoring at least once during the study period. Of those monitored for blood glucose, only 20.1% were done at baseline, 38.7% were monitored within the first 90 days (Table 1). More than half (57.5%) of the SGA new users had blood glucose tests within the first 180 days. "Furthermore, utilization data among the SGA new users' cohort monitored for

Table 1
Aggregated glycaemic control monitoring for new users of second-generation antipsychotic (SGA) medicines (n = 25,603) in older people.

Monitoring timeframes (days)	Initial dispensings	SGAs subsequent dispensings	Subtotal monitored	Percent (%)
Baseline (≤30)	3173	88	3261	20.05
31–60	1535	68	1603	9.86
61–90	1373	54	1427	8.78
91–180	2923	137	3060	18.82
181–270	1886	100	1986	12.21
271–365	1389	61	1450	8.92
> 1 year	3275	199	3474	21.36
Total people monitored	15554	707	16261	100