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Diabetes and substance use: a perspective within drug rehabilitation

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Abstract

Diabetes mellitus has become increasingly more common and diagnosed within the global population. Coupled with the continued prevalence of substance use, there are some distinct considerations for users suffering (knowingly or unknowingly) from type 1 or type 2 diabetes. The various different types of drugs of abuse including central nervous system stimulants, depressants, and hallucinogens present varying direct and indirect complications for diabetes based on their physiological and psychological effects ranging from non-compliance with medication to an increased risk of hypoglycaemia, hyperglycaemia, and/or ketoacidosis. This perspective highlights these issues supported by the drug history and toxicological findings in patients undergoing drug rehabilitation in the United Arab Emirates (UAE) demonstrating the use of alcohol, amphetamines, benzodiazepines, cannabis, opiates/opioids (especially tramadol), pregabalin, and synthetic cannabinoids. Physicians and drug clinic professionals should be aware of the contraindications of substance use and diabetes with a view to educating patients and healthcare professionals within such clinical settings.

Keywords

Substance use, diabetes, alcohol

Introduction

There are numerous drugs that are prescribed for medicinal purposes in the treatment of acute and chronic conditions or other medical issues and events. Whilst various prescription drugs may also be misused (e.g., benzodiazepines, opiates/opioids, gabapentinoids, etc.), there are a variety of drugs used recreationally [e.g., heroin, cocaine, cannabis, amphetamine-type stimulants (ATS), etc.]. The use of prescription drugs and drugs of abuse can result in therapeutic or desired effects, respectively, along with negative effects that can

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include adverse effects such as toxic effects. Often the production of these effects primarily depends on the dose consumed and any acquired tolerance to the effects of the drug. However, there can also be tolerance-independent side effects of a physiological (e.g., rashes, headache, etc.) and psychological nature (e.g., depression, other mood changes, memory, and cognitive impairment, etc.).

Diabetes mellitus is a medical condition that has become increasingly more common and diagnosed within the global population, often related to changes in modern society and obesity. It is essentially a metabolic disorder in which the body is unable to appropriately regulate blood glucose levels, leading to an increase in blood glucose produced from the metabolism of sugar [1]. Glucose levels are regulated by the hormone insulin secreted from β -cells of islets of Langerhans in the pancreas. Complications of untreated diabetes are severe and can cause diabetic ketoacidosis, hyperosmolar hyperglycaemic state, or death [2]. Serious long-term complications include cardiovascular disease (high blood pressure leading to increased risk of coronary heart disease), stroke (as well as cerebrovascular disease including transient ischaemic attack), chronic kidney disease (including nephropathy), neuropathy (with associated pain or numbness), limb issues (peripheral vascular disease leading to limb and foot damage and potentially gangrene) and damage to the eyes (including retinopathy, cataracts and glaucoma) [3].

Diabetes occurs either due to the failure of the pancreas to produce enough insulin or the impairment of body cells' proper permeability in response to insulin secretion. There are three main types of diabetes mellitus: type 1, type 2, and gestational diabetes [3]. Type 1 diabetes or insulin-dependent diabetes (IDD), as previously defined; also known as juvenile or adolescent diabetes, results from the failure of the pancreas to produce enough insulin as a consequence of loss or damage to beta cells caused by an autoimmune response. The cause of this autoimmune response is unknown (idiopathic). Type 2 diabetes originates from body cell resistance to insulin, whereby cells fail to respond to insulin properly. Taking insulin itself may be required by the patient as the disease progresses. This form was previously referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". Lastly, gestational diabetes occurs when pregnant women without a previous history of diabetes develop high blood glucose levels.

Due to the intended and unintended effects of drugs, the use of drugs by diabetic individuals can create a variety of associated consequences, both directly (i.e. use of drug causing memory impairment which may result in the patient not taking their insulin or anti-diabetic medication) as well as indirectly as part of the patient's physiological status (i.e. medical and disease state as a result of diabetes and/or other comorbidities) [4, 5]. Whilst diabetic patients being prescribed drugs (for diabetes itself or other medical issues) may be monitored closely, this may not be the case for individuals that may be using illicit drugs of abuse. Equally, the impact of using such drugs within a diabetic disease state has not been widely discussed within the medical, pharmaceutical, or toxicological literature. The aim of this article is to highlight the potential issues associated with substance use within the medical context of diabetes, including some initial data pertaining to such drugs used by diabetic patients within a drug rehabilitation setting at the National Rehabilitation Center (NRC) in Abu Dhabi, United Arab Emirates (UAE).

Diabetes and substance use

Substance use is common amongst many age groups, including individuals suffering from type 1 and type 2 diabetes. In the UK, a questionnaire study found that 29% of young adults (aged 16–30) with type 1 diabetes responded that they regularly used illicit drugs [6]. In terms of type 2 diabetes which is a developmental condition, some studies have suggested that when used alone or in combination, alcohol, and illicit drugs, might be associated with an earlier onset of type 2 diabetes [7]. Aside from the potential adverse impact on self-care through substance use (e.g., poor nutrition, etc.) that may have an effect of inducing or hindering diabetic control, there can be direct physiological effects of substance use and drugs of abuse in particular. Such drugs are typically associated with certain central nervous system (CNS) and pharmacodynamic effects resulting in categorisation as stimulant, depressant, or hallucinogenic in nature [8].

Stimulants and hallucinogens

Commonly abused stimulants include cocaine and ATS [e.g., amphetamine, methamphetamine, and 3,4methylenedioxymethylamphetamine (MDMA)]. The subsequent effect on the CNS increases the heart rate of an individual and produces an increase in activity. Thereby, potentially increasing carbohydrate metabolism may result in hypoglycaemia in a diabetic individual without the necessary dietary replenishment [5, 8]. In addition, stimulant drug action such as cocaine involves triggering the adrenal medulla to release catecholamines such as noradrenaline (norepinephrine) and adrenaline (epinephrine) [2]. This is coupled with increased concentrations of cortisol and corticotropin, all of which can ultimately increase glucose concentrations in the blood as well as being a direct potentiator of diabetic ketoacidosis through excess hepatic ketoacid production [2]. Associated with this, researchers have indicated a potential increased risk of diabetic ketoacidosis occurring in individuals using cocaine and/or methamphetamine [2, 9]. Furthermore, cocaine acts as an appetite suppressor which would alter dietary intake thus hampering diabetic individuals from following a balanced diet which is a core element in controlling blood sugar levels.

Commonly abused hallucinogens include lysergic acid diethylamide (LSD), "magic mushrooms", phencyclidine, and ketamine. Whilst no direct impact on biochemical glycaemic control has been reported, the use of hallucinogens results in various physiological and psychological effects that could result in difficulty in maintaining appropriate glucose concentrations in the body as well as the taking of medication (including insulin). Physiologically, nausea and vomiting may occur that can cause dehydration and could potentiate ketoacidosis. Psychological effects including psychedelia and disorganized thoughts may last for variable amounts of time, further impacting and complicating the individual's self-management of diabetes [8].

Depressants and cannabis

Commonly abused CNS depressants include opiates (morphine/heroin, codeine) opioids (methadone, tramadol, fentanyl), and benzodiazepines, along with ethanol (alcohol). The use of such depressant drugs can produce reduced motor and cognitive functions (including movement and impaired judgment) in the individual. As for other drugs of abuse mentioned elsewhere, this could lead to poor self-care (including poor nutrition and/or insufficient glucose monitoring) and/or non-compliance or chaotic use of diabetic medication, all of which could impede glycaemic control as well as leading to potential ketoacidosis. Furthermore, cocaine and heroin also act as an appetite suppressor with subsequent potential issues with sufficient dietary intake. Additionally, supported by animal studies, people with heroin dependency have been found to be suffering from defective pancreatic β -cell response to glucose stimulation and hyperglycaemia [4, 10, 11].

In terms of alcohol, whilst moderate alcohol intake is not officially contraindicated, when a type 1 diabetic or a type 2 diabetic consumes alcohol, their blood sugar levels will increase thereby disrupting glycaemic control with an unpredictable risk of hypoglycemia and hyperglycemia. Related to this is the high quantity of carbohydrates in beverages which further impact such control and increase the risk of hyperglycaemia. In addition, alcohol also hampers the liver and prevents it from releasing glycogen (complex polymer of glucose) which is required to prevent a reduction in glucose concentrations, especially if insulin is taken. Thus, patients with both type 1 and type 2 diabetes can develop hypoglycaemia.

Knowledge about cannabis (especially its multitude of cannabinoids) and its health impacts remains a developing topic with new discoveries being revealed frequently. Indeed, recently reported animal studies have indicated a potential anti-inflammatory effect of delta-9-tetrahydrocannabinol (THC) in hyperinsulinemia often associated with type 2 diabetes [12]. However, again as mentioned elsewhere for other drugs, the use of cannabis can adversely affect cognitive abilities such as judgement, memory, and ability to make decisions as well as acting as an appetite stimulant. This may impact the individual maintaining a balanced diet as well as potentially impeding their use of anti-diabetic medication (e.g., forgetfulness and/or sporadic use). Furthermore, potential vomiting and hyperemesis can lead to dehydration which, along with a potential increase in glucose concentrations through increased intake of

sugary/fatty food, increases the risk of ketoacidosis. Also, cannabis use in type 2 diabetics is associated with an increased risk of peripheral artery occlusion and myocardial infarction. The chances of developing kidney problems are also higher in cannabis users, whether they have type 1 or 2 diabetes.

Substance rehabilitation diabetic patients

The NRC provides medical care on an in- and out-patient basis within the context of drug rehabilitation in the UAE [13]. For the purpose of this study, the drug history of 62 patients (55 male, 4 female; aged 22–73 years, median 46 years) who suffer from type 1 (n = 18, insulin-dependent) or type 2 (n = 44) diabetes was noted. The types of substances used and the associated frequency proportion of patients are shown in Table 1.

Drug	Туре	Total	Patients (%)
Amphetamines	Stimulant	30	51
Alcohol	Depressant	26	44
Cannabis	Depressant	22	37
Pregabalin	Depressant	21	36
Benzodiazepines	Depressant	16	27
Opiates/Opioids	Depressant	12	20
Tramadol	Depressant	8	14
Synthetic cannabinoids	Stimulant/Depressant/Hallucinogen	1	2

Table 1. Drug types used within a drug rehabilitation patient population with toxicological analysis

The most frequent substances involved were amphetamines, alcohol, cannabis, and pregabalin with no particular trend for type 1 or type 2 diabetic patients. As tramadol accounted for 40% of total opiates/ opioid cases including combined use of tramadol along with heroin, statistics for tramadol were shown separately. Overall, many patients exhibited poly-drug abuse with CNS depressants predominating, often in combination with amphetamines. Not only does this reflect the drug situation in the region but also reflects the potential challenges and contraindications highlighted elsewhere for these substance types [14]. Of particular note was one patient who was a user of synthetic cannabinoids. These are a class of new psychoactive substances (NPS, formerly referred to as "designer drugs") that have been used within Europe for nearly 20 years but are relatively new for the region. The issue with these particular substances is that they have a particularly complex pharmacological effect that is beyond that of cannabinoids from the cannabis plant due to their interaction with the endocannabinoid system [type 1 cannabinoid (CB_1) and type 2 cannabinoid (CB_2) receptors] [15]. Synthetic cannabinoids exhibit CNS stimulant (i.e. cardiovascular), depressant (i.e. movement and respiratory), and hallucinogenic (i.e. acute and extreme psychosis) effects. Their direct and indirect impacts on diabetes have not been studied, but given the varying physiological and psychological effects, they arguably pose a significant contraindication and due to the frequency of diabetes in the general population, it is likely that many synthetic cannabinoid users are diabetics. Hence, further study of this sub-population would be of benefit.

Conclusion

Given the increased number of diagnoses of diabetes in the global population as well as the continued prevalence of substance use worldwide, there continues to need to be an understanding of the direct and indirect issues associated with glycaemic control and diabetes as a whole. Many drugs of abuse produce psychological and physiological effects that impede an individual's ability to self-care, coupled with contraindications for dealing with the disease and its wider impact on patient health status and clinical care.

Abbreviations

CNS: central nervous system

Declarations

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Author contributions

AEAA: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing—original draft. WE: Conceptualization, Methodology, Visualization, Writing—original draft. AA, SAM, MAR, and MA: Formal Analysis, Investigation, Methodology, Resources. SE: Formal Analysis, Investigation, Methodology, Validation, Visualization, Writing—original draft, Writing—review & editing.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Ethical permissions in relation to the National Rehabilitation Center Ethics Committee were followed for patient involvement.

Consent to participate

Informed consent to participate in the study was obtained from all participants.

Consent to publication

Not applicable.

Availability of data and materials

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