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Drug-induced weight gain in the last 10 years: a descriptive study

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Medication-induced weight gain can be frustrating to patients and health care providers. Drug-induced weight gain is a profound side effect of numerous commonly used medications. The present study aimed to investigate FAERS reports about drug-induced weight gain in the last ten years. Using the US FDA Adverse Event Reporting System (FAERS) between 2012 and 2021, a retrospective, descriptive analysis was conducted to analyze the major reported Adverse Events about weight gain. During the last ten years, 137370 reports were submitted to FAERS about drug-induced weight gain. The most common drugs that are reported by the patients and that are associated with weight gain were risperidone (11.55%), adalimumab (3.94%), pregabalin (3.86%), aripiprazole (3.1%), etanercept (2.72%), and prednisone (2.70%). In conclusion, the present study showed that drug-induced weight gain is a common side effect of several medications frequently used to treat chronic diseases. Healthcare providers should educate their patients about the medicines that may cause weight gain.

1. Introduction

Adverse events related to medications are common in primary care, and many of these events are ameliorable or preventable (Gandhi et al. 2003). Baile et al. stated that adverse drug events are unintended and harmful consequences of medications use (Bailey et al. 2016). Sonawane et al. (2018) reported that more than 770 thousand patients are injured or die annually from adverse drug events and that from 1998 to 2005, there was a 2.6-fold increase in the reports of serious adverse drug events.

The FDA Adverse Event Reporting System (FAERS) is a database for post-marketing drug safety monitoring and is publicly available healthcare information. The database contains valuable information about medication errors, patient demographics, adverse drug events, and more (Fang et al. 2009; Pratt and Danese 2009). It was initiated by the US Food and Drug Administration in 1969 and was redesigned in 1998 (FDA 2015). Besides those from manufacturers, the reports can be submitted by the public and health care professionals (Sakaeda et al. 2013).

The prevalence of obesity continues to rise globally, resulting in concurrent increases in metabolic disorders such as hypertension and type 2 diabetes, and poses a significant public health concern (Rotermann et al. 2014; CDC 2017). The increased use of medications in the previous decade may, in part, contribute to the high rates of overweight and obesity worldwide (Wharton et al. 2018). Medication-induced weight gain can be frustrating to patients and health care providers (Wharton et al. 2018). Drug-induced weight gain is a profound side effect of numerous commonly used medications. It decreases compliance with therapy and leads to the worsening of comorbid conditions related to obesity (Ness-Abramof and Apovian 2005).

Medication-induced weight gain occurs frequently, and it can be prevented. However, insufficient data are available on medication-induced weight gain (Leslie et al. 2007). So, the present study aimed to investigate FAERS reports about drug-induced weight gain in the last ten years.

2. Investigations and results

Using the US FDA Adverse Event Reporting System (FAERS) between 2012 and 2021, a retrospective, descriptive analysis was conducted to analyze the major reported Adverse Events about weight gain. "Abnormal weight gain, Overweight, Weight gain poor, Weight increased" Keywords were used to search for drug-induced weight gain. The FDA Adverse Event Reporting System (FAERS) is a database that contains adverse event reports, product quality complaints, and medication error reports that were submitted to Food and Drug Administration. The reports that were submitted by healthcare professionals, consumers, and manufacturers were included in the study.

The collected data included the total number of reports, number of serious reports, the specialty of the reporters, gender of the patients, the age of the patients, the number of annual reports that were submitted to FAERS during the study period, and the most common drugs that are reported by the patients and that are associated with weight gain. The descriptive results were represented as numbers and percentages.

During the last ten years, 137370 reports were submitted to FAERS about the drug-induced weight gain (121628 cases reported a weight increase, 11500 cases reported abnormal weight gain, 3281 cases reported as overweight, and 1208 cases reported poor weight gain). Among the 137370 cases, 68294 cases were reported as serious cases. Among the 68294 serious cases, 2144 cases were reported as dead. Regarding the specialty of the reporters, 1267 reporters did not specify whether they are healthcare providers or not, so they were excluded from Table 1. More than 62% of the reporters were consumers, and only 37.27% were healthcare providers. The specialty of the reporters is shown in Table 1.

Table 1: The specialty of the reporters

Category	Number of cases	Percentage
Healthcare Professional	50,727	37.27
Consumer	85,376	62.73
Total	136103	100.00

Table 2 shows the gender of the patients. The gender was not specified in 10863 reports, so they were excluded from Table 2. More than 63% of the patients were females.

Table 2: Gender of the patients

Category	Number of cases	Percentage
Female	80,241	63.43
Male	46,266	36.57
Total	126507	100.00

Table 3 shows the age of the patients. The age was not specified in 59,761 patients, so they were excluded from Table 3. The age of 68.40% of the patients was between 18 and 64 years, and the age of 23.63% of them was between 65 and 85 years.

Table 3: Age of the patients

Category	Number of cases	Percentage
0-1 Month	114	0.15
2 Months-2 Years	267	0.34
3-11 Years	2,355	3.03
12-17 Years	2,712	3.49
18-64 Years	53,086	68.40
65-85 Years	18,338	23.63
More than 85 Years	737	0.95
Total	77609	100.00

Table 4 shows the number of annual reports submitted to FAERS during the study period.

Table 4: The number of annual reports submitted to FAERS during the study period

Category	Number of cases	Percentage
2021	19,568	14.24
2020	15,340	11.17
2019	16,134	11.74
2018	14,757	10.74
2017	20,313	14.79
2016	13,117	9.55
2015	15,232	11.09
2014	8,853	6.44
2013	7,415	5.40
2012	6,641	4.83

Table 5 shows the most common drugs reported by the patients and associated with weight gain. More than 2000 different drugs were reported. So, only the drugs with more than 1000 individual reports were included in Table 5. The most common drugs that are reported by the patients and that are associated with weight gain were risperidone (11.55%), adalimumab (3.94%), pregabalin (3.86%), aripiprazole (3.1%), etanercept (2.72%), prednisone (2.70%), levothyroxine sodium (2.59%), olanzapine (2.18%), infliximab (2.09%), and tocilizumab (2.02%).

Table 5: The most commonly reported drugs

Category	Number of cases	Percentage
Risperidone	15,869	11.55
Adalimumab	5,409	3.94
Pregabalin	5,309	3.86
Aripiprazole	4,263	3.10
Etanercept	3,735	2.72
Prednisone	3,711	2.70
Levothyroxine Sodium	3,559	2.59
Olanzapine	2,991	2.18
Infliximab	2,866	2.09
Tocilizumab	2,771	2.02
Levonorgestrel	2,709	1.97
Methotrexate	2,592	1.89
Paliperidone	2,592	1.89
Rituximab	2,571	1.87
Tofacitinib Citrate	2,439	1.78
Etonogestrel	2,353	1.71
Sacubitril\Valsartan	2,261	1.65
Quetiapine Fumarate	2,121	1.54
Calcium Chloride\Dextrose\ Magnesium Chloride\Sodium Chloride\Sodium Lactate	1,875	1.36
Abatacept	1,780	1.30
Paliperidone Palmitate	1,590	1.16
Lenalidomide	1,576	1.15
Ruxolitinib	1,571	1.14
Ambrisentan	1,570	1.14
Omalizumab	1,558	1.13
Gabapentin	1,475	1.07
Leflunomide	1,436	1.05
Infliximab-Dyyb	1,359	0.99
Certolizumab Pegol	1,352	0.98
Insulin Glargine	1,336	0.97
Teriparatide	1,292	0.94
Brexpiprazole	1,202	0.88
Acetaminophen	1,197	0.87
Duloxetine Hydrochloride	1,181	0.86
Golimumab	1,174	0.85
Treprostinil	1,174	0.85
Sertraline Hydrochloride	1,119	0.81
Macitentan	1,105	0.80
Leuprolide Acetate	1,105	0.80
Metformin Hydrochloride	1,050	0.76
Venlafaxine Hydrochloride	1,022	0.74
Insulin Lispro	1,000	0.73

3. Discussion

Drug-induced weight gain is a serious side effect of several frequently used medications, leading to noncompliance with treatment and exacerbating patients' conditions. The most common drugs that are associated with weight gain are diabetes medications (such as insulin, thiazolidinedione therapy, and insulin secretagogues), psychotropic agents (such as olanzapine, quetiapine, clozapine, and risperidone), antidepressants (such as some serotonin reuptake inhibitors, mirtazapine, and amitriptyline), mood stabilizers (such as lithium), and antiepileptic drugs (such as carbamazepine, valproate, and gabapentin) (Ness-Abramof and Apovian 2005). Saunders et al. (2016) reported that drug-induced weight gain is a common adverse event for antidiabetic drugs (including insulin, meglitinides, sulfonylureas, and thiazolidinediones), antihypertensives (such as alpha-adrenergic blockers, beta-adrenergic blockers (including atenolol, metoprolol, nadolol, and propranolol), antidepressants (such as amitriptyline, doxepin, imipramine, mirtazapine, paroxetine, and nortriptyline).

The most common drugs reported by the patients and associated with weight gain were risperidone, adalimumab, pregabalin, aripiprazole, etanercept, prednisone levothyroxine sodium, olanzapine, infliximab, and tocilizumab. Dayabandara et al. (2017) reported that antipsychotic-induced weight gain is the main treatment problem for physicians and that patient's weight increases after starting antipsychotics and continue for the long term. Bak et al. (2014) reported that the use of antipsychotics increases the weight of patients (≥7% from baseline). Oh et al. (2015) stated that the risk of clinically relevant weight increase in patients with schizophrenia was most significant with the use of quetiapine, clozapine, and olanzapine. Hoppe et al. (2008) informed that pregabalin use is associated with a high risk for weight gain depending on total anticonvulsant drug load. Moreover, Preuss et al. (2021) reported that pregabalin's most reported adverse events were dizziness, drowsiness, blurred vision, edema, dry mouth, difficulty concentrating, and weight gain.

In addition to antidepressants, antipsychotics, and antiepileptic agents, our study showed that weight gain was also associated with monoclonal antibodies, TNF-α Inhibitors, the endocrine disorders medications such as corticosteroids and levothyroxine. Lutf and Hammoudeh (2012) reported that weight gain was observed in 13.3% of the patients who used anti-TNF therapy and that weight gain and hair loss may be one reason for discontinuing the anti-TNF therapy. Patsalos et al. (2020) reported that patients gained an average of 0.90 kg under infliximab, 2.34 kg under etanercept, and 2.27 kg during treatment with adalimumab. Lepp et al. (2020) informed that approximately 60% of Crohn's disease patients experience weight gain within the first six weeks of using infliximab. Moreover, Choi et al. (2020) stated that weight and the leptin-adiponectin ratio increased after tocilizumab treatment in patients with rheumatoid arthritis (Choi et al. 2020). Wung et al. (2008) reported that despite their benefits in several diseases, glucocorticoids also have several side effects, including weight gain. Berthon et al. (2015) found that oral corticosteroids are an efficacious treatment for asthma exacerbations, but the development of undesirable adverse effects such as weight gain may reduce patient adherence to therapy. Furthermore, previous studies showed that weight gain and inability to lose weight occur in patients with treated hyperthyroidism and hypothyroidism (Hamilton et al. 2008; Hoogwerf and Nuttall 1984).

In conclusion, the present study showed that drug-induced weight gain is a common side effect of several medications frequently used to treat chronic diseases. Healthcare providers should educate their patients about the medicines that may cause weight gain. In most cases, the clinician can prescribe alternative other drugs that offer the same beneficial effect without causing excess weight gain, but if there is no alternative for the medicine, adjunctive therapies should be considered.

Conflicts of interest: None declared.

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