Non-health Care Facility Medication Errors Associated with Hormones and Hormone Antagonists in the United States

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Abstract

Introduction Hormones and hormone antagonists are frequently associated with medication errors and may result in important adverse outcomes. The purpose of this study is to investigate non-health care facility (non-HCF) medication errors associated with hormones and hormone antagonists in the United States (US).

Methods A retrospective analysis of National Poison Data System data was conducted to identify characteristics and trends of unintentional non-HCF therapeutic errors involving hormones and hormone antagonists among individuals of all ages from 2000 to 2012.

Results From 2000 to 2012, US poison control centers received 169,695 calls regarding unintentional non-HCF therapeutic errors associated with hormone therapies, averaging 13,053 medication error calls annually. The rate of reported errors increased significantly by 162.6% ($p < 0.001$), from 2.24 per 100,000 US residents in 2000 to 5.89 per 100,000 in 2012. Two thirds of the errors (65.2%) occurred among females. The medications most commonly associated with errors were thyroid preparations (23.2%), corticosteroids

(21.9%), and insulin (20.0%). All nine deaths and 93.2% of major effects were attributed to hypoglycemic agents. Sulfonylureas alone accounted 43.9% of major effects. The number and rate of therapeutic errors increased significantly for all medication categories except estrogen and thiazolidinediones. Most errors were managed at the site of exposure (82.9%) and did not result in serious medical outcomes (95.6%).

Conclusions This study provides an overview of non-HCF medication errors associated with hormones and hormone antagonists in the US. While most errors did not result in adverse outcomes, their increasing frequency places a greater burden on the health care system.

Keywords Unintentional therapeutic error · Hormones · Hormone antagonists · Oral hypoglycemic medications · Poison control center

Abbreviations

AAPCC	American Association of Poison Control Centers
AMA	Against medical advice
HCF	Health care facility
CCU	Critical care unit
CI	Confidence interval
NPDS	National Poison Data System
OR	Odds ratio
PCC	Poison control center
US	United States

Introduction

Medication errors are a leading cause of morbidity and mortality in the United States (US), with non-health care facility

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(HCF) medication errors increasing in recent years [1–5]. Prior research using US poison control center (PCC) data found that compared with other drug categories, hormones and hormone antagonists are ranked third, behind cardiovascular drugs and analgesics, for the annual number of reported medication errors resulting in moderate to severe medical outcomes [2].

The drug category of hormones and hormone antagonists includes several medications previously identified as being associated with a substantial number of adverse drug events, including hypoglycemics and corticosteroids [6–11]. In addition, medication errors associated with many of these drugs are increasing. For example, a study utilizing data from nine regional PCCs in the US found a 495% increase in unintentional therapeutic errors involving insulin from 2000 to 2009 [6].

The continuing increase in hormone and hormone antagonist use and associated medication errors supports the need for further research to identify the characteristics and trends associated with these errors. Prior studies of hormone and hormone antagonist medication errors have either briefly discussed these medications as part of a broader study including a variety of drug categories, or described errors associated with a specific hormone or hormone antagonist [2–14]. This is the first comprehensive study describing the epidemiology of hormone- and hormone antagonist-related unintentional therapeutic errors reported to PCCs in the US.

Methods

Data Source

This study retrospectively analyzed 2000–2012 data from the National Poison Data System (NPDS) to characterize non-HCF unintentional therapeutic errors involving hormones and hormone antagonists among individuals of all ages. The NPDS is maintained by the American Association of Poison Control Centers (AAPCC) and receives near real-time data collected from calls to regional PCCs in the US and its territories [15].

Case Selection Criteria

The AAPCC Micromedex Joint Coding Group's generic substance coding system was used to identify exposures to hormones, hormone antagonists, and oral hypoglycemics (Appendix Table 4) [15]. In the event of a multiple-substance exposure, PCC specialists rank substances based on their likely contribution to the reported clinical effects. This study includes only cases for which a hormone, hormone antagonist, or oral hypoglycemic was ranked first.

Exposures in this study were limited to those that were classified by PCC specialists as “unintentional therapeutic errors,” defined by the AAPCC as “an unintentional deviation from a proper therapeutic regimen that results in the wrong dose, incorrect route of administration, administration to the wrong person, or administration of the wrong substance” [15]. The terms “Unintentional therapeutic error” and “medication error” are used interchangeably in this article. Unless otherwise specified, insulin is included in all calculations involving “hypoglycemics” or “hypoglycemic agents” and is not included in calculations regarding “oral hypoglycemics” or “oral hypoglycemic agents.” Exposures were excluded from this study if they occurred outside the 50 US states or the District of Columbia, or if they involved confirmed non-exposures, intentional abuse or malicious intent, or occurred in a HCF, nursing home, or prison.

Study Variables

Data were analyzed by hormone medication category (Appendix), type of therapeutic error, level of health care received, and medical outcome. Level of health care received was categorized as treated/evaluated and released, admitted (to a critical care unit [CCU] or non-critical care unit [non-CCU]), patient refused referral/did not arrive at HCF, patient lost to follow-up/left against medical advice, or no HCF treatment received (including those who were managed at the site of exposure). Medical outcomes included serious medical outcomes (death, major effect, or moderate effect), minor effect, no effect, and not followed/unable to follow. The AAPCC defines medical outcomes as follows: major effect (symptoms are life-threatening or result in significant residual disability or disfigurement), moderate effect (symptoms are more pronounced, prolonged, or systemic than minor symptoms and usually require treatment), and minor effect (symptoms are minimally bothersome and usually resolve rapidly) [16].

For some analyses, age was grouped into three subsets: younger children (0–5 years), older children (6–19 years), and adults (≥ 20 years). Other variables analyzed included gender, exposure site (own residence, other residence, public area, restaurant/food service, school, workplace, other, or unknown), management site (on site at a non-HCF location, patient already in or en route to a HCF when PCC called, patient referred by PCC to a HCF, other, or unknown), clinical effects, therapies performed, and exposure chronicity (acute, acute-on-chronic, or chronic). Acute exposures consist of “a single, repeated, or continuous exposure occurring over a period of 8 h or less” [16]. Acute-on-chronic exposures are defined as “a single exposure that was preceded by continuous, repeated, or intermittent exposure” over a period of > 8 h [16]. Chronic exposures are a “continuous, repeated or intermittent exposure of the same substance lasting longer than 8 h” [16].

Statistical Analysis and Ethical Statement

Data were analyzed using SPSS 21.0 (IBM Corp., Armonk, NY) software. US Census Bureau July 1 intercensal and postcensal population estimates for 2000–2012 were used to calculate exposure rates [17, 18]. Simple linear regression was used to determine the statistical significance of exposure trends over the study period. Statistical significance was determined at $\alpha = 0.05$. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to compare different types of hormones and hormone antagonists with respect to hospital admission (admitted to a CCU or non-CCU) or major effects. This study was deemed exempt by the Institutional Review Board of the authors' institution.

Results

General Characteristics and Trends

From 2000 to 2012, there were 169,695 non-HCF unintentional therapeutic errors attributable to hormones and hormone antagonists reported to US PCCs, averaging 13,053 exposures annually. The rate of reported medication errors increased by 162.6% ($p < 0.001$) from 2.24 per 100,000 US residents in 2000 to 5.89 in 2012. Most exposures (65.3%, $n = 110,866$) occurred among females (Table 1) and the rate of medication errors increased significantly ($p < 0.001$) for both males and females during the study period (Fig. 1). Within the age groups of 0–5 years and 6–19 years, 58.5 and 55.4% of reported errors were among males, respectively. However, males accounted for only 29.1% of errors among individuals 20 years of age and older.

The frequency of reported therapeutic errors peaked at ages 0–1 years and again between ages 50–65 years (Fig. 2). Hormone and hormone antagonist-related error rates were highest among older individuals, peaking at 10.42 per 100,000 US residents among 80-year-olds. The lowest rates were among individuals 18–29 years old (Fig. 2). In this study, 11.6% of reported exposures involved more than one substance.

Types of Therapeutic Error

The most common types of therapeutic errors reported to poison control centers were “inadvertently took/given medication twice” (32.9%) and “wrong medication taken/given” (20.2%) (Table 1). “Inadvertently taking/giving the medication twice” was the most common error type for all hypoglycemic agents except insulin. Medication errors involving insulin were most frequently attributed to “wrong medication taken/given” (45.7%). The most common types of therapeutic error varied among age groups. “Inadvertently took/given medication

twice” was the most common error among children 0–5 years old and adults ≥ 20 years old, representing 29.7% and 35.2% of errors, respectively. Among older children 6–19 years old, 27.9% of errors were attributable to “inadvertently took/given someone else's medication.”

Exposure Chronicity, Exposure Site, and Management Site

A majority (62.8%, $n = 106,607$) of reported exposures were attributable to an acute administration of the medication, 34.2% ($n = 58,012$) were acute-on chronic, and 2.9% ($n = 4838$) were chronic. Most exposures occurred at the individual's own residence and were managed on site without HCF involvement (96.6%, $n = 163,902$ and 82.9%, $n = 140,635$, respectively). A small percentage of reported medication errors (8.6%, $n = 14,610$) were referred to a HCF by the PCC, and 6.4% were already in or en route to a HCF when the PCC was called.

Clinical Effects, Therapies, and Level of Health Care Received

Ninety percent (90.1%, $n = 152,839$) of reported medication errors resulted in no observable clinical effects, and for 59.9% ($n = 101,589$) of cases, no therapies were performed. Overall, 7.8% of medication errors were treated/evaluated and released at a HCF, 1.4% were admitted to a non-critical care unit, and 0.7% were admitted to a critical care unit (Table 1). The percentage of exposures that were treated at a HCF (treated/evaluated and released, or admitted to a CCU or non-CCU) was highest among adults (10.9%) and lowest among children ≤ 5 years (4.3%).

Medical Outcomes

More than two thirds (67.5%) of reported exposures were not followed up after initial contact with the PCC, primarily because the PCC specialist determined that the exposure was likely to result in only minimal clinical effects (42.5%) or was nontoxic (20.8%) (Table 1). In nearly one fourth (24.2%) of cases, the medical outcome was “no effect,” while 3.9% had minor effects, 4.2% had moderate effects, and 0.1% resulted in major effects. All of the nine fatalities occurred among adults, and all were admitted to a CCU ($n = 8$) or non-CCU ($n = 1$) prior to death.

Medication Characteristics and Trends

Hypoglycemic agents (insulin and all oral hypoglycemics) were associated with 92.1% ($n = 3306$) of reported hospital admissions (Table 2) and individuals exposed to hypoglycemic agents had higher odds (OR 15.95, 95% CI

Table 1 Characteristics of non-health care facility medication errors associated with hormones and hormone antagonists, National Poison Data System 2000–2012

Characteristics	Age group, <i>n</i> (%)			Total <i>n</i> (%) [*]
	0–5 years	6–19 years	≥ 20 years	
Gender				
Female	5874 (41.2)	8462 (44.6)	95,995 (70.8)	110,866 (65.3)
Male	8341 (58.5)	10,518 (55.4)	39,526 (29.1)	58,628 (34.5)
Unknown	37 (0.3)	12 (0.1)	104 (0.1)	201 (0.1)
Therapeutic error ^a				
Inadvertently took/given medication twice	4229 (29.7)	3530 (18.6)	47,789 (35.2)	55,829 (32.9)
Wrong medication taken/given	1602 (11.2)	3577 (18.8)	28,902 (21.3)	34,217 (20.2)
Other incorrect dose	2183 (15.3)	2866 (15.1)	18,848 (13.9)	24,015 (14.2)
Inadvertently took/given someone else's medication	2182 (15.3)	5297 (27.9)	15,004 (11.1)	22,551 (13.3)
Medication doses taken/given too closely together	1222 (8.6)	1118 (5.9)	8944 (6.6)	11,326 (6.7)
Incorrect formulation/concentration given	513 (3.6)	665 (3.5)	5279 (3.9)	6492 (3.8)
Confused units of measure	780 (5.5)	408 (2.1)	2480 (1.8)	3687 (2.2)
Health professional iatrogenic error	458 (3.2)	309 (1.6)	1679 (1.2)	2470 (1.5)
Other/unknown therapeutic error	1745 (12.2)	2122 (11.2)	12,438 (9.2)	16,432 (9.7)
Level of care				
No HCF treatment received	13,496 (94.7)	17,238 (90.8)	112,890 (83.2)	144,291 (85.0)
Treated/evaluated and released	513 (3.6)	1059 (5.6)	11,641 (8.6)	13,252 (7.8)
Individual lost to follow-up/left AMA	117 (0.8)	246 (1.3)	4477 (3.3)	4934 (2.9)
Individual refused referral/did not arrive at HCF	25 (0.2)	127 (0.7)	3423 (2.5)	3595 (2.1)
Admitted to non-critical care unit	72 (0.5)	238 (1.3)	2142 (1.6)	2455 (1.4)
Admitted to critical care unit	29 (0.2)	82 (0.4)	1021 (0.8)	1135 (0.7)
Admitted to psychiatric facility	0 (0.0)	2 (0.0)	31 (0.0)	33 (0.0)
Medical outcome				
Not followed, minimal clinical effects possible	6672 (46.8)	8799 (46.3)	56,261 (41.5)	72,067 (42.5)
Not followed, judged as nontoxic	4401 (30.9)	5136 (27.0)	25,552 (18.8)	35,260 (20.8)
No effect	2721 (19.1)	3650 (19.2)	34,551 (25.5)	41,073 (24.2)
Unable to follow, judged as potentially toxic	87 (0.6)	326 (1.7)	6679 (4.9)	7224 (4.3)
Minor effect	302 (2.1)	705 (3.7)	5623 (4.1)	6649 (3.9)
Moderate effect	64 (0.4)	360 (1.9)	6734 (5.0)	7176 (4.2)
Major effect	5 (0.0)	16 (0.1)	216 (0.2)	237 (0.1)
Death	0 (0.0)	0 (0.0)	9 (0.0)	9 (0.0)
Total (row %)	14,252 (8.4)	18,992 (11.2)	135,625 (79.9)	169,695 (100.0)

Percentages may not sum to 100.0% due to rounding error

HCF health care facility; PCC poison control center, AMA against medical advice

^{*}Total includes 826 exposures for which the individual's age is unknown

^aTherapeutic error percentages may sum to > 100.0% due to multiple error types

14.12–18.01) of hospital admission than those exposed to other medication categories. Combined, insulin and sulfonylureas accounted for 77.0% of CCU admissions and 78.8% of non-CCU admissions. Although thyroid preparations and corticosteroids were associated with 23.2% and 21.9% of reported medication errors, they comprised only

3.1% and 2.8% of hospital admissions, respectively. Sulfonylureas accounted for 6.9% of reported exposures, but they represented 42.6% of hospital admissions; sulfonylurea exposures had 11.40 times (95% CI 10.64–12.22) greater odds of hospital admission than exposures to other medications.

Fig. 1 Annual frequency and rate of non-health care facility medication errors associated with hormones and hormone antagonists by gender, National Poison Data System 2000–2012

The medications associated with errors varied by age group. Eighty percent (80.1%) of reported exposures among children 0–5 years old were related to corticosteroids. Corticosteroids (34.4%) were also most frequently associated with medication errors among children 6–19 years old, followed by thyroid preparations (24.5%). Among adults, thyroid preparations (24.4%) and biguanides (14.4%) were linked to the most cases. Serious medical outcomes related to insulin and oral hypoglycemic medications were more frequent among adults (Table 3).

The number and rate of reported therapeutic errors increased significantly ($p = 0.011$) during the study period for all hormones except estrogen, unknown hormones or hormone antagonists, and thiazolidinediones. From 2000 to

2012, insulin-related medication errors increased in frequency (675.2%) and rate (596.9%) ($p < 0.001$) (Fig. 3). Similar increases were seen for thyroid preparations and corticosteroids (Fig. 3). The rate of reported medication errors associated with estrogen displayed a significant decrease over the study period ($p = 0.002$), while medication errors associated with thiazolidinediones increased early in the study period ($p = 0.001$) and then decreased beginning in 2005 ($p < 0.001$).

Among the nine fatal exposures, five were attributed to biguanides, three to sulfonylureas, and one to insulin (Tables 2 and 3). Hypoglycemics (insulin and all oral hypoglycemics) were associated with 93.2% of all major effects, with sulfonylureas alone accounting for 43.9% of these

Fig. 2 Frequency and rate of non-health care facility medication errors associated with hormones and hormone antagonists by age, National Poison Data System 2000–2012

Table 2 Frequency of non-health care facility medication errors associated with hormones and hormone antagonists by medication type, age group, HCF level of care, and serious medical outcomes, National Poison Data System 2000–2012

Medication description	Age group			HCF level of care			Serious medical outcomes				Total, <i>n</i> (%)
	0–5 years	6–19 years	≥20 years	CCU	Non-CCU	Total admitted, <i>n</i> (%)	Death	Major effect	Moderate effect	Total serious, <i>n</i> (%)	
Misc. hormones/antagonists											
Thyroid preparations	1546	4660	33,056	43	68	111 (3.1)	0	6	169	175 (2.4)	39,430 (23.2)
Corticosteroids	11,421	6525	19,086	30	69	99 (2.8)	0	4	152	156 (2.1)	37,217 (21.9)
Insulin	134	829	32,844	418	861	1279 (35.6)	1	85	4419	4505 (60.7)	33,996 (20.0)
Oral contraceptives	248	1540	2939	0	3	3 (0.1)	0	0	27	27 (0.4)	4773 (2.8)
Estrogens	108	410	2915	0	1	1 (0.0)	0	1	13	14 (0.2)	3448 (2.0)
Progestins	179	699	2258	1	8	9 (0.3)	0	1	9	10 (0.1)	3164 (1.9)
Other hormones	241	1012	1718	21	22	43 (1.2)	0	2	44	46 (0.6)	2988 (1.8)
Other hormone antagonists	98	274	2032	4	3	7 (0.2)	0	2	10	12 (0.2)	2417 (1.4)
Selective estrogen receptor modulators	27	174	1987	4	6	10 (0.3)	0	0	13	13 (0.2)	2197 (1.3)
Androgens	16	58	566	0	1	1 (0.0)	0	0	6	6 (0.1)	648 (0.4)
Unknown hormones or hormone antagonists	0	2	15	0	0	0 (0.0)	0	0	0	0 (0.0)	17 (0.0)
Oral hypoglycemics											
Biguanides	88	1807	19,501	105	213	318 (8.9)	5	20	442	467 (6.3)	21,488 (12.7)
Sulfonylureas	79	612	10,961	456	1074	1530 (42.6)	3	104	1626	1733 (23.3)	11,690 (6.9)
Thiazolidinediones	54	240	3364	22	62	84 (2.3)	0	4	115	119 (1.6)	3669 (2.2)
Other or unknown	13	150	2383	31	64	95 (2.6)	0	8	131	139 (1.9)	2553 (1.5)
Total	14,252	18,992	135,625	1135	2455	3590 (100.0)	9	237	7176	7422 (100.0)	169,695 (100.0)

Percentages may not sum to 100.0% due to rounding error

HCF health care facility, CCU critical care unit

exposures. In contrast, the more frequently reported exposures to thyroid preparations and corticosteroids accounted for 2.5 and 1.7% of major effects, respectively. Individuals who were exposed to hypoglycemics had greater odds (OR 18.17, 95% CI 10.94–30.19) of experiencing major effects than individuals exposed to other medication categories.

Discussion

An average of approximately 13,000 hormone-related medication errors were reported annually to US PCCs during the 13-year study period. Calls to PCCs regarding hormone-related medication errors increased steadily over this period; in the final year of the study, PCCs received 18,491 calls for an average of one call every 28 min. Meanwhile, all human exposure calls to PCCs increased from 2000 to 2007 before declining from 2007 to 2012 [15]. The increase in hormone-related calls may be attributed to the frequent and increasing prescribing of multiple categories of hormones and hormone antagonists in the US, such as hypoglycemics, corticosteroids, and androgen medications [19–25]. The decrease in

medication errors associated with estrogen and thiazolidinediones is likely due to a decline in prescribing for both of these medication categories [12, 19, 24, 26, 27]. Estrogen prescriptions decreased significantly after the hormone was linked to increased risk of stroke during menopausal hormone therapy trials [28, 29]. Thiazolidinedione prescriptions likely declined due to concerns about cardiovascular events related to the use of rosiglitazone, a drug in the thiazolidinedione class [19, 24, 30, 31].

Overall, approximately two thirds of reported medication errors were among females. However, among individuals < 20 years old, a greater proportion of reported errors were among males. For each drug category included in this study except androgens, a greater proportion of medication errors were among females. This includes hypoglycemic agents, despite the fact that there are more males diagnosed with diabetes in the US than females [32]. The reason for this discrepancy could not be determined using the NPDS data, but it is consistent with prior research demonstrating a greater proportion of reported medication errors among adult females than males [2]. The higher error frequency among adult females may be because they are more likely to make these errors, or

Table 3 Characteristics of non-health care facility medication errors associated with insulin and oral hypoglycemics, National Poison Data System 2000–2012

Medication Category and Serious Medical Outcomes, <i>n</i> (%)												
Characteristics	Insulin			Biguanides			Sulfonylureas			Other or unknown oral hypoglycemics		
	Death	Major effects	Moderate effects	Death	Major effects	Moderate effects	Death	Major effects	Moderate effects	Death	Major effects	
Age												
0–5 years	0	2 (2.4)	21 (0.5)	0	0	2 (0.5)	0	1 (1.0)	19 (1.2)	0	1 (8.3)	
6–19 years	0	5 (5.9)	130 (2.9)	0	0	29 (6.6)	0	11 (10.6)	136 (8.4)	0	20 (8.1)	
≥ 20 years	1 (100.0)	78 (91.8)	4257 (96.3)	5 (100.0)	20 (100.0)	411 (93.0)	3 (100.0)	92 (88.5)	1467 (90.2)	0	11 (91.7)	
Unknown	0	0	11 (0.2)	0	0	0	0	0	4 (0.2)	0	0	
Gender												
Female	0	30 (35.3)	2642 (59.8)	4 (80.0)	6 (30.0)	294 (66.5)	2 (66.7)	52 (50.0)	1004 (61.7)	0	6 (50.0)	
Male	1 (100.0)	55 (64.7)	1776 (40.2)	1 (20.0)	14 (70.0)	148 (33.5)	1 (33.3)	52 (50.0)	622 (38.3)	0	6 (50.0)	
Unknown	0	0	1 (0.0)	0	0	0	0	0	0	0	0	
Chronicity of exposure												
Acute	0	44 (51.8)	2179 (49.3)	0	10 (50.0)	250 (56.6)	0	65 (62.5)	1198 (73.7)	0	8 (66.7)	
Acute-on-chronic	0	34 (40.0)	2138 (48.4)	0	6 (30.0)	158 (35.7)	1 (33.3)	22 (21.2)	340 (20.9)	0	4 (33.3)	
Chronic	1 (100.0)	5 (5.9)	88 (2.0)	4 (80.0)	4 (20.0)	33 (7.5)	2 (66.7)	14 (13.5)	79 (4.9)	0	5 (2.0)	
Unknown	0	2 (2.4)	14 (0.3)	1 (20.0)	0	1 (0.2)	0	3 (2.9)	9 (0.6)	0	3 (1.2)	
Therapeutic error ^a												
Inadvertently took/given medication twice	0	4 (4.7)	254 (5.7)	0	3 (15.0)	123 (27.8)	0	9 (8.7)	272 (16.7)	0	58 (23.6)	
Wrong medication taken/given	0	30 (35.3)	2281 (51.6)	0	1 (5.0)	73 (16.5)	2 (66.7)	23 (22.1)	298 (18.3)	0	2 (16.7)	
Other incorrect dose	0	26 (30.6)	744 (16.8)	2 (40.0)	3 (15.0)	64 (14.5)	0	14 (13.5)	154 (9.5)	0	3 (25.0)	
Inadvertently took/given someone else's medication	0	0	66 (1.5)	0	2 (10.0)	92 (20.8)	0	32 (30.8)	613 (37.7)	0	80 (32.5)	
Medication doses taken/given too closely together	0	3 (3.5)	38 (0.9)	0	0	18 (4.1)	0	1 (1.0)	51 (3.1)	0	11 (4.5)	
Incorrect formulation/concentration given	1 (100.0)	5 (5.9)	602 (13.6)	0	0	6 (1.4)	0	1 (1.0)	27 (1.7)	0	4 (1.6)	
Confused units of measure	0	3 (3.5)	193 (4.4)	0	1 (5.0)	5 (1.1)	0	1 (1.0)	5 (0.3)	0	0	
Health professional iatrogenic error	0	3 (3.5)	77 (1.7)	0	1 (5.0)	14 (3.2)	3 (100.0)	15 (14.4)	73 (4.5)	0	16 (6.5)	
Other/unknown therapeutic error	0	19 (22.4)	423 (9.6)	3 (60.0)	9 (45.0)	68 (15.4)	0	23 (22.1)	205 (12.6)	0	30 (12.2)	
Total, <i>n</i> (%)	1 (100.0)	85 (100.0)	4419 (100.0)	5 (100.0)	20 (100.0)	442 (100.0)	3 (100.0)	104 (100.0)	1626 (100.0)	0 (0.0)	246 (100.0)	

^a Therapeutic error percentages may sum to > 100.0% due to some cases involving multiple types of error

because, once an error has occurred, they are more likely to call a PCC.

Insulin had the largest increase in medication error frequency, increasing nearly eightfold over 13 years. This finding is consistent with prior research and is at least partially explained by the fact that the number of individuals diagnosed with diabetes in the US increased 77.7% from 2000 to 2012 [6, 33]. Insulin use has likewise increased in recent years, with greater numbers of individuals being prescribed insulin for the treatment of type 2 diabetes, particularly in newer formulations and as part of combination therapies [34]. Although the frequency of medication error calls to PCCs for insulin, corticosteroids, and thyroid preparations was similar in 2012, insulin's narrower therapeutic window and more severe toxicity likely explain its much higher proportion of serious medical outcomes. Insulin overdoses can result in severe hypoglycemia, seizures, coma, or death. Insulin underdoses may cause hyperglycemia or ketoacidosis [35]; however, PCCs are less likely to be called for medication underdosing than overdosing.

Collectively, hypoglycemic agents (including insulin) were associated with 43.3% of reported medication errors, but constituted 92.1% of hospital admissions and 93.8% of serious medical outcomes, including all nine fatalities in this study. Sulfonylureas alone accounted for 42.4% of hospital admissions and 23.3% of serious medical outcomes despite comprising only 6.9% of reported errors. Medication errors related to sulfonylureas increased significantly over the study period, despite the fact that the number of prescriptions for these drugs remained constant from 2003 to 2012 [19]. Biguanides accounted for the largest proportion of calls attributed to oral hypoglycemics and also increased significantly over the study period, a finding that is consistent with the 97% increase in biguanide prescriptions from 2003 to 2012 [19].

A greater proportion of adults than children were treated at HCFs for medication errors related to hormone and hormone antagonists. This is likely due to differences in hormone use by age group. For example, 80.1% of medication errors among children 0–5 years old were related to corticosteroids and 2.6% to hypoglycemic agents, while 50.9% of reported errors among adults involved hypoglycemics.

The most common type of therapeutic error associated with hormones and hormone antagonists was inadvertently taking/giving the medicine twice, accounting for one third of all calls. The prevention of this type of error may be helped by the use of a child-resistant scheduling medication box for non-liquid medications or a medication container with technology that signals when a dose is due. Among older children, the most frequent scenario was inadvertently taking/giving someone else's medication. Adult supervision during medication administration, even among older children, and efforts by manufacturers to ensure that medications have different appearances and names may help prevent this confusion. Medication labeling that follows recommendations for health

literacy and numeracy is also recommended. The use of food, oral or intravenous glucose, glucagon, and octreotide are available secondary prevention measures to combat the development of hypoglycemia in the event of a hypoglycemic medication error leading to overdose.

Unlike other hypoglycemic agents, most insulin-related medication errors were attributed to “wrong medication taken/given.” This may be associated with confusion between rapid- and long-acting formulations of insulin. While our data could not be used to confirm this reason for the insulin-related errors in this study, prior studies have identified this as a topic of concern [36]. Prevention strategies to reduce the risk of this type of error include greater differentiation of insulin packaging and storing rapid- and long-acting insulins in separate locations [36].

Study Limitations

This study has several limitations. We could not determine if hospitalizations were a result of the medication error or an underlying health condition. In addition, the proportion of cases that were admitted to a HCF for monitoring of potential late medication effects that did not manifest is unknown. The NPDS underestimates the true number of hormone and hormone antagonist-related medication errors because it only includes errors voluntarily reported to a PCC. Some cases may be treated in a HCF without a report being filed with a PCC. Although PCC specialists follow up with cases to resolution whenever feasible based on follow-up protocols, it is possible that a patient could exhibit clinical effects or seek medical care after completing contact with the PCC, resulting in an underestimate of the severity of the exposure. In addition, PCCs rely on self-reported information and cannot completely verify information for reported exposures, including the substance, medication error, and medical outcome. Reported medication error exposures do not necessarily indicate a poisoning or overdose. In the event of exposures involving multiple substances, we only examined cases based on the highest ranked substance. Other medications may have influenced medical outcomes; however, only 11.6% of reported exposures involved more than one substance; therefore, the effect of multiple substances was likely small. Despite these limitations, the NPDS is a national database containing extensive information about reported medication errors in the US and is a valuable tool for investigating non-HCF medication errors related to hormones and hormone antagonists.

Conclusions

This is the first comprehensive study done at the national level to investigate non-HCF medication errors reported to poison control centers involving all types of hormones and hormone antagonists. The annual number of these reported errors

Fig. 3 Top three hormones and hormone antagonists associated with non-health care facility medication errors: medication error frequency by year, National Poison Data System 2000–2012

increased throughout the study period to more than 18,000 in 2012. While most of these errors did not lead to a clinically significant outcome, some exposures, especially those associated with hypoglycemic agents, have the potential to result in serious medical outcomes for the individual and burden the health care system.

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Compliance with Ethical Standards

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Conflict of Interest The authors declare that they have no conflicts of interest.

Appendix

Table 4 AAPCC generic codes for hormones and hormone antagonists included in this study

Hormone/hormone antagonist group	Generic code	Generic code name
Miscellaneous hormones and hormone antagonists		
	201000	Androgens
	132000	Corticosteroids
	155000	Estrogens
	236000	Insulin
	202000	Progestins
	201121	Selective estrogen receptor modulators
	044000	Thyroid preparations (including synthetics and extracts)
	068000	Oral contraceptives
	077822	Other hormones
	077823	Other hormone antagonists
	077824	Unknown hormones or hormone antagonists
Oral hypoglycemics		
	201118	Oral hypoglycemics: biguanides
	233000	Oral hypoglycemics: other or unknown
	201119	Oral hypoglycemics: sulfonylureas
	201120	Oral hypoglycemics: thiazolidinediones

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