ADVERSE REACTION REPORTING FOR ENERGY DRINKS AND CAFFIENATED PRODUCTS

SUMMARY OF DATA FROM HEALTH CANADA'S ADVERSE REACTION REPORTING FOR SPECIFIC PRODUCTS DATABASE

DAVID HAMMOND, JESSICA REID & SARA ZUKOWSKI

UNIVERSITY OF WATERLOO
FACULTY OF APPLIED HEALTH SCIENCES
School of Public Health and Health Systems

SUGGESTED CITATION

HAMMOND D, READ JR, ZUKOWSKI S. ADVERSE REACTION REPORTING FOR ENERGY DRINKS AND CAFFIENATED PRODUCTS: SUMMARY OF DATA FROM HEALTH CANADA'S ADVERSE REACTION REPORTING FOR SPECIFIC PRODUCTS DATABASE. MARCH 2017.

CONTACT

DAVID HAMMOND PHD
PROFESSOR
SCHOOL OF PUBLIC HEALTH & HEALTH SYSTEMS
UNIVERSITY OF WATERLOO
WATERLOO, ON CANADA
N2L 3G1
DHAMMOND@UWATERLOO.CA
WWW.DAVIDHAMMOND.CA

DESCRIPTION

Health Canada's *Adverse Reaction Reporting for Specific Products* was searched for adverse reactions associated with energy drinks and for 'coffee' related beverages.

Canada Vigilance Program

The Canada Vigilance Program is Health Canada's post-market surveillance program that collects and assesses reports of suspected adverse reactions to health products marketed in Canada. Post-market surveillance enables Health Canada to monitor the safety profile of health products once they are marketed to ensure that the benefits of the products continue to outweigh the risks. The Canada Vigilance Program has collected reports of suspected adverse reactions since 1965. Adverse reaction reports are submitted by health professionals and consumers on a voluntary basis either directly to Health Canada or via Market Authorization Holders. The information collected by the program can be accessed through the Canada Vigilance Online Database.[1]

The following limitations should be taken into account when interpreting the data:

1. The data has been collected primarily by a spontaneous surveillance system in which suspected adverse reactions to health products are reported to market authorization holders (manufacturers) and Health Canada on a voluntary basis.

2. There is under reporting of adverse reactions with both voluntary and mandatory surveillance systems.

3. Adverse reaction reports are suspected associations which reflect the opinion or observation of the individual reporter. The data presented reflects, as much as possible, the reporter's observations and opinions, and does not reflect any Health Canada assessment of association between the health product and the reaction(s).

4. Inclusion of a particular reaction does not necessarily mean that it was caused by the suspected health product(s). Certain reported reactions may occur spontaneously. They provide a background rate in the general population and may have a temporal, but not necessarily a causal, relationship with the health product. The purpose of the Canada Vigilance Program is to detect possible signals of adverse reactions associated with health products. Additional scientific investigations are required to validate signals from the Canada Vigilance Program and to establish a cause and effect relationship between a health product and an adverse reaction. Assessment of causality must include other factors such as temporal associations, the possible contribution of concomitant medication or therapies, the underlying disease, and the previous medical history.

5. This database contains only a small proportion of adverse reactions reported following receipt of vaccines, and is reflective of serious reactions reported to market authorization holders as required under the Food and Drugs Act.

[1] Health Canada. Canada Vigilance Program. Verbatim description accessed 12 Aug 2016 from: http://www.hc-sc.gc.ca/dhp-mps/medeff/vigilance-eng.php

6. The number of reports received should not be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients exposed to the health product is known.

7. Numerical comparisons should not be made between reactions associated with different health products on the basis of the data in these line-listings.

8. Where a health product has multiple ingredients, it may not be possible to determine which, if any, of the substances in the combination product were responsible for a particular reaction.

9. In order to be entered into the database, information from adverse reaction report is coded using key words (reaction terms) which represent the reaction(s) described in the case report. The coding of adverse reaction reports is subject to limitations of coding terminology dictionaries. Each report relates to a single patient, however, more than one reaction may have been described and therefore coded per case report.

10. The data provided do not represent all known safety information concerning the suspected health product(s) and should not be used in isolation to make decisions regarding an individual's treatment regimen; other sources of information, including the prescribing information for the product, should be consulted.

11. The assistance of a health care professional should be sought to aid in the interpretation of the information contained herein.

12. The database is routinely checked for duplicate reports. Duplicate reports are reports related to the same patient and event received from more than one source (e.g., pharmacist and consumer). It is not always possible to detect duplicate reports, often because the documentation in the original report may be variable or incomplete. Each duplicate report received will appear separately on the summary and will be identified as duplicate in the Link/Duplicate Report Information field.

13. When follow-up reports of a single case or event are received, only the latest version of the report is included in the output.[2]

METHODS

The Canada Vigilance Online Database was searched for entries between 1999 and 2013. Separate searches were conducted to identify adverse reactions reported for energy drinks and coffee-related products. The following terms were used to search for energy drinks (with the number of reports retrieved for each term shown in parentheses): 'Energy' (n=99), 'Red bull' (n=30), 'Monster' (n=17), 'Rockstar' (n=16), '5-Hour Energy' (n=17), 'NOS' (n=7), 'Full throttle' (n=3), 'Rage' (n=1), 'Guru' (n=1), 'Xenergy/Xyience' (n=0), and Amp (n=0).

The following search terms were used to identify adverse reactions for coffee-related products: 'coffee' (n=20), 'caffeine' (n=52), 'espresso'/'expresso' (n=0), 'Starbucks' (n=0), 'Folger's (n=0), 'Van

[2] Health Canada. Caveat, Privacy Statement and Interpretation of Data - Search the Canada Vigilance Adverse Reaction Online Database http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/conditions_search-recherche-eng.php

Houtte' (n=0), 'Nestle' (n=0), 'Maxwell' (n=0), Nescafe (n=0), Second Cup (n=0), and Tim Hortons (n=0).

RESULTS

Number of adverse reactions reported

A total of 104 adverse reaction reports were identified, including 91 cases involving an energy drink (86.7%) and 14 cases involving a coffee beverage (13.3%). One case involved both a coffee and an energy drink and was counted separately in each category.

Table 1 shows the number of adverse reactions by energy drink brand. Three brands—*Red Bull*, *Monster* and *5-Hour Energy*—accounted for 66% of all adverse reaction cases.

Table 1: Number of adverse reaction cases involving an energy drink, by brand (n=91)

	Frequency (n)	**Percentage**
Red Bull	29	31.9%
5-Hour Energy	16	17.6%
Monster	15	16.5%
Rockstar	14	15.4%
NOS	6	6.6%
Full Throttle	3	3.3%
Sobe	2	2.2%
Mountain Dew	2	2.2%
Rage	1	1.1%
Guru	1	1.1%
Rip It	1	1.1%
Turbo	1	1.1%

Table 2 shows the adverse reactions for energy drinks, alone and in combination with another substance. The majority (69.2%) of adverse reaction cases involving an energy drink were **not** in combination with another substance.

Table 2: Number of adverse reaction cases involving an energy drink, alone and in combination with other substances (n=91)

	Frequency (n)	Percentage
Energy drink(s) alone	63	69.2%
Energy drink in combination with another substance	28	30.8%
Energy drink + prescription	12	13.2%
Energy drink + ethanol	6	6.6%
Energy drink + OTC	5	5.5%
Energy drink + ethanol + medication (Rx or OTC)	2	2.2%
Energy drink + ethanol + marijuana	1	1.1%
Energy drink + coffee	1	1.1%
Energy drink + tobacco	1	1.1%

Table 3 shows the adverse reactions for coffee, alone and in combination with another substance. Nearly all (~93%) adverse reactions involved coffee in combination with another substance.

Table 3: Number of adverse reaction cases involving coffee, alone and in combination with other substances (n=14)

	Frequency (n)	Percentage
Coffee alone	1	7.1%
Coffee in combination with another substance	13	92.9%
Coffee + prescription	10	71.6%
Coffee + OTC	1	7.1%
Coffee + ethanol + medication (Rx or OTC)	1	7.1%
Coffee + energy drink (missing)	1	7.1%

Types of adverse reactions

Table 4 shows the most frequently reported types of adverse reactions involving energy drinks. Across the 91 cases involving energy drinks, there were a total of 350 reported instances of adverse reactions (some cases involved multiple types of adverse reactions). The top three most frequent adverse reactions for cases involving energy drinks were increased or irregular heartbeat, malaise or feeling abnormal and vomiting. An increased or irregular heartbeat was observed in 61.5% of all cases involving energy drinks.

Table 4: Most frequently reported adverse reactions for cases involving energy drinks

	Frequency (n)	**% of *all* adverse reactions** (n=350)	**% of cases affected** (n=91)
Increased or irregular heartbeat (tachycardia/arrhythmia/palpitations/atrial or ventricular fibrillation)	56	16.0%	61.5%
Malaise or feeling abnormal	15	4.3%	16.5%
Vomiting	14	4.0%	15.4%
Psychomotor hyperactivity (muscle contractions involuntary/hyperkinesia/muscle spasms or twitching/tremor)	11	3.1%	12.1%
Blood pressure increased or hypertension	9	2.6%	9.9%
Sleep disorder, initial insomnia or insomnia	9	2.6%	9.9%
Chest discomfort or pain	8	2.3%	8.8%
Nausea	8	2.3%	8.8%
Fatigue or lethargy	8	2.3%	8.8%
Disturbance in attention, disorientation or delirium	8	2.3%	8.8%

Table 5 shows the most frequently reported types of adverse reactions for cases involving coffee. Across the 14 cases involving coffee, there were a total of 48 reported adverse reactions (some cases involved multiple types of adverse reactions). Only the top 5 most frequent adverse reactions for cases involving coffee are listed; all other adverse reactions had a frequency of one. The most frequently reported adverse reactions were food interaction and psychomotor hyperactivity, observed in 42.9% and 35.7% of cases involving coffee, respectively.

Table 5: Most frequently reported adverse reactions for cases involving coffee

	Frequency (n)	**% of *all* adverse reactions** (n=48)	**% of cases affected** (n=14)
Food interaction	6	12.5%	42.9%
Psychomotor hyperactivity (muscle contractions involuntary/hyperkinesia/muscle spasms or twitching/tremor)	5	10.4%	35.7%
Alanine/aspartate aminotransferase increased	2	4.2%	14.3%
Dizziness	2	4.2%	14.3%
Headache or migraine	2	4.2%	14.3%

Table 6 shows the most frequent Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class affected by adverse reactions for cases involving energy drinks.[3] Across the 91 cases involving energy drinks, there were a total of 350 reported instances of adverse reactions (some cases involved multiple types of adverse reactions and thus, multiple MedDRA System Organ Classes). "Nervous system disorders" were the most common MedDRA System Organ Class affected for cases involving energy drinks, at 72.5%.

Table 6: Most frequent MedDRA System Organ Class affected by adverse reactions for energy drinks

	Frequency (n)	**% of all adverse reactions** (n=350)	**% of cases affected** (n=91)
Nervous system disorders	66	18.9%	72.5%
Investigations*	50	14.3%	55.0%
General disorders and administration site conditions	46	13.1%	50.5%
Psychiatric disorders	40	11.4%	44.0%
Cardiac disorders	38	10.9%	41.8%
Gastrointestinal disorders	35	10.0%	38.5%
Skin and subcutaneous tissue disorders	13	3.7%	14.3%
Respiratory, thoracic and mediastinal disorders	11	3.1%	12.1%
Injury, poisoning and procedural complications	11	3.1%	12.1%
Vascular disorders	9	2.6%	9.9%

Table 7 shows the most frequent MedDRA System Organ Class affected by adverse reactions for cases involving coffee. Across the 14 cases involving coffee, there were a total of 48 reported instances of adverse reactions (some cases involved multiple types of adverse reactions and thus, multiple MedDRA System Organ Classes). "Nervous system disorders" were the most common MedDRA System Organ Class affected for cases involving coffee, at 85.7%, followed closely by "General disorders and administration site conditions" at 78.6%.

[3] Medical Dictionary for Regulatory Activities. http://www.meddra.org/

Table 7: Most frequent* MedDRA System Organ Class affected by adverse reactions for coffee

	Frequency (n)	**% of all adverse reactions** (n=48)	**% of cases affected** (n=14)
Nervous system disorders	12	25.0%	85.7%
General disorders and administration site conditions	11	22.9%	78.6%
Gastrointestinal disorders	6	12.5%	42.9%
Psychiatric disorders	3	6.3%	21.4%
Investigations*	3	6.3%	21.4%
Skin and subcutaneous tissue disorders	3	6.3%	21.4%
Eye disorders	2	4.2%	14.3%
Immune system disorders	2	4.2%	14.3%
Vascular disorders	2	4.2%	14.3%

*All other MedDRA System Organ Classes (not shown) had a frequency of 1.