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Discontinuation of Direct Oral Anticoagulants in Response to Attorney Advertisements: Data From the FDA Adverse Event Reporting System

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The impact of attorney advertisements on patients' decisions to discontinue a direct oral anticoagulant (DOAC) prematurely is not well examined, although some studies have documented misinformation in attorney advertisements associated with medical products.[1-3] In 2016, the American Medical Association recommended that attorney advertisements include clear warnings that patients should not discontinue medications without physician consultation, reflecting a consensus that attorney advertisements may deter consumers from taking their medications.[4]

We searched the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) to identify US reports of patients who discontinued or reduced the dose of their DOACs (ie, dabigatran, rivaroxaban, apixaban, and edoxaban) after viewing an attorney advertisement, received by FDA from approval of each DOAC through November 15, 2017. Using SAS version 9.4 (SAS Institute Inc, Cary, NC), we conducted a narrative search of all DOAC reports for terms that could indicate DOAC use modification in reference to a television advertisement. We included reports where a DOAC was discontinued or dose reduced after viewing an attorney advertisement. We excluded reports unrelated to the subject of interest, duplicates, or reports with insufficient information.

We identified 66 reports that described patients who viewed an advertisement and then discontinued (n = 65) or reduced (n = 1) the dose of a DOAC, including 7 deaths (Table 1). In most reports (64/66, 97%), DOAC discontinuation occurred without physician consultation. We classified the advertisements into 3 categories: "attorney" advertisements (n = 25) clearly describe a law firm advertisement; advertisements described as "1-800-BAD-DRUG" advertisements (n = 13) appear to be announcements advising consumers to contact a law firm[5]; and "unspecified" advertisements were those without enough information to classify the advertisement but that mentioned nonspecific terms such as

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Declaration of Conflicting Interests

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negative television commercials (n = 28). Among the 25 reports referencing an "attorney" advertisement, most patients (18/25, 72%) experienced a stroke (n = 13), thromboembolism (n = 4), or a transient ischemic attack (TIA) (n = 1) following DOAC discontinuation; 3 patients died. Most patients who viewed "1-800-BAD-DRUG" advertisements (11/13, 85%) experienced a stroke (n = 8) or a thromboembolism (n = 3); 2 patients died. Similarly, of the remaining 28 patients who viewed "unspecified" advertisements, more than half (17/28, 61%) experienced a stroke (n = 12), thromboembolism (n = 4), or TIA (n = 1); 2 patients died.

Our findings provide evidence consistent with a previous study showing attorney advertising influenced patients to discontinue rivaroxaban.[2] We found that attorney advertisements may influence patients to discontinue or reduce the dose of their DOAC without medical advice, which places this group at heightened risk of thromboembolic events. Although it is expected that DOAC discontinuation contributed to the thromboembolic outcomes, it is unknown how many events would have occurred despite drug continuation. However, in the ROCKET-AF trial, an increased risk of stroke was observed among rivaroxaban patients who temporarily or permanently discontinued anticoagulation.[6] Limitations of our assessment are consistent with those of spontaneously reported data and include underreporting, selective reporting, and the lack of event adjudication. The FDA uses its regulatory authority to ensure that prescription drug promotion by manufacturers is truthful, balanced, and not misleading. Furthermore, the regulation of attorney advertisements is typically through state attorney ethics rules.[5] Given the severity of the outcomes reported to the FDA, we believe that it is imperative for clinicians to counsel DOAC users about the risks of therapy modification in the absence of medical consultation.

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Table 1.

Characteristics of FAERS Reports of DOAC Discontinuation or Dose Reduction After Viewing Attorney Advertisements (n = 66 Reports).[a]

Selected Characteristics		n (%)
Age (years), n = 35[b]	Range	30-90
	Median	70
	Mean	68
Sex	Male	27 (41)
	Female	28 (42)
	Unknown	11 (17)
Reason for use	Atrial fibrillation	36 (55)
	Thromboembolism	13 (20)
	Unknown	17 (25)
DOAC	Rivaroxaban	55 (83)
	Dabigatran	8 (12)
	Apixaban	3 (5)
	Edoxaban	0
Reporter	Health care professional	50 (76)
	Consumer	16 (24)
Advertisement type	Attorney[c]	25 (38)
	1-800-BAD-DRUG[d]	13 (20)
	Unspecified	28 (42)
Advertisement medium	Television ads	38 (58)
	Direct mail ads	1 (2)
	Unknown	27 (40)
Disposition of therapy after viewing advertisement	Discontinued	65 (98)
	Dose reduced	1 (2)
DOAC discontinuation or dose reduction resulted in a reported adverse event	Yes	47 (71)
	No	19 (29)
Subsequent reported adverse event	Stroke	33 (50)
	Thromboembolism[e]	11 (17)
	Transient ischemic attack	2 (3)
	Not reported[f]	1 (2)
	Unknown	19 (29)
Serious outcomes[g,h]	Death	7 (11)
	Life-threatening	1 (2)
	Hospitalization	26 (39)
	Other serious	24 (36)
	Disability	1 (2)
	Unknown	13 (20)

Abbreviations: DOAC, direct oral anticoagulant; FAERS, US Food and Drug Administration Adverse Event Reporting System.

[a] As of November 15, 2017.

[b] Refers to the number of cases in which the specific demographic data were provided; balance of total had incomplete data.

[c] Attorney advertisements: clearly described a law firm advertisement.

[d] 1-800-BAD-DRUG ads: Announcements referencing “bad drug” that appear to be public service announcements describing side effects of a product advising consumers to contact a third party or a law firm.

[e] Thromboembolic events include pulmonary embolism, deep-vein thrombosis, splenic infarct, and “blood clots.”

[f] Report of death, but adverse event was not specified.

[g] More than 1 serious outcome is possible.

[h] Per 21 CFR 314.80, the regulatory definition of serious is any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, a congenital anomaly/birth defect, and other serious important medical events.