ELSEVIER

Blood 142 (2023) 3745–3747

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Risk of Venous Thromboembolic Events Among Obese Hormonal Contraceptive Users

Divyaswathi Citla Sridhar, MD[1,2], *Nancy Sokkary, MD*[3,4], *Lakshmi Venkat Srivaths, MD*[5,6], *Rachel P. Rosovsky, MD*[7,8], *Bethany T. Samuelson Bannow, MD MCR*[9,10], *Madhvi Rajpurkar, MD*[11,12]

[1] University of Arkansas for Medical Sciences, Little Rock, AR
[2] Arkansas Children's Hospital, Little Rock, AR
[3] Dept of Obstetrics and Gynecology, Emory school of Medicine, Atlanta, GA
[4] Division of Pediatric and Adolescent Gynecology, Children's Healthcare of Atlanta, Atlanta, GA
[5] Gulf States Hemophilia and Thrombophilia Center, Houston, TX
[6] University of Texas Health Science Center at Houston, Houston, TX
[7] Division of Hematology & Oncology, Department of Medicine, Massachusetts General Hospital, Boston, MA
[8] Harvard Medical School, Boston, MA
[9] The Hemophilia Center At OHSU, Portland, OR
[10] Department of Medicine, Division of Hematology, Oregon Health and Science University, Portland, OR
[11] Division of Hematology Oncology, Central Michigan University, Detroit, MI
[12] Children's Hospital of Michigan, Detroit, MI

Background: Obesity and hormonal contraception (HC) are independent risk factors for venous thromboembolism (VTE). Thirty eight percent of women in the United States (US) are obese, and the prevalence of childhood obesity in the US is among the highest in the world. Obesity (BMI>30 kg/m2), increases VTE risk via several mechanisms, and the VTE risk in obese individuals is 2.5 times higher than that of their non-obese peers. More than half of women aged 15-49 years use some form of contraception, and 14% report using oral contraceptive pills specifically. The overall VTE risk with combined hormonal contraception (CHC) is approximately two-fold higher than an individual's baseline risk, with further increase depending on the type/dose of progesterone and estrogen, and route of administration.

To date case-control and cohort studies have demonstrated an increased VTE risk among obese contraceptive users. But these data do not include adolescents and were derived from populations with relatively low rates of obesity.

This study aimed to assess and compare the VTE risk among obese females, age 10-44 years, who were prescribed HC compared to non-obese HC users and obese non-users utilizing a national electronic-medical record database. Using a large national database allowed the inclusion of females from diverse ethnic, economic, and geographic background.

Methods: Population level data was collected from TriNETX, LLC, an administrative database that contains comprehensive inpatient and outpatient data from 56 tertiary care hospitals in US. Prevalence data regarding the type and dose of progesterone and estrogen and mode of administration was assessed.

Data on females ages 10-44 years from 1/1/2000 to 12/30/2022, who received a new prescription for any HC as identified by the prescription name in pharmaceutical claims and procedure codes was analyzed. Recorded BMI was used to divide the cohort into obese and non-obese individuals as per CDC guidelines. VTE events were defined as presence of ≥1 ICD 9 or 10 codes for VTE diagnosis and presence of a prescription for an anticoagulant drug within the first year after hormonal prescription. Data was summarized descriptively and VTE rates were calculated.

Results: Of the 97,026,002 females who met inclusion criteria, 1,370,481 were obese and 2,649,987 were non-obese. The overall rate of VTE for obese vs. non-obese users was 0.9% vs. 0.5% ($p<-0.001$) and obese HC users vs. obese non-users was 0.9 and 1.06% ($p<0.05$).

VTE rates among obese users versus non-obese users was significantly higher for most progesterone only options ($p<0.001$), excluding drospirenone only pills and high dose norethindrone (Table 1). A similar pattern of higher VTE rates in obese vs non-obese users was observed for the majority of CHC preparations with few exceptions ($p<0.001$). (Table 1)

In general, VTE rates were higher among obese non-users compared to obese users. However, the rate of VTE was significantly higher among obese users of oral norethindrone 5mg and all medroxyprogesterone acetate users ($p<0.001$). (Table 2)

Discussion: Utilizing the data from a large inpatient/outpatient administrative database, our study shows that obese HC users have a higher VTE rate within one year of initiating HC when compared to non-obese HC users, for progesterone only options (excluding drospirenone, high dose norethindrone) and most CHCs.
With few exceptions, obese HC non-users had a higher rate of VTE when compared to obese users. This observation is likely due to confounding by indication bias as prescribers may avoid HC in individuals with underlying risk factors for VTE. Applying propensity score analysis and examining different subcategories of obesity may help overcome this bias in future analysis.
Our study highlights the utility of large databases to study healthcare outcomes of VTE risk in females with and without obesity and HC users and non-users. Although limited by the use of administrative claims data and acknowledging that all statistically significant results may not be clinically significant, our study suggests obesity as a VTE risk factor in females for most HCs.

Disclosures Rosovsky: *Pulmonary Embolism Response Team:* Membership on an entity's Board of Directors or advisory committees, Other: President-Elect; *BMS:* Consultancy; *Dova:* Consultancy; *Janssen:* Consultancy, Other: Research funding is to my institution, Research Funding; *Abbott:* Consultancy; *Penumbra:* Consultancy, Other: National Lead Investigator for STORM PE; *Inari:* Consultancy.

https://doi.org/10.1182/blood-2023-184567

Table 1: Rates of VTE among obese vs non-obese

	Obese			Non obese			
	Number of users	Number of VTE events	Rate	Number of users	Number of VTE events	Rate	p value
PROGESTERONE ONLY							
Pills							
NTE - Total	73086	570	0.78%	185089	727	0.39%	<0.0001
NTE - oral (except 5mg/35mcg)	20853	165	0.79%	69944	179	0.26%	<0.0001
NTE 5mg	3536	62	1.75%	4597	62	1.35%	0.1398
NTE 35mcg	6577	59	0.90%	12400	49	0.40%	<0.0001
DP - Total	12746	45	0.35%	49775	128	0.26%	0.0659
DP - oral (except 4mg)	2412	1	0.04%	18470	18	0.10%	0.7165
DP - oral 4mg	292	1	0.34%	300	1	0.33%	0.9842
Subdermal implant							
Etonorgestrel - total	46160	251	0.54%	78157	329	0.42%	0.0021
Etonorgestrel - implant	9813	35	0.36%	14516	50	0.34%	0.8741
Intrauterine Device							
Levonorgestrel - total	87819	811	0.92%	173018	767	0.44%	<0.0001
Levonorgestrel - IUD	19934	174	0.87%	35115	162	0.46%	<0.0001
Injectables							
MPA - Total	76377	946	1.24%	80202	692	0.86%	<0.0001
MPA - Intramuscular	25149	248	0.99%	28948	179	0.62%	<0.0001
COMBINED HORMONAL CONTRACEPTIVES							
Pills							
Levonorgestrel + EE - Total	50426	329	0.65%	99616	290	0.29%	<0.0001
Levonorgestrel + EE - Oral	8498	31	0.36%	20292	41	0.20%	0.0117
Drospirenone + EE - Total	18449	108	0.59%	53739	151	0.28%	<0.0001
Drospirenone + EE - ORAL	5517	22	0.40%	15206	61	0.40%	0.9808
Desogestrel + EE- Total	14360	106	0.74%	34666	122	0.35%	<0.0001
Desogestrel + EE - Oral	3387	15	0.44%	8478	22	0.26%	0.1057
Ethynodiol + EE- Total	1473	1	0.07%	3265	16	0.49%	0.0245
Ethynodiol + EE - Oral	575	0	0.00%	866	0	0.00%	N/A
Norethindrone + EE - Total	65883	461	0.70%	156409	486	0.31%	<0.0001
Norethindrone + EE -Oral	19204	92	0.48%	42200	87	0.21%	<0.0001
Norgestrel + EE - Total	6967	34	0.49%	15346	55	0.36%	0.1546
Norgestrel + EE - Oral	2360	12	0.51%	5120	16	0.31%	0.1971
Norgestimate + EE - Total	57063	306	0.54%	125170	312	0.25%	<0.0001
Norgestimate + EE - Oral	17226	74	0.43%	35718	66	0.18%	<0.0001
Estetrol+ Drospirenone - Total	30	0	0.00%	64	0	0.00%	N/A
Estetrol+ Drospirenone - Oral	21	0	0.00%	41	0	0.00%	N/A
Patch							
Levonorgestrel +EE - Total	50426	329	0.65%	99616	290	0.29%	<0.0001
Levonorgestrel +EE -Topical	20	0	0.00%	54	0	0.00%	N/A
Norelgestromin +EE - Total	9036	41	0.45%	15530	57	0.37%	0.2985
Norelgestromin +EE - Topical	3862	1	0.03%	7462	13	0.17%	0.0332
Ring							
Segesterone + EE - total	136	0	0.00%	335	0	0.00%	N/A
Segesterone + EE - vaginal	25	0	0.00%	62	0	0.00%	N/A
Etonogestrel + EE - total	23994	17	0.10%	35202	92	0.26%	<0.0001
Etonogestrel + EE - Vaginal	9353	42	0.40%	15902	39	0.25%	0.0057

EE: ethinyl estradiol, NTE: norethindrone acetate, DP: drospirenone

Table 2: Rates of VTE among obese users vs non-users

	Obese Users			Obese NON-Users			
	Number of users	Number of VTE events	Rate	Number of non-users	Number of VTE events	Rate	p value
PROGESTERONE ONLY							
Pills							
NTE - Total	73086	570	0.78%	1347797	14259	1.06%	<0.0001
NTE - oral (except	20853	165	0.79%	1347797	14259	1.06%	0.0002
NTE 5mg	3536	62	1.75%	1347797	14259	1.06%	<0.0001
NTE 35mcg	6577	59	0.90%	1347797	14259	1.06%	0.2031
DP - Total	12746	45	0.35%	1347797	14259	1.06%	<0.0001
DP - oral (except 4mg)	2412	1	0.04%	1347797	14259	1.06%	<0.0001
Drosperinone - oral 4mg	292	1	0.34%	1347797	14259	1.06%	0.2321
Subdermal implant							
Etonorgestrel - total	46160	251	0.54%	1347797	14259	1.06%	<0.0001
Etonorgestrel - implant	9813	35	0.36%	1347797	14259	1.06%	<0.0001
Intrauterine Device							
Levonorgestrel - total	87819	811	0.92%	1347797	14259	1.06%	0.0002
Levonorgestrel - IUD	19934	174	0.87%	1347797	14259	1.06%	0.0111
Injectables							
MPA - Total	76377	946	1.24%	1347797	14259	1.06%	<0.0001
MPA -Intramuscular	25149	248	0.99%	1347797	14259	1.06%	0.2697
COMBINED HORMONAL CONTRACEPTIVES							
Pills							
Levonorgestrel + EE - Total	50426	329	0.65%	1347797	14259	1.06%	<0.0001
Levonorgestrel + EE - Oral	8498	31	0.36%	1347797	14259	1.06%	<0.0001
Drospirenone + EE - Total	18449	108	0.59%	1347797	14259	1.06%	<0.0001
Drospirenone + EE - Oral	5517	22	0.40%	1347797	14259	1.06%	<0.0001
Desogestrel + EE- Total	14360	106	0.74%	1347797	14259	1.06%	0.0002
Desogestrel + EE - Oral	3387	15	0.44%	1347797	14259	1.06%	0.0005
Ethynodiol + EE- Total	1473	1	0.07%	1347797	14259	1.06%	0.0002
Ethynodiol + EE - Oral	575	0	0.00%	1347797	14259	1.06%	0.0132
Norethindrone + EE - Total	65883	461	0.70%	1347797	14259	1.06%	<0.0001
Norethindrone + EE -Oral	19204	92	0.48%	1347797	14259	1.06%	<0.0001
Norgestrel + EE - Total	6967	34	0.49%	1347797	14259	1.06%	<0.0001
Norgestrel + EE - Oral	2360	12	0.51%	1347797	14259	1.06%	0.0091
Norgestimate + EE - Total	57063	306	0.54%	1347797	14259	1.06%	<0.0001
Norgestimate + EE - Oral	17226	74	0.43%	1347797	14259	1.06%	<0.0001
Esterol+Drospirenone - Total	30	0	0.00%	1347797	14259	1.06%	0.5711
Esterol+Drospirenonee - Oral	21	0	0.00%	1347797	14259	1.06%	0.6356
Patch							
Levonorgestrel +EE - Total	50426	329	0.65%	1347797	14259	1.06%	<0.0001
Levonorgestrel +EE -Topical	20	0	0.00%	1347797	14259	1.06%	0.6438
Norelgestromin +EE - Total	9036	41	0.45%	1347797	14259	1.06%	<0.0001
Norelgestromin +EE - Topical	3862	1	0.03%	1347797	14259	1.06%	<0.0001
Ring							
Segesterone + EE - total	136	0	0.00%	1347797	14259	1.06%	0.2279
Segesterone + EE - vaginal	25	0	0.00%	1347797	14259	1.06%	0.6051
Etonogestrel + EE - total	23994	17	0.10%	1347797	14259	1.06%	<0.0001
Etonogestrel + EE - Vaginal	9353	42	0.40%	1347797	14259	1.06%	<0.0001

EE: ethinyl estradiol, NTE: norethindrone acetate, DP: drospirenone

Figure 1