

18th ANNUAL PHARMA MIDDLE EAST CONGRESS

November 05-07, 2018 Abu Dhabi, UAE

Association between Proton Pump Inhibitors use and New Onset of Ischemic Stroke in A Tertiary Hospital, King Abdul-Aziz Medical City-Central Region Saudi Arabia: Retrospective Study

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Background: Stroke is a rapid loss of brain function due to disruption of blood supply to the brain and a major cause of mortality and morbidity worldwide. In Saudi Arabia the incidence of ischemic stroke is 69%. Risk factors are: hypertension, diabetes mellitus, smoking, dyslipidemia. Proton pump inhibitors (PPIs) one of the world's most frequently prescribed medications contributed to many adverse effects. Retrospective study found a significant increase in risk of new onset ischemic stroke in the PPIs users. Prospective cohort study found no association.

Aim: assess the likelihood of developing new onset ischemic stroke among patients who were using PPIs for 6 months or more versus patients who were not using PPIs.

Method: Case-control study at King Abdulaziz Medical City central region, from January2016 to January2017. Sample size calculations based on probability type I error of 0.05, 80% power, estimated to be 400 [200 ischemic stroke (cases) and 200 non-ischemic stroke (controls)]. Each group obtained by simple random sampling, medications reviewed if patients were using PPIs. The association between PPIs use, demographic data, clinical factors and development of ischemic stroke evaluated by using Odds Ratio (OR) and 95% confidence interval (CI). Continuous data expressed as mean \pm SD. Categorical data analyzed using the Chi-square test.

Result: 128 patients met the inclusion criteria. 64 patients with 47 on PPIs had new onset ischemic stroke (mean age 69.14 \pm 11.57, 53.13% were male), 64 patients with 39 on PPIs without ischemic stroke (mean age 60.88 \pm 12.49, 54.69% were female). Primary endpoint: there was insignificant association between patients with previous exposure to PPIs and ischemic stroke (Odds Ratio (OR) 0.396; 95% (CI) 0.111-1.415). In comparison to the retrospective study. For secondary endpoint: the incidence of ischemic stroke was insignificant between patients who used different doses, 20mg orally daily in ischemic and non-ischemic stroke (29.79% Vs. 48.72%, respectively), and 40mg orally daily in ischemic stroke and non-ischemic stroke (70.21% Vs. 51.28%, respectively), P=0.0723.

Table (1) Baseline Characteristics

Characteristics	Outcome		p-value
	Ischemic (N=64)	Non-Ischemic (N=64)	
Age (years)	69.14 (11.57)	60.88 (12.49)	0.0003
Gender			0.3767
Male	53.13%	45.31%	
Female	46.88%	54.69%	
Weight	75.50 (14.46)	84.54 (19.32)	0.0031
Height	159.88 (10.22)	160.44 (9.17)	0.8338
Smoking			0.3436
Yes	1.56%	3.13%	
No	56.25%	43.75%	
Not available	42.19%	53.13%	
Previous medical history			
Hypertension	92.19%	54.69%	<0.0001
Diabetes mellitus	67.19%	67.19%	1.0000
Dyslipidemia	68.75%	73.44%	0.5586
Heart Failure	7.81%	14.06%	0.2573
Myocardial Infarction	0.00%	4.69%	0.0797
Atrial Fibrillation	12.50%	3.13%	0.0481
Coronary Artery Disease	21.88%	20.63%	0.8644
Chronic Kidney Disease	9.38%	7.81%	0.7525
Peripheral Vascular Disease	1.56%	3.13%	0.5591
Carotid Artery Stenosis	9.38%	0.00%	0.0121
Chronic Kidney Disease	73.44%	60.94%	0.1321
Peripheral Vascular Disease	51.56%	37.50%	0.1095
Carotid Artery Stenosis	21.88%	21.88%	1.0000
Doses			0.0723
20mg orally once daily	29.79%	48.72%	
40mg orally once daily	70.21%	51.28%	
Indications			
Refractory gastroesophageal reflux disease	1.56%	3.13%	0.5591
Non-Steroidal Anti-inflammatory Drugs use	3.13%	6.25%	0.4030
Other	3.13%	17.19%	0.0085

Table (2) Predictors risk factors of ischemic stroke.

Parameter	p-value	OR	95% Confidence Interval
Proton pump inhibitors use	0.1541	0.396	0.111-1.415
Weight	0.0380	0.961	0.925-0.998
Gender	0.1649	0.303	0.056-1.633
Heart failure	0.0302	13.367	1.282-139.333
Hypertension	<.0001	43.642	7.544-252.461

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Conclusion: Association between PPIs use with different doses prior the occurrence of new onset ischemic stroke is insignificant, after accounting PPIs indications, several factors contributed to the risk of ischemic stroke.

Inclusion criteria:

Patients 25 years or older with/without a medical history of hypertension, diabetes, dyslipidaemia, ischemic heart disease, heart failure, myocardial infarction, atrial fibrillation, chronic kidney disease on haemodialysis or peritoneal dialysis, who were using anticoagulant and nonsteroidal anti-inflammatory medications.

Exclusion criteria:

Patients with history of ischemic stroke, transient ischemic attack, haemorrhagic stroke, neurological diseases, brain tumor, encephalitis, meningitis, pregnant women.

Primary endpoint: To assess the association between PPIs use and the risk of development new onset ischemic stroke.

Secondary endpoint: To determine the relationship between dose and frequency of PPIs and development of new onset ischemic stroke.

Biography

Maha AlMolaiki has completed her PharmD from King Saud University and has worked assisting as Patient Cares, both in outpatient and inpatient at King Abdulaziz Medical City-Central region. She is currently a Pharma Resident at Pharmacy Residency at King Abdulaziz Medical City-Central Region.

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