A Comparative Effectiveness Study of Generic versus Brand-name Pioglitazone in Patients with Type II Diabetes Mellitus in Thailand

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G-I-N 2011 Conference, Inchon Memorial Hall Korea University, Seoul, Korea, Aug 28-31, 2011

Background

- Diabetes mellitus (DM) is an important chronic disease.
- Thiazolidinediones (TZDs) are commonly used in Thailand.
- Pioglitazone is only TZD available in Thailand

Ministry of public health Thailand, Thailand health profile, 2010, Kosachunhanan N, J Med Assoc Thai 2006

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Background

- A bioequivalent study indicated generic pioglitazone was equivalent to brand pioglitazone.
  - Only pharmacokinetic study
  - Single dose
- Therapeutic equivalent study is still needed.

Chatsiricharoenkul S, J Med Assoc Thai 2007

Objectives

To compare the clinical effectiveness between generic pioglitazone and the brand.

Methods

Study design & Data source	- Retrospective cohort study - Electronic patient databases from a University-affiliated hospital.

Databases	- Demographic data - Pharmacy data - Diagnosis data - Laboratory data

Study subjects	- Patient receiving pioglitazone in year 2007-2009 *Inclusion criteria* 1) 18 years or older 2) had received pioglitazone at least 6 months 3) HbA1C >7% within 180 days before starting pioglitazone 4) had HbA1C result(s) in 60-270 days after starting pioglitazone

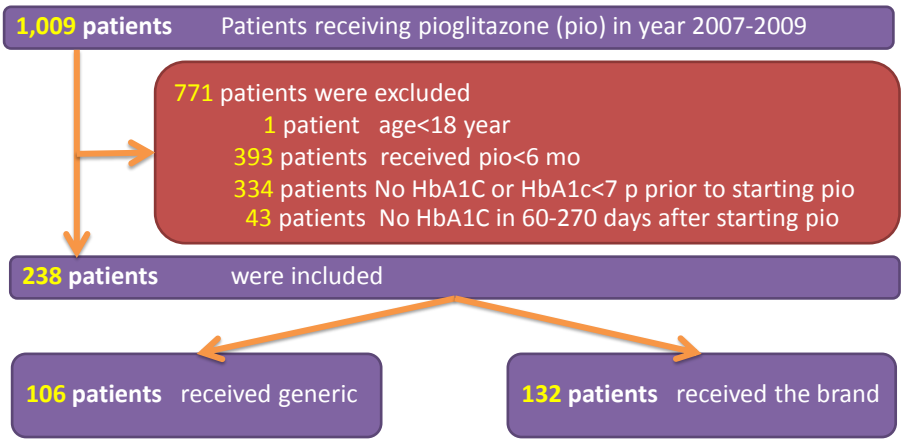
Exposure & Comparator	**Exposure:** Generic pioglitazone **Comparator:** The brand pioglitazone

Study outcomes	**Primary outcomes:** - Changes in HbA1C level from baseline **Secondary outcomes:** - No. of patients who met the HbA1C goal (<7%)

Statistical analysis	**Multivariable analysis:** **- For 1° outcomes:** - Multivariable linear regression with propensity score (PS) adjustment **- For 2° outcomes:** - Multivariable logistic regression with PS adjustment **Propensity score:** **-** Multivariable logistic regression - Factors included age, sex, concurrent medication, co-morbidity, insurance and baseline HbA1C

Results

Patients' Inclusions



Patients' Characteristics

Parameters	The generic	The brand	P-value
Age, mean (SD)	58.6±1.1	63.5±0.95	0.009*
% Male	61.3%	69.7%	0.18
Health insurance			
Universal coverage	62 (58.49)	39 (29.55)	0.001*
Government employee	39 (36.79)	90 (68.18)	
Social security schemes	5 (4.72)	3 (2.27)	
Baseline HbA1C	8.77±1.54	8.82±1.68	0.80

* Statistical significant

Patients' Characteristics

Parameters	The generic	The brand	P-value
Concurrent medication (N,%)			
Insulin	17 (12.88)	3 (2.83)	0.005*
Metformin	116 (87.88)	86 (81.13)	0.149
Sulfonylureas	99 (75.00)	82 (77.36)	0.672
Repaglinide	2 (0.76)	1 (1.89)	0.694
Voglibose	13 (9.85)	3 (2.83)	0.032*

* Statistical significant

Patients' Characteristics

Parameters	The generic	The brand	P-value
Co-morbidities (N,%)			
Hypertension	96 (72.73)	76 (57.58)	0.860
Stroke	3 (2.27)	6 (4.55)	0.173
Dyslipidemia	101 (76.52)	91 (68.94)	0.070
Hyperthyroidism	16 (12.12)	5 (3.79)	0.045*
Ischemic heart disease	17 (12.88)	8 (6.06)	0.182
Hypoglycemic episode	1 (0.76)	2 (1.52)	0.438

* Statistical significant

Statistical analysis

	%HbA1C (Mean ± SD)		
	baseline	60-270 days after starting pio	Differences
The generic	8.77 ± 1.54	8.05 ± 1.67	-0.72 ± 1.67
The brand	8.82 ± 1.68	7.70 ± 1.50	-1.11 ± 1.49
PS- adjusted multivariable linear regression#	**Adjusted mean difference:** 0.32 (95%CI; -0.04 to 0.68)		

Adjusted by age, sex, PS, insurance, baseline HbA1c, dose of pioglitazone, Concurrent medication (insulin, voglibose and rapaglinide), and comorbidity (DLP, thyroid,stroke, hypoglycemic episode, IHD)
Abbreviation: PS; Propensity score, HbA1C; hemoglobin A1C, pio; pioglitazone

Statistical analysis

	No. of Patient who met HbA1c goal (HbA1C <7.0%)		
	HbA1C <7% (Meet goal)	HbA1C ≥7% (Not meet goal)	% patients met goal
The generic	33	73	31.1%
The brand	44	88	33.3%
PS- adjusted multivariable logistic regression#	**Adjusted odds ratio:** 0.95 (95%CI; 0.50-1.82)		

Adjusted by age, sex, PS, insurance, baseline HbA1c, dose of pioglization, Concurrent medication (insulin and voglibose), and comorbidity (HTN, thyroid, and IHD)
Abbreviation: PS; Propensity score, HbA1C; hemoglobin A1C,

Discussions

Discussions

- These findings revealed that the magnitude of HbA1c level reduction was not different.
- Factors were not considered:
  - Non-pharmacological treatment
  - Adherence
- Low statistical power (47% power)
- Misclassifications might be occurred.

Conclusions

- Once the sample size was insufficient, equivalence cannot be concluded.
- Further studies are still needed.

Acknowledgement

- Our research team:
  - Ornrat Lohitnavy,
  - Nathorn Chaiyakunapruk,
  - Pattamapron Komemee,
  - Prattarapron Parnmangmee
  - Krit Keawsomneik

http://rgj.trf.or.th

- Thailand Research Fund through the Royal Golden Jubilee PhD program

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