中文題目：急性冠心症住院患者早期使用伐尼克蘭 Varenicline 的安全性和有效性；亞洲群族數據

英文題目：Safety and Efficacy of Early Varenicline Prescription in Hospitalized Patients with Acute Coronary Syndrome; Asian Population Data

作　　者：羅健賢[1] 李麗青[1] 顏啟華[2] 李佳燕[3] 李京郁[3] 詹貴川[1]

服務單位：[1]中山醫學大學附設醫院內科部,[2]中山醫學大學附設醫院家庭醫學科,[3]中山醫學大學附設醫院護理部

Introduction

Acute coronary syndrome (ACS) is one of the leading causes of death worldwide. Smoking is a strong risk factor and smoking cessation is of critical importance in these patients, which reduces the risk of recurrent MI, cardiovascular death and further cardiac event as much as 50%[1] and associated with a life expectancy gain of 3 years after coronary artery bypass surgery. The majority of hospitalized smokers with cardiac disease want to quit smoking. Few trials have examined the efficacy of smoking cessation pharmacotherapies in hospitalized patients with ACS. In-hospital initiation of nicotine replacement therapy, although frequently prescribed in North America, however relevant trials were less.

Varenicline is an α4β2 nicotinic acetylcholine receptor partial agonist that reduces cravings and withdrawal symptoms during smoking abstinence and also decreases the reinforcing effects of nicotine. Although varenicline has been shown to be effective for smoking cessation in both healthy smokers and patients with stable cardiovascular disease,[2] little is known about its efficacy in patients with acute cardiovascular
disease. Previous studies have reached mixed conclusions regarding the safety of varenicline among smokers.[2,3]

Previous trial, EVITA (Evaluation of Varenicline in Smoking Cessation for Patients Post-Acute Coronary Syndrome)[4], reported that patients who received varenicline prescribed in-hospital patients with acute coronary syndrome, had significantly higher rates of smoking abstinence and also low adverse events. However the study population was from Canada or United States, and was also not powered to examine safety end points. Snaterse et al.

pointed that majority of patients who quit immediately after a life-threatening ACS shown more successful quitters and remained abstinent through 1 year of follow-up.[5] For this reason, we assessed the safety as well as efficacy of varenicline in a high risk patient population of smokers hospitalized with ACS in East Asian population.

Methods

This is a prospective observational study in which we collected data from a single institution on hospitalized patients due to ACS who were prescribed Varenicline treatment after cardiac catheterization.

Patient selection

This data was collected from July 2020 to June 2021, patients underwent percutaneous coronary intervention for ACS, including ST-segment elevation myocardial infarction (STEMI), non ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). Patients with chronic coronary syndrome, never smoke, smoked <10 packed-year were excluded. All the enrolled patients were high-intensity counselling and force prescribed Varenicline treatment for smoking cessation.

Intervention and Follow-Up

Patients were received varenicline 0.5 mg once/d x 3 days, followed by 0.5 mg twice/d x 4 days, followed by 1.0 mg twice/d for the remainder of the 8 week treatment period. At follow-ups, patients who failed to abstinence smoking were encouraged to receive the second similar treatment course. Patients were instructed by their cardiologists at regular outpatient clinic visits and their clinical condition followed by specialist health educating staff. All the patients were traced for any adverse effect at weeks 4, 8, and 12. Further efficacy and safety information of varenicline was also followed at weeks 24. Side effects symptoms of withdrawal, discomfort, medication adherence, and smoking status were assessed during follow-up contacts.

End Point Assessment

The primary end point was set as safety of varenicline, any serious adverse

cardiac event including recurrent MI, non-fatal stroke or death 24 weeks after medication. Efficacy of smoking abstinence was also assessed as self-report of complete abstinence in a week before the 24 week clinic visit.

Results

Baseline Characteristics

Among the 100 patients, 39 patients were excluded (33 patients was not ACS, 6 patients refused to use medications). A rest of patients were agreed to receive Varenicline treatment for smoking cessation. In brief, 61 patients who smoked ≥10 cigarettes/d and ≥10 packed-year, who were hospitalized with ACS were enrolled. The baseline characteristics were summarized in Table 1. Mean age was 58.2 (31-78) years. 95% of study patients were male. About 37.7% was STEMI, 31.1% were NSTEMI and UA respectively. Patients smoked a mean of 31.5 (10-110) packed year at the time of hospital admission.

Hospital Course

All patients had cardiac catheterization and underwent percutaneous coronary intervention. Rare cases developed treatable ventricular arrhythmia, heart failure, pulmonary edema or recurrent ischemia during hospitalization. Median time from admission to 1st dose of study medication was 2.2 (0-13) days. Most patients received the first dose of varenicline during hospitalization. Nearly all patients, at least received the medication at first outpatient clinic within a week and only one patient delay use of medicine at day 13 of event. Mean duration of drug intake was 4.5 days.

Outcome

During the follow-up at 4, 8 and 12 weeks, no patients meet the safety end point (i.e., serious adverse cardiac event including recurrent MI, non-fatal stroke or death). Only minor side effects were reported (headache 1.6%, GI upset 8.2%, constipation, 1.6% irritability 1.6% and insomia 6.5%). At 24 weeks, only one patient had died and no more patients who develop other serious adverse cardiac event. For efficacy, the rate of smoking abstinence was 79% at 24 weeks (Table 2).

Conclusion

Early use of varenicline was safe in hospitalized patients with ACS just undergoing percutaneous coronary intervension. It is also efficacious for smoking cessation in this high-risk patient population. Our data may represent the first report about the safety and efficacy of early prescription of varenicline in Asian population who hospitalized due to ACS.

References

1. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2012;11:CD000146.
2. Rigotti NA, Pipe AL, Benowitz NL, Arteaga C, Garza D, Tonstad S. Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease: a randomized trial. Circulation 2010;121:221-9.
3. Prochaska JJ, Hilton JF. Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis. BMJ 2012;344:e2856.
4. Eisenberg MJ, Windle SB, Roy N, et al. Varenicline for Smoking Cessation in Hospitalized Patients With Acute Coronary Syndrome. Circulation 2016;133:21-30.
5. Snaterse M, Scholte Op Reimer WJ, Dobber J, et al. Smoking cessation after an acute coronary syndrome: immediate quitters are successful quitters. Neth Heart J 2015;23:600-7.

Table 1: Baseline characteristics of smokers with acute coronary syndrome

Demographic		
Age, year, mean	58.2	(31-78)
Male sex	58	95.00%
Cigarettes duration (packed-year) at baseline	31.5	(10-110)
Medical history		
Hyperlipidemia	50	81.90%
Hypertension	45	73.70%
Diabetes	40	65.50%
Prior ischemic stroke	35	57.30%
Hospital admission		
ST-segment elevation myocardial infarction	23	37.70%
Non ST-segment elevation myocardial infarction	19	31.10%
Unstable angina	19	31.10%
Percutaneous coronary intervention	61	100.00%
Length of stay, median	3.5 day	(3-7 days)
Time from admission to first dose of study medication, median	2.2 day	(day 0-13)

Table 2: Efficacy and safety outcomes

	No. of patient	%
Smoking abstinence rate	48	79.00%
Serious adverse events		
Death	1	1.60%
MI	0	0.00%
Stroke	0	0.00%
Other minor adverse events		
GI upset	5	8.20%
Insomia	4	6.50%
Headache	1	1.60%
Constipation	1	1.60%
Irritable	1	1.60%
Malaise	1	1.60%