PSYCHIATRY

Safety and Efficacy of Viva QS® for Smoking Cessation among Industrial Workers in Kerteh and Kuantan, Malaysia

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ABSTRACT

Objective: **To evaluate the safety and efficacy of Viva QS®, an herbal medication consists of a combination of twelve herbs for smoking cessation in Malaysian adult smokers.**

Methods: **A randomized, double-blind placebo-controlled study was conducted in the industrial factories in Kerteh and Kuantan, Malaysia. The subjects were recruited from those attended mobile smoking cessation programme (MSCP), agreed to sign written consent and fulfilled study criteria. Demographic and smoking history information, modified Fagerstrom test for nicotine dependence (FTND) score and carbon monoxide (CO) level were obtained at baseline. Follow-up was conducted by phone calls and/or face-to-face meetings at three time points. Viva QS® and placebo were supplied for 24 weeks.**

Results: **One hundred and fifty-five subjects were randomized from 1st April 2008 to 26th October 2008 in the study. Biochemically verified 7-days point prevalence demonstrated Viva QS® significantly increased quit rate vs. placebo; 42.7% vs. 26.2% ($p = 0.038$) at week 4, 32.0% vs. 16.7% ($p = 0.031$) at week 12 and 30.7% vs. 13.9% ($p = 0.015$) at week 24. Adverse events reported were similar between groups. The most frequently reported adverse events were sore throat and dry mouth (36.6% and 17.8%, respectively for Viva QS® vs. 28.8% and 16.9% for placebo).**

Conclusions: **Viva QS is safe and effective to aid smokers quit smoking in this population sample.**

KEY WORDS

safety, efficacy, herbal medication, smoking cessation

INTRODUCTION

Addiction to nicotine is so strong that alcoholics and drug addicts asserted it would be less painful to quit these substances, as compared to nicotine[1)]. In 2006, according to the Third National Health and Morbidity Survey (NHMS3) carried out by the Ministry of Health, Malaysia in 2006 found out that 27% of the population are ever smokers, 21.5% are current smokers and only 5.4% were categorized as ex-smokers[2)]. It was also reported that 70.6% of current smokers attempted to quit and on average, smokers had 2.1 times quit attempts in the past one year.

The search for new alternative treatments or interventions for smoking cessation remains an area of research agenda. Herbal medications have been used long time ago as alternative interventions, in addition to the current pharmacological treatment available. We conducted a study to assess the efficacy and safety of an herbal medication namely Viva QS® as an alternative intervention for smoking cessation. Viva QS® is consisted of twelve herbs mainly found in Korea and China. It was originally developed from Viva®, a medication used in suppressing opiate withdrawal symptoms and acted as therapeutic nutrient to detoxify drug addiction[3)]. Through observation during the treatment, patients also admitted distaste to cigarettes, thus Viva QS® was developed for the purpose of smoking cessation, but some adjustments were done in the amount of certain herbs, as in Table 1.

MATERIAL AND METHODS

Study design

This study was a randomized, double-blind placebo-controlled trial of 155 industrial-worker smokers. Study was conducted at 11 industrial workplaces in Kerteh and Kuantan, Malaysia. Subjects were selected conveniently from those attended mobile smoking cessation programme (MSCP), handled by a team consisted of pharmacists and family medicine specialists. MSCP was conducted to assist hard-to-reach smokers to help them quit smoking. Recruitment was promoted by emphasizing the importance of smoking cessation and the opportunity to participate in the study. Each subject was given a set of self-administered demographic and smoking history questionnaires, and an informed consent to read through. Smokers who agreed to quit and to sign the consent form were screened for eligibility and those fulfilled the inclusion and exclusion criteria were selected for enrolment.

Screening

Subjects were screened for inclusion and exclusion criteria. Nicotine dependence level was assessed using the modified FTND test. Upon signing the informed consent form, eligible subjects filled in the given questionnaires. Baseline smoking status was determined by measuring the level of carbon monoxide (CO) using PiCO+ Smokerlyzer in an exhaled air sample. The peak expiratory flow rate

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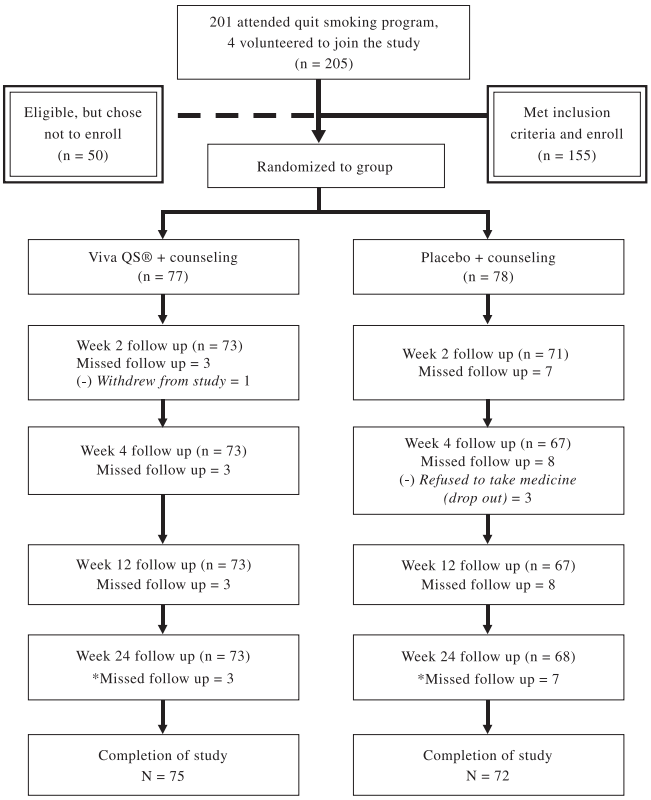

* Three (3) subjects from placebo group and one, (1) subjects from Viva QS® group were excluded from final analysis because they were lost from being follow-up since the beginning of study.

Figure 1. Flowchart of Subjects' Recruitment and Follow-up

(PEFR) was obtained using peak flow meter. Each subject was given a booklet, contained a form to record the daily cigarette smoked, if any, from the date of commencement until the end of week-24, and a withdrawal symptoms score sheets, modified based on the revised Nicotine Withdrawal Scale (MNSW-R)[4] to record any withdrawal symptom from week 1 until week 5. Subjects were required to select a 'target quit date' to quit smoking.

Inclusion criteria

1. Male smokers age 18 to 60 years old.
2. Subjects should be able to speak English or Malay.
3. Fagerström score test is 4 or more.
4. Give consent to be involve in the study.

Exclusion criteria

1. History of dependence on alcohol or drug abuse within the past year.
2. Current or past history of medical treatment on these chronic diseases, i.e. asthma, any cardiovascular disease, HIV or AIDS, cancer, mental disorders and serious liver or renal disease or history of transplantation.
3. Current used of nicotine replacement therapy or bupropion SR.
4. Drinking more than 8 cups of coffee per day (75 ml each cup).

Randomization

Subjects satisfied the study criteria were randomly assigned to receive a 24-week supply of Viva QS® or placebo. Subjects were randomized between April 1, 2008, and October 26, 2008, with the last 6-month follow-up session completed in May 17, 2009. The manufacturer was responsible for the randomization; the medication packs were numbered from 1 to 155. Subjects were assigned to a specific treatment number based on the provided randomization code. There was no difference between placebo and Viva QS® in appearance, color and shape of the capsules, and were packaged in identical blisters packaging and boxes. Viva QS® used was from the same production batch. The administration of the capsules was conducted on a double-blind basis i.e. all subjects and the researchers had no information on who received Viva QS® or placebo.

Table 1. Dosage of Study Medication

Treatment week	Dosage (Viva QS® / placebo)
Week 1	2 capsules 2 times per day (2 BD)
Week 2 and week 3	1 capsule 2 times per day (1 BD
Week 4 to week 24	1 capsule once a day (1 OD)

Treatment and follow-up period

The duration for this period was 24 weeks (Figure 1). The manufacturer fixed the dosing regimen as shown in Table 1. Compliance was assessed based on self-reporting and capsules counting. Subjects were instructed to quit smoking on their target-quit date; we suggested on the eighth day after they consumed the medication. At week 2 subjects were contacted by telephone call to obtain the quit date. At week 4 subjects were follow-up by telephone calls to assess smoking status and adverse events experienced by subjects at that time point. Subjects received brief counseling of 5-10 minutes during the follow-up. One same researcher was responsible to perform all counseling and follow-up by telephone. Subjects were continuously contacted until reachable; if the subjects were still unreachable at this time point, subjects were included as missing in the analysis.

At week 12, subjects were met individually face-to-face at their workplaces or at an organized meeting location. At this time point, three researchers were involved to provide individual brief counseling session (5-10 minutes) as well as assessing the smoking status. In order to avoid biases and variability in the follow-up reports, a standard follow-up form was used. Smoking status was assessed by self-report and confirmed with CO test; and smoking abstinence was confirmed by expired CO levels < 8 ppm[5].

At this time point, subjects who were unable to be follow-up face-to-face, were contacted by telephone calls. Abstinence was recorded according to self-report; self-reported smoking status alone was accepted to be documented, even without validation with CO test. At this time point, CO test was not compulsory, thus follow up via telephone calls or face-to-face were both accepted. Adverse events were documented according to self-reports from the subjects, thus, there was no difference in terms of documenting the adverse effects; either by face-to-face or telephone call as no physical examination was conducted in the assessment.

Study completion

Subjects completed the treatment period at the end of week 24. Researchers met the subjects again at the workplaces or at an organized meeting location for this final visit. In addition to self-reported smoking status, validation of abstinence at the end of study was conducted using CO test and measurement of cotinine in urine and/or saliva. Subjects who were unable to be met at this point were follow-up by telephone calls or by contacting the medical personnel in-charge at the workplaces to confirm the smoking status but subjects without biochemical markers validation were considered smokers.

Biochemical validation

Carbon monoxide (CO) measurement was taken at week 12 and week 24. At the end of study, cotinine level was obtained by measuring samples from urine and/or saliva of the subjects, regardless of their self-reported smoking status. For cotinine level in urine sample, cut-off point of 50 ng/ml[6] was applied to differentiate a smoker from a non-smoker, while a cut-off value of 8 ppm[5] was applied for the CO monitoring. For saliva NicAlert®, a cut-off value of 1 (presenting 10-30 ng/ml) was used[6], meaning the actual cut-off value considered is 10 ng/ml.

Biochemical instruments for validation

1. Pico+ Smokerlyzer was used to measure carbon monoxide (CO) level in an exhaled air sample.
2. Saliva NicAlert® was used to measure cotinine level in saliva samples.

Table 2. Baseline Demographic Characteristics

Characteristics	Viva QS® (n = 75)	Placebo (n = 72)	Total (n = 147)	*p* value (2-tailed)
Age (years), n (%)				
18-30	24 (32.0)	28 (38.9)	52 (35.4)	0.594
31-45	37 (49.3)	34 (47.2)	71 (48.3)	
46-60	14 (18.7)	10 (13.9)	24 (16.3)	
Race, n (%)				
Malay	74 (98.7)	71 (98.6)	145 (98.6)	0.741
Others	1 (1.3)	1 (1.4)	2 (1.4)	
Marital status, n (%) a				
Married	63 (86.3)	62 (87.3)	125 (86.8)	0.856
Never married or divorced	10 (13.7)	9 (12.7)	19 (13.2)	
Education, n (%)				
Secondary school	16 (21.3)	26 (36.1)	42 (28.6)	0.116
Certificate	10 (13.3)	10 (13.9)	20 (13.6)	
Degree/ Diploma	49 (65.3)	36 (50.0)	85 (57.8)	
Employment, n (%)				
Management	17 (22.7)	14 (19.4)	31 (21.1)	0.632
Technical	58 (77.3)	58 (80.6)	116 (78.9)	
Age begin smoking (years), n (%)				
10-15	22 (29.3)	19 (26.4)	41 (27.9)	0.692
16-20	42 (56.0)	45 (62.5)	87 (59.2)	
21-40	11 (14.7)	8 (11.1)	19 (12.9)	
Baseline tobacco use (No. of cigarette smoked per day), n (%)				
1-10 sticks	19 (25.3)	16 (22.2)	35 (23.8)	0.216
11-20 sticks	42 (56.0)	49 (68.1)	91 (61.9)	
> 20 sticks	14 (18.7)	7 (9.7)	21 (14.3)	
Baseline Fagerstrom test score for nicotine dependence, n (%)				
4-6	61(52.6)	55 (47.4)	116 (78.9)	0.463
7-10	14 (45.2)	17 (54.8)	31 (21.1)	
Mean carbon monoxide (CO) level (ppm), (SD)	11.63 (4.834)	11.38 (4.294)	11.50 (4.564)	0.739
Mean Fagerstrom test score for nicotine dependence, (SD)	4.91 (1.317)	5.15 (1.469)	5.03 (1.394)	0.286

[a] n = 144. Three subjects with missing data.

Table 3. Baseline Tobacco Used Characteristics

Characteristics	Viva QS® (n = 75)	Placebo (n = 72)	Total (n = 147)	*p* value (2-tailed)
Previous cessation attempted, n (%)[a]	64 (85.3)	61 (84.7)	125 (85.0)	0.917
Duration of quitting (years), n (%)[a]				
< 1	57 (89.1)	51 (83.6)	108 (86.4)	0.374
1-3	7 (10.9)	10 (16.4)	17 (13.6)	
Reasons for previous relapse, n (%)[a]				
Difficulty in concentration	32 (50.0)	37 (60.7)	69 (55.2)	0.231
Craving for cigarette	38 (59.4)	25 (41.0)	63 (50.4)	0.040*
Impatience	21 (32.8)	22 (36.1)	43 (34.4)	0.702
Frustration and uncontrolled anger	20 (31.3)	22 (36.1)	42 (33.6)	0.569
Bad temper	14 (21.9)	18 (29.5)	32 (25.6)	0.328
Insomnia	16 (25.0)	14 (23.0)	30 (24.0)	0.789
Increased appetite	10 (15.6)	13 (21.3)	23 (18.4)	0.412
Influence by friends	10 (15.6)	8 (13.1)	18 (14.4)	0.689
Awakening at night	6 (9.4)	8 (13.1)	14 (11.2)	0.508
Depression	6 (9.4)	3 (4.9)	9 (7.2)	0.493**
Reasons for current quit attempt, n (%)				
Health	67 (89.3)	61 (84.7)	128 (87.1)	0.405
Family, friends and loved ones	52 (69.3)	46 (63.9)	98 (66.7)	0.484
Economy	30 (40.0)	36 (50.0)	66 (44.9)	0.223
Job requirement	8 (10.7)	6 (8.3)	14 (9.5)	0.630
Religion	5 (6.7)	2 (2.8)	7 (4.8)	0.268

[a] n = 125 (22 subjects had never attempted to quit prior to the study).

*$p < 0.05$

** Fischer's exact test.

Table 4. Biochemically Verified 7-Days Point-prevalence Abstinence Rate at Week 24

	Viva QS® (n = 75)	Placebo (n = 72)	OR (95% CI)	*p* value (2-tailed)
Total quitters, n (%)	23 (30.7)	10 (13.9)	2.74 (1.20-6.28)	0.015
Verified abstinence by saliva cotinine test (ng/ml), n (%) [a, d]	13/27 (48.1)	10/27 (37.0)		
Verified abstinence by urine cotinine test (ng/ml), n (%) [b]	10/13 (76.9)	0/7 (0.0)		
Verified abstinence by carbon monoxide (CO) test (ppm), n (%) [c]	30/41 (73.2)	21/34 (61.8)		

[a] Scale (ng/ml): 0 = 1-10, 1 = 10-30, 2 = 30-100, 3 = 100-200, 4 = 200-500, 5 = 500-2000.

[b] Scale (ng/ml): 0 = not detectable, 1 = 1-20, 2 = 20-50, 3 = 50-100, 4 = 100-200, 5 > 200

[c] Scale (ppm): 1 = 0 - 7, 2 = 8 - 10, 3 = 11 - 20, 4 > 20.

[d] Subjects (n = 54) provided urine samples as well for validation of cotinine level in urine. Samples were unable to be analyzed due to technical problem in the laboratory. Final analysis used saliva samples only for validation of cotinine level in these subjects.

Table 5. 7-Days Point-prevalence Abstinence Rates at Two Time Points

No of week after quit date	7-Days point-prevalence abstinence rates, n (%)	OR (95% CI)	*p* value
Week 4 (n = 147)			
Viva QS®	32 (42.7)	2.08 (1.035-4.163)	0.038
Placebo	19 (26.2)		
Week 12 (n = 147)			
Viva QS®	24 (32.0)	2.35 (1.071-5.169)	0.031
Placebo	12 (16.7)		

Note. At week 12, 29 subjects were follow-up face-to-face and smoking status were confirmed and validated with CO test, whereas 111 subjects were follow-up by telephone call to confirm the smoking status but without CO test for validation.

Table 6. Rates of Continuous Abstinence at Two Different Periods

Period of follow-up	Continuous abstinence rates, n (%)	OR (95% CI)	*p* value
Week 4 to week 12 [a]			
Viva QS®	22/75 (29.3)	2.30 (1.02-5.19)	0.041
Placebo	11/72 (15.3)		
Week 4 to week 24 [a]			
Viva QS®	19/75 (25.3)	2.38 (0.99-5.67)	0.048
Placebo	9/72 (12.5)		

[a] n = 147 (subjects with missing data were analyzed as smokers during these two periods).

Table 7. Adverse Events According to Severity, by Treatment Groups

Adverse events	Viva QS® (n = 73)[a] n(%)	Placebo (n = 71)[a] n(%)	*p* value *
Sore throat	21 (28.8)	26 (36.6)	0.894
Dry mouth	13 (17.8)	13 (16.9)	0.625
Cough	8 (11.0)	6 (8.4)	0.321
Anxiety	6 (8.2)	2 (2.8)	0.116
Headache	4 (5.5)	4 (5.6)	0.889
Bloating	3 (4.1)	3 (4.2)	0.667
Stomach disturbances	2 (2.8)	5 (6.6)	0.371
Rhinitis	2 (2.7)	2 (2.8)	0.543
Vomiting	2 (2.8)	0 (0.0)	0.182

[a] n = 144, 3 subjects with missing reports.

* No significant difference in both groups in all events (all $p > 0.05$).

Table 8. Differences in Withdrawal Symptoms Reported by Subjects at Two Time Points

Withdrawal symptoms	Difference in symptoms compared with placebo group (95% CI)	*p* value *
Viva QS®		
Week 2		
Craving for cigarettes	-0.204 (-0.670 to 0.261)	0.387
Difficulty in concentration	0.273 (-0.132 to 0.677)	0.185
Increase appetite	0.125 (-0.342 to 0.592)	0.597
Depression	-0.066 (-0.432 to 0.299)	0.720
Bad temper	-0.144 (-0.511 to 0.223)	0.439
Impatience	0.239 (-0.139 to 0.616)	0.213
Insomnia	-0.242 (-0.606 to 0.122)	0.191
Frustration and uncontrolled anger	-0.222 (-0.542 to 0.099)	0.173
Awakening at night	-0.124 (-0.377 to 0.129)	0.333
Week 5		
Craving for cigarettes	-0.121 (-0.490 to 0.249)	0.519
Difficulty in concentration	-0.063 (-0.298 to 0.171)	0.593
Increase appetite	0.046 (-0.270 to 0.362)	0.773
Depression	-0.024 (-0.217 to 0.169)	0.807
Bad temper	-0.060 (-0.202 to 0.081)	0.400
Impatience	0.033 (-0.140 to 0.206)	0.704
Insomnia	-0.065 (-0.224 to 0.094)	0.420
Frustration and uncontrolled anger	-0.105 (-0.240 to 0.030)	0.128
Awakening at night	-0.087 (-0.215 to 0.040)	0.178

* No significant difference in both groups in all events (all $p > 0.05$).

3. High performance liquid chromatography with ultra-violet (HPLC-UV) detection to measure cotinine level in urine samples. This method was done in a laboratory based at the International Islamic University Malaysia.

Efficacy evaluation

Self-reported 7-days point prevalence tobacco[7] and continuous abstinence rates[8] at two time points were assessed for quit rates measurement. Primary dichotomous outcome or end-point is 7-days point prevalence at 6 months i.e. week 24. 7-days point prevalence at week 4 and week 12; and continuous abstinence rates from week 4 through week 12 and week 4 through week 24 were evaluated as secondary outcomes.

Self-reported non-quitting status or at the time when CO level was 8 ppm or higher, or when saliva or urine cotinine test result was higher than the cut-off values, subjects were considered smokers dur-

ing treatment and follow-up period. In the case of continuous abstinent end-points missed visit or follow-up: if at the next visit or follow-up there was a self-report of no smoking, a status of not smoking was applied for the missed session[9]. Subjects who considered themselves smokers at week 4, week 12 and week 24, data was collected on the number of cigarettes smoked and their current smoking behaviors, in addition to CO and cotinine samples. Subjects with missed CO value but met other abstinence criteria, and provided self-reported non-smoking status, were considered as non-smokers at week 4 and week 12. At week 24, this condition was not applied as non-smoking status should be confirmed with biochemical markers.

Safety evaluation

Adverse events were assessed according to subjects' self-reported and were not through observation by researchers. Any serious adverse effects experienced by subjects or any case of hospitalization either due to intervention or not, were documented and reported to the manufacturer.

STATISTICAL METHODS

Analysis of the data was done using SPSS version 12.0 for windows. Cross-tabulation and comparison of means were used to summarize baseline demographic data and baseline tobacco use. The chi-square test and comparison of means were used to compare treatments on primary and secondary end-points. Types of adverse events over the entire period were compared between groups using cross-tabulation and independent t-test. Comparison of means was used to analyze mean in both groups. The test was considered significant if $p < 0.05$.

RESULTS

Baseline demographic and tobacco use characteristics

There were no significant differences in the baseline characteristics of participants between treatment groups (Table 2). The average age of the subjects was 35.2 ±8.36. On average, baseline Fagerstrom test score for nicotine dependence (FTND) was 5.03 ±1.39. On average, the subjects started smoking at the age of 17.7 ±3.35. Table 3 showed tobacco used characteristics at baseline. The most commonly reported motivational factors for current quitting attempt were health (87%), family, friends and their loved ones (67%) and economy (45%). The most common reasons for previous relapsed reported among subjects were difficulty in concentration (55%), craving for cigarettes (50%), impatience (34%) and, uncontrolled anger and frustration (34%).

Primary outcome

Abstinence rate at the end of study i.e. week 24 was assessed as primary outcome. Self-reported abstinence at this time point was biochemically validated by measuring cotinine level in saliva and/or urine samples, in addition to self-report and CO test. Table 4 showed the biochemically validated 7-days point-prevalence abstinence for the treatment and control groups. The abstinence rate for Viva QS® was significantly better than the placebo at the end of the treatment period (30.7% vs. 13.9%; $p < 0.05$; OR, 2.74).

Saliva samples (n = 54) and urine samples (n = 20) were managed to be collected to measure cotinine level at the end of study. A percentage of 42.6% (23/54) from saliva samples and 50% (10/20) from urine samples demonstrated confirmed abstinence status. From CO level measurement, results showed 68% (51/75) subjects were confirmed abstinence, but 18 out of those 51 subjects showed dissimilar results for saliva and urine tests. Thus, subjects were considered smokers; as measurement of cotinine level in saliva and/or urine sample was the principal biochemical validation method. One subject only agreed for CO test and refused to provide either saliva or urine sample, thus he was classified as smoker.

Secondary outcomes

The 7-days point-prevalence abstinence rates at week 4 and week 12 were assessed as secondary outcomes. The abstinence rates were higher in Viva QS® as compared to placebo at all time points (Table 5). Results showed significant differences between groups; Viva QS® vs. placebo (42.7% vs. 26.2%; $p = 0.038$; OR, 2.08) at week 4, and (32.0% vs. 16.7%; $p = 0.031$; OR, 2.35) at week 12.

Continuous abstinence rates from week 4 through week 12, and from week 4 through week 24 were assessed as secondary outcomes (Table 6). Abstinence rates of Viva QS® were higher than placebo at both periods. The continuous abstinence rate from week 4 through week 12 differed significantly between treatment groups (Viva QS®: 29.3% vs. placebo: 15.3%; $p = 0.041$; OR, 2.30). Significantly, Viva QS® showed higher abstinence rates than placebo from week 4 through week 24 (Viva QS®: 25.3% vs. placebo: 12.5%; $p = 0.048$; OR, 2.38).

Measures of safety

54% subjects in Viva QS® group and 51% subjects in placebo group reported at least one adverse event ($p = 0.69$). Adverse events reported at any time of the study contact points throughout 24 weeks of treatment period were similar between groups (Table 7). Sore throat and dry mouth were the most commonly reported adverse events in both groups (Viva QS®, 28.8% and 17.8%; placebo, 36.6% and 16.9%). The least frequently reported adverse events in both groups were rhinitis (Viva QS®, 2.7%; placebo, 2.8%) and vomiting (Viva QS®, 2.8%; not reported in placebo group). Stomach disturbances showed lower incidents in Viva QS® (2.8%) as compared to placebo (6.6%).

Measures of withdrawal

Withdrawal symptoms were reported in 132 subjects (Viva QS®, n = 69; placebo, n = 63); no withdrawal (n = 1) and not reported (n = 14). Table 8 showed no significant difference in withdrawal symptoms scores in both groups at all events at two time points.

DISCUSSIONS

Majority of subjects in this study were aged 31 to 45 years (49%), followed by group aged 18 to 30 years old (35%). Subjects were randomly chosen from different group ages, to represent the "real world" of adult population. Highest number of subjects was group age 31 to 45 years as commonly at most workplaces, most workers were about these ages.

In measuring efficacy in this study, we based respectively on the ratio and the differences in the 7-days point prevalence abstinence rates at three time points between groups, with the abstinence rate at week 24 as primary outcome. Self-reported abstinence at week 24 required validations with biochemical markers, by measuring cotinine level in saliva and/or urine samples, plus exhaled breath carbon monoxide (CO) level. Secondary outcomes in this study were the 7-days point prevalence abstinence rates at week 4 and week 12, and continuous abstinence rates at two time frames.

Prior to commencement of the study, an abstinence rate of 21% for intervention group and 16% for placebo were targeted. Results obtained were different; with higher abstinence rates in intervention group and lower in placebo. This study was the first randomized control trials (RCTs) conducted to assess the efficacy of Viva QS® for smoking cessation and with limited studies involved herbal medications for smoking cessation, thus no standard reference were available. As a result, standard quit rates as in previous studies involved NRTs, bupropion and varenicline were adopted.

It was common when smokers reported quitting "on their own" through self-help either by "cold turkey", or cutting down gradually the number of cigarettes smoked, however, with the assistance of a cessation programmes such as MSCP and pharmacotherapy, the quit rates are usually higher on average, i.e. more than 20%. Intensive clinical interventions for 6 to 12 weeks of individual or group counseling led by professionals are generally more successful than self-help[1]. Combining two or more methods for smoking cessation including pharmacologic and non-pharmacologic therapies may also produce bigger success[10].

Pharmacological interventions are most effective when combine with behavioral interventions, so most studies evaluating the use of pharmacotherapy generally incorporated at least limited behavioral therapy within the study protocol[11]. In this study, a combination of both behavioural and pharmacologic therapies was applied to aid the smokers quit, with the intention-to-treat method. Intention-to-treat (ITT) is an important strategy to treat smokers in any clinical trials

involving smoking cessation, for the analysis of randomized controlled trials that compares patients in the groups to which they were originally randomly assigned[12].

In this study, adverse events reports were used to assess safety of the herbal medication at any time point. No mortality case happened throughout the study. Two subjects were hospitalized during the study in two separated cases, but were not related to study medication. As Viva QS® was developed from twelve herbs and contained various ingredients; the tolerable adverse events suggested the herbs used in the medication might not be harmful to be taken. However more researches should be done to study the each of the herbs involved.

Withdrawal symptoms reported were assessed using modified version of revised Minnesota withdrawal scale (MNWS-R)[4]. Each symptom was rated from 0 (absent) to 4 (severe). No significant difference was found between groups; concluded that Viva QS® is not effective to reduce withdrawal symptoms. Initially, results were unable to suggest Viva QS® is helpful to reduce craving or any other withdrawal symptoms. For analysis, the mean symptoms score were compared between withdrawals at week 2 and week 5, to assess the severity of withdrawal symptoms at the early stage of quitting (week 2) and after 5 weeks of quitting. Reduction in mean symptoms was found in both groups; results were concordance as in other previous studies and theories that withdrawal symptoms usually will be overcome by the subjects after 4 to 5 weeks of quitting[13,14].

There are several limitations in this study. The study population were mostly middle-aged Malay males, thus findings may not be generalized to other populations of smokers. Furthermore, subjects were recruited from those who were motivated and voluntarily to quit, which limits the generalization, but does represent the group of smokers for whom pharmacotherapy may be most appropriate.

Self-reported smoking status at all time points were not verified except during final follow-up at week 24; thus results were unable to be verified biochemically at other times. We estimated medication compliance by self-reports and therefore could not be certain that subjects assigned to receive Viva QS® actually took the medication as directed. To avoid confusion, the significant differences in quit rates were observed at all time points, and assumed that Viva QS® was being taken as directed.

This study was not initially designed to detect chemically which components among the twelve herbs of Viva QS® contributed to the cessation effect, but was designed to compare the overall effectiveness of the medication as a whole and not to distinguish among the components.

To strengthen the study, future research should be done to investigate the pharmacotherapy and therapeutic effects of the combination of the herbs in Viva QS® in details. Further studies could investigate the relative benefit of each component in Viva QS® and to find the main component contributes to the cessation effect. Another issue is regarding weight gain problem after cessation. Thus, future study should investigate if Viva QS® is also effective to help quitters managing problem with weight gain.

CONCLUSIONS

Viva QS® is effective and safe to be used as an aid for smoking cessation in adult smokers, but further studies should be done to confirm the results in other population samples, such as adolescents and elderly.

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