

The Effect of Anchovy Sauce on Severity and Progression of Glaucoma

Research Article

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Abstract

Introduction: Anchovy sauce is a known appetizer in many Asian's cuisines. Based on the bio-physical content of anchovy sauce, there is a possibility of the frequent consumption can affect severity and progression of glaucoma. The aim of this study was to determine the association of anchovy sauce intake in severity and progression of glaucoma.

Methods: A cross-sectional study was conducted involving 91 primary glaucoma patients who were compliance and achieved target intraocular pressure, non-smoker and without a family history of glaucoma. Direct face-to-face interview on the dietary recall of anchovy sauce consumption was conducted between May 2013 and December 2013. The complete ocular examination was performed including intraocular pressure measurement. Hoddap-Parrish-Anderson criterion was used to assess the severity of glaucoma based on the latest reliable and reproducible of two consecutive Humphrey visual fields 24-2. The association between anchovy sauce and glaucoma severity was determined using Fisher's exact test. Multiple logistic regression analysis was performed to determine the association of anchovy sauce intake with glaucoma progression.

Results: A total of 46 male and 45 female with primary glaucoma were recruited with a mean age of 66.4 (SD10.1) years old. 56 patients consumed anchovy sauce with 19% occasionally, 44.6% weekly, 16.1% daily and 5.4% in every meal. There was no significant association of anchovy sauce intake with severity and progression of primary glaucoma after a mean of 6.4 years of follow-up.

Conclusion: Anchovy sauce has potential protective effect against progression and severity of glaucoma. However, it was not reflected in this study due to small sample size and poor quantification of the amount of anchovy sauce as a condiment to the main dish.

Keywords: Glaucoma; Anchovy Sauce; Progression.

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Introduction

Glaucoma is a progressive optic neuropathy characterized by specific visual field defects due to the loss of retinal ganglion cells and damage to the optic nerve head (ONH) [1]. It is a leading cause of irreversible blindness worldwide [1]. It was estimated that 60.5 million people were affected by glaucoma by year 2010, and further increase to 79.6 million by year 2020 [2]. Triad of mechanical pressure induced by intraocular pressure (IOP), degenerative changes of retina ganglion cells and ocular perfusion impairment to ONH are postulated to cause progression of glaucoma [3-5]. Dietary intake such as coffee is also believed to play a role in severity and progression of glaucoma [6-10].

Anchovy sauce, also known as 'budu' locally is a popular appetizer in the east coast of Peninsular Malaysia, particularly in the state of Kelantan [11, 12]. It is also available in Indonesia. In South Thailand, it is known as 'nam-pla, and 'patis' in Philippines [11-14]. 'Budu' is fermented anchovy sauce made by mixing the anchovy with high concentration of salt in the range of ratio of 2:1 to 6:1, and water. Anchovy sauce contains various biogenic

and biochemical nutrition, which potentially give either harmful or protective effect towards diseases [15-18]. Based on the high content of sodium and omega-3 fatty acid of anchovy sauce, assumption of its role as the risk for progression of glaucoma is inevitable. The main objective of this study was to determine the association between dietary intake of anchovy sauce with severity and progression of glaucoma.

Material and Method

A cross-sectional study was conducted involving 91 patients diagnosed with primary open angle glaucoma (POAG) and primary angle closure glaucoma (PACG) seen in Eye Clinic, Hospital Universiti Sains Malaysia, Kelantan between May 2013 and December 2013. The sample size was calculated based on the prevalence of glaucoma from Singapore Malay Eye Study. Based on 3.4% prevalence, the estimated sample size was 66 glaucoma patients (includ-

ing 30% missing data). This study received ethical approval from Research and Ethics Committee of Universiti Sains Malaysia (Ref no: 00007718) and was conducted in accordance to Declaration of Helsinki for human research.

Glaucoma patients who were compliance to topical pressure lowering medications were recruited. Only patients who were able to produce two consecutive reliable (false negative and false positive less than 33%, fixation loss less than 20%) and reproducible Humphrey visual field analysis (HVF) were recruited. Patients with media opacities especially cataract more than grade 2 of LOCS II grading, vitreous haemorrhage and corneal opacities were excluded. Those with retina pathology such as retinitis pigmentosa and diabetic retinopathy were also excluded. Those with the history of surgical intervention especially filtering surgery were also excluded except for cataract surgery.

A questionnaire on dietary recall of the intake of anchovy sauce

Figure 1. Questionnaire on anchovy sauce consumption.

B. Dietary intake

Anchovy sauce intake- Yes/No

If yes, state frequency:

	Frequency of Intake				Amount of serving taken (1 teaspoon per serving)
	How many times per day	How many times per week	How many time per month	How many times per year	
Anchovy sauce intake					

was designed and validated. The questionnaire was adopted from food frequency questionnaire (FFQ) [19] (Figure 1). Anchovy sauce was not included in the original FFQ, to ensure clarity of the questionnaire a pilot study was conducted on 10 glaucoma patients. A direct face-to-face interview was conducted by ophthalmologist in training (NAAA and ANFA) and postgraduate student (NAS). Patients who have problem in remembering their food intake were excluded.

Ocular examination was conducted including slit lamp biomicroscopy and fundus examination. The IOP was measured using Goldmann applanation tonometry (GAT). Visual field test was performed using Humphrey Statpac 2 pattern deviation probability map of 24-2, SITA Standard, using a 31.5-apostilb background with a white Goldmann size III (0.43°) stimulus, (Carl Zeiss Meditec, Dublin, CA, USA). The Hoddap-Parrish-Anderson (H-P-A) criteria were used to evaluate the severity of glaucoma based on mean deviation (MD). A MD value less than -6dB is categorized as early defect, MD less than -12dB is moderate and MD more than -12dB is severe defect [20]. The severity and progression of glaucoma was determined by the glaucoma specialists (LS and AY) [20-23]. Progression was defined as the changes of HPA category at the initial diagnosis and at the recruitment process. Changes of more than -4 MD from baseline was considered significant and defined as progression of glaucoma.

Data were analysed using SPSS Version 20. Association between anchovy sauce and glaucoma severity was determined using Fisher's exact test. Multiple logistic regression was applied to determine associated factors of anchovy sauce intake with glaucoma progression. All variables with p-value less than 0.25 during uni-

variate analysis were included on the multivariate analysis. Backward and forward stepwise logistic regression was used for the variable under interest (Glaucoma progression and not progress) which was binary. The final model was obtained using the likelihood ratio based on maximum likelihood estimate. Model fitness for final model was checked by using the Hosmer-Lemeshaw test, over all classification of correct outcome and area under the receiver operating characteristic (ROC) curve. For the categorical variables results are presented as the frequency and its percentage and for numerical variables results are presented as the mean±SD. However for the multivariate analysis were presented with adjusted odds ratios with 95% confidence intervals, likelihood ratio test statistics and p-value. Significance level was set at p=0.05.

Result

A total of 91 patients were recruited with the mean age of 66.4 years old (SD 10.1). Majority of patients were Malays (n=66, 72.5%) (Table1). There was almost equal distribution among male (n=46) and female (n=45) patients; 50.5% and 49.5% respectively. Majority of the patients were diagnosed with POAG (n=80, 87.9%) (Table1). Mean IOP at initial presentation was measured at 23.8mmHg (SD 9.3). Based on HPA classification, majority were at severe stage of glaucoma during the recruitment period followed by moderate and mild severity; 42.9%, 31.9% and 25.3% respectively (Table 2). A total of 57 (62.6%) patients showed progression of the disease.

56 (61.5%) glaucoma patients recalled taking anchovy sauce in their diet with nearly half of them reported taking anchovy sauce once a week (Table 3). However, there was no significant differ-

Table 1. Demographic characteristic.

Variable	n (%)
Sex	
Male	46 (50.5)
Female	45 (49.5)
Race	
Malay	66 (72.5)
Chinese	25 (27.5)
Age in years	
Mean (SD)	66.4(10.1)
Diagnosis	
POAG	80 (87.9)
PACG	11 (12.1)
Glaucoma severity at recruitment	
Mild	23 (25.3)
Moderate	29 (31.9)
Severe	39 (42.9)
Duration of follow up in years	
Mean (SD)	6.9(4.4)
Systemic Comorbidity	
Diabetes Mellitus	44 (48.4)
Hypertension	64 (70.3)
Hyperlipidaemia	23 (25.3)
Ischaemic heart disease	15(16.5)
Asthma	4 (4.4)
IOP at initial presentation(mmHg)	
Mean (SD)	23.8(9.3)
IOP at recruitment (mmHg)	
Mean (SD)	16.2(2.9)
HVF at initial presentation (mean, SD)	
Mean deviation	-10.12(8.20)
Pattern standard deviation	5.69(3.66)
HVF at recruitment (mean, SD)	
Mean deviation	-12.60(9.54)
Pattern standard deviation	6.40(3.73)

SD=standard deviation; IOP=intraocular pressure; HVF=Humphrey Visual Field

Table 2. Clinical parameters and anchovy sauce intake.

Variable	Anchovy sauce intake n(%)	Non anchovy sauce intake n (%)	P value
Age in years			
<60	16 (66.7)	8 (33.3)	0.547 ^a
60 and above	40(59.7)	27(47.3)	
Sex			
Male	27(58.7)	19(41.3)	0.668 ^a
Female	29(64.4)	16(35.6)	
Race			
Malay	44(66.7)	22(33.3)	0.147 ^a
Chinese	12(48.0)	13(52.0)	
IOP at initial presentation			

Mean (SD)	23.18(7.62)	24.74 (11.50)	0.437 ^b
IOP at recruitment			
Mean (SD)	16.81(5.26)	18.8(11.39)	0.366 ^b
HVF at initial presentation(mean, SD)			
Mean deviation	-9.45(7.99)	-11.10(8.51)	0.366 ^b
Pattern standard deviation	6.31(4.18)	4.57(2.75)	0.078 ^b
HVF at recruitment (mean, SD)			
Mean deviation	-12.57(9.75)	-12.89(9.36)	0.858 ^b
Pattern standard deviation	6.99(4.03)	5.43(2.98)	0.094 ^b

^a Fisher Exact Test, ^b Independent T test.

IOP=intraocular pressure; HVF=Humphrey Visual Field

Table 3. The association of anchovy sauce intake with glaucoma severity.

Variable	Glaucoma severity at recruitment, n (%)			P value
	Mild	Moderate	Severe	
Anchovy sauce intake				
Yes	14(25.0)	18(32.1)	24(42.9)	0.996 ^a
No	9(25.7)	11 (31.4)	15 (42.9)	
Frequency of intake (n=56)				
Every meal	1(33.3)	2(66.7)	0(0.0)	0.466 ^a
Daily	2(22.2)	1(11.1)	6(66.7)	
Weekly	7(28.0)	9(36.0)	9(36.0)	
Occasional	4(21.1)	6(31.6)	9(47.4)	

^aFisher exact test.

Table 4. The association of anchovy sauce intake and glaucoma progression.

Variable	n (%)		p-value
	Non-progression	Progression	
Type of glaucoma			
POAG	32(40)	48(60)	0.161 ^a
PACG	2(18.2)	9(81.8)	
IOP at initial presentation (mmHg)			
Mean(SD)	22.76(8.35)	24.39(9.81)	0.423 ^b
IOP at recruitment (mmHg)			
Mean(SD)	15.20(3.45)	15.95(2.93)	0.273 ^b
HVF at initial presentation			
MD, Mean (SD)	-7.17(6.55)	-11.84(8.61)	0.006 ^b
PSD, Mean (SD)	3.97(2.46)	6.20(3.82)	0.019 ^b
HVF at recruitment			
MD, Mean (SD)	-6.64(6.82)	-16.10(9.21)	<0.001 ^b
PSD, Mean (SD)	4.11(2.26)	7.34(3.81)	
Number of topical medication			
1	14(46.7)	16(53.3)	0.418 ^a
2	13(34.2)	25(65.8)	
More than 2	7(30.4)	16(69.6)	
Anchovy Sauce intake			

Yes	22 (39.3)	34 (60.7)	0.663 ^a
No	12 (34.3)	23 (65.7)	
Frequency of intake (n=56)			
Every meal	2 (66.7)	1 (33.3)	0.144 ^a
Daily	3 (33.3)	6 (66.7)	
Weekly	13 (52.0)	12 (48.0)	
Occasional	4 (21.1)	15 (78.9)	

^aFisher Exact Test, ^bIndependent T test.

POAG= Primary open angle glaucoma, PACG= Primary angle closure glaucoma, IOP=intraocular pressure; HVF=Humphrey Visual Field.

Table 5. Factors associated with glaucoma progression.

Variable	Regression coefficient (b)	Adjusted OR (95% CI)	Wald statistic	p-value
Glaucoma severity at recruitment				
Mild	-	-	-	-
Moderate	-0.20	0.82(0.12,5.60)	0.04	0.838
Severe	5.11	165.5(8.00,3428)	10.92	0.001
Duration of follow up (years)	0.47	1.60(1.13,2.26)	7.16	0.007
Frequency of anchovy sauce intake				
Every meal	-	-	-	-
Once daily	-3.47	0.31(0.00, 8.95)	1.44	0.230
Weekly	-1.97	0.04(0.00,12.94)	0.73	0.394
Occasional	-3.20	0.73(0.01, 96.88)	0.02	0.898

Backward LR Multiple Logistic Regression was applied.

Multicollinearity and interaction term were checked and not found.

Hosmer-Lemeshow test (p=0.364), classification and area under curve (91.6%) were applied to check the model fitness.

ence in severity of glaucoma among those taking anchovy sauce in their diet (Table 3).

There were evidence of progression of the disease in 34 (60.7%) glaucoma patients who were taking anchovy sauce daily after at least 6 years of follow-up (Table 4). However, there was no significant association of anchovy sauce intake and the frequency of intake with progression of glaucoma (Table 4). Even after the adjustment for age, gender, systemic comorbidity and disease duration using multivariate logistic regression analysis, there was still no significant association between anchovy sauce intake and glaucoma progression.

Discussion

In general, the main aim of the management of glaucoma is to retard progression of the disease. The IOP has been identified as modifiable risk factor for development and progression of glaucoma. Identification of another modifiable risk factor such as dietary intake is important to halt further retinal nerve fibre layer damage in glaucoma patients.

However, in the present study there was no significant association of anchovy sauce with severity and progression of glaucoma. High content of protein up to 24.88% and mean value of salt 25.10% was found in anchovy sauce produced in the state of Kelantan, Malaysia [11, 12]. Anchovy sauce contains biological active compounds particularly angiotensin converted enzyme 1 (ACE-1) inhibitor [15, 18] and other important biogenic amines; histamine and tyramine [17, 18, 24, 25]. These compounds may exert both protective and damaging effect on the optic nerve [17].

ACE-1 inhibitor isolated from fermented anchovy sauce was found to have inhibitory activity in vitro [15, 18]. ACE-1 inhibitor and histamine is a known vasodilator. Tyramine causes vasoconstrictor effect [11]. High salt content in anchovy sauce may aggravate the effect of tyramine and cause reduction in optic nerve head perfusion [17, 18, 25]. The high content of omega-3 in anchovy sauce is believed to reduce the risk of glaucoma. Low consumption of omega-3 increased the risk of glaucoma based on epidemiology study [26]. Clinical based studies also found the higher risk of glaucoma in patients with low consumption of omega-3 [27-29]. It was found that higher consumption of omega-3 facilitates aqueous outflow and reduces the IOP [30]. However, there was no significant difference in IOP at diagnosis and at recruitment between those consumed anchovy sauce and those who are not in this present study. Furthermore, higher consumption of omega-3 reduces the risk of Alzheimer's disease [31-35]. Alzheimer disease may share similar pathogenesis with glaucoma [29, 33].

There is high possibility that anchovy sauce may associate with protective effect against glaucoma and perhaps retard further progression. Based on multiple regression analysis, anchovy sauce seems to reduce the risk of progression. This may also explain the lack of association of anchovy sauce consumption with severity of glaucoma. In this study, the questionnaire was designed to be patient's friendly without proper quantification of the amount of intake (estimation of 1 teaspoon). Quantification of anchovy sauce is not easy due to the small amount of intake as condiment with many local dishes [12]. Perhaps, due to the similar reason the frequency of intake may not be a good tool to estimate the amount of anchovy sauce.

However, the current study may not be a true representative of

the effect of anchovy sauce on glaucoma due to relatively small sample size. Ideally, the number of patients should be divided equally among those who consumed anchovy sauce and those who are not. This will give a clearer picture of the effect of anchovy sauce on severity and progression. A prospective cohort study will give more accurate outcome compared to cross sectional study. The questionnaire used in this current study is exclusively concentrate on anchovy sauce intake. There is no information on other dietary intake. The protective effect against progression and severity of glaucoma may not entirely due to anchovy sauce alone. Perhaps, it is due to combination effect of other dietary intake. Complete dietary recall questionnaire particularly food rich with omega-3 is important to determine the role of anchovy sauce in progression of glaucoma.

In the current study, Hodapp Parish and Anderson (HPA) criteria is adopted to define severity and progression. Although HPA is quite reliable and easy to use but it only provides a crude staging of glaucoma severity [24]. We excluded those glaucoma patients with family history of glaucoma and non-compliance to medications. Perhaps we had eliminated some of significant confounding towards glaucoma progression [26]. The main confounding factor was relatively small sample size. The calculation was based on the prevalence of glaucoma due to unavailability of previous studies on anchovy sauce and glaucoma. This is not ideal.

Nevertheless, this study provides a preliminary data on the potential effect of anchovy sauce on glaucoma. A better constructed questionnaire with proper quantification of anchovy sauce may give a better reflection of the effect of anchovy sauce on glaucoma patients.

Conclusion

Anchovy sauce has potential effect on progression and severity of glaucoma. Quantification of intake of anchovy sauce is a challenge due to small volume of intake as condiment to the main dishes. A larger sample size is needed to give a better understanding of the effect of anchovy sauce in glaucoma patients.

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