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Polymorphisms of CYP2E1 rs2031920 is not Associated with Risk of Nasopharyngeal Carcinoma in Minangkabau Ethnic Group

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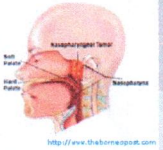
Background

- Nasopharyngeal carcinoma (NPC) is a cancer in the nasopharyngeal epithelium that is globally rare.
- NPC is a unique cancer with incidence varies widely according to geographic location and ethnic background.
- The incidence is high in certain regions such as in southern China and in Southeast Asia, including Indonesia
- In southern China the incidence is up to 50 cases per 100,000 populations per year, whereas in Europe and US the incidence of this malignancy is less than 1 / 100,000.



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Background

- The exact etiology of nasopharyngeal cancer is unknown, but it is thought to be a multi factorial interaction.
- Epstein-Barr virus (EBV) infection interacts with genetic susceptibility, and environmental are the main etiological factors.
- Various environmental factors have been reported related to the incidence of Nasopharyngeal Carcinoma (NPC), including consumption of salted fish containing nitrosamines
- Clinical epidemiology study on NPC at Dr.M. Djamil Hospital Padang did not find this association.

Background

- Nitrosamines are activated by the CYP2E1 enzyme.
- Activation of nitrosamines can cause the growth of several malignancies.
- Several studies have found that CYP2E1 is also expressed on the nasal and nasopharyngeal mucosa
- CYP2E1 mutation can cause nasopharyngeal mucosa susceptible to growth of NPC

Background

- Study in Taiwan and Thailand populations found CYP2E1 RsaI (rs2031920) polymorphism in the promoter associated with an increased risk of NPC
- while Guo at al. who conducted studies in the Chinese population did not find an increased risk of NPC in mutant homozygote individuals variants of CYP2E1-RsaI (rs2031920).
- Several studies have reported in several ethnic groups that have inconsistent results.

Objectives

- Our study was conducted to analyze the association of the CYP2E1 rs2031920 polymorphisms with the incidence of NPC in the Minangkabau ethnic group.

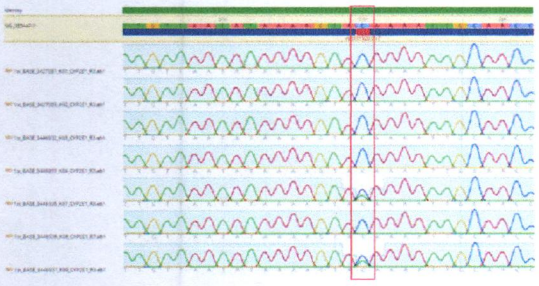
METHODS

- The subjects of this study were newly diagnosed NPC Minangkabau patients, while the controls were healthy people who were also Minangkabau ethnic.
- A total of 23 cases of NPC and 23 aged and sex-matched controls participated in this study.
- Informed consent was obtained and blood samples were taken.
- The study was approved by the ethics committee of Faculty of Medicine, Andalas University, Padang, Indonesia (No.422/KEP/FK/2018).

Methods

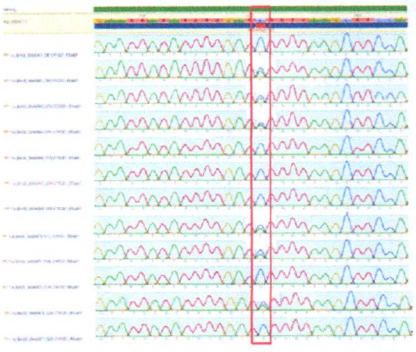
- The method used to identify these polymorphisms is PCR sequencing.
- All PCR product samples were sequenced at 1stBASE, Singapore.
- The results of sequencing data are then processed with Genious 11.1.2 software.
- The presence of mutation of CYP2E1 gene is indicated by the changes in CC base to CT or TT.
- In individuals who have CYP2E1 rs2031920
  - no change in CC base is called a wild type →not experience polymorphism
  - change from CC to CT are called heterozygote mutants
  - change from CC to TT are called homozygote mutants.
- Sequencing results are then aligned with the reference genes (NG_055447.1)

Alignment of some sequencing of NPC group with reference genes CYP2E1



Sample K01, K02,K03, K04, K07, K08 dan K09
Heterozigote mutations in the two samples; K07 and K09

Alignment of sequencing of some control group samples with the CYP2E1 reference gene.



Heterozigote Mutation in six samples : S09, S10, S11, S17, S18 and S24

Results

Association of CYP2E1 Polymorphism (rs2031920) with NPC

Polymorphisms	Group		p
	NPC f (%)	Control f (%)	
Wild type (CC)	21 (91.3)	17 (73.9)	0.243
Heterozigote Mutation (CT)	2 (8.7)	6 (26.1)	
Homozigote Mutation (TT)	0 (0)	0 (0)	
Total	23(100)	23(100)	

- CYP2E1 gene polymorphism was found in both the NPC and control group
- In the NPC group there were 8.7% heterozygote mutants while in the control group there were 26.1% heterozygote mutants

RESULTS

- there were no homozygote mutants in the two groups, and statistically none a significant relationship between CYP2E1 gene polymorphism and the incidence of NPC, with p> 0.05.
- In NPC group, there were only heterozygote mutations in the two samples (K07 and K09), there were no homozygote mutations,
- whereas in the control group there were six samples, also in the form of heterozygote mutants (S09, S10, S11, S17, S18 and S24)

Discusssion

- In this study, Minangkabau ethnicity in both NPC and controls group found only heterozygote mutantion (c1c2), and not related to the incidence of NPC.
- The similiar result was reported by Lourembam et al. who conducted a study in India in areas with high insidence of NPC also found only heterozygote polymorphisms and also did not find a significant relationship with the incidence of NPC

- Several studies have reported in several ethnic groups that have inconsistent results.
- The meta-analysis study in various ethnicities found a correlation between CYP2E1 rs2031920 gene polymorphism and the incidence of NPC
- Most of these studies found homozigote mutation.
- No association with the incidence of NPC if it was only heterozygote mutation.

- Various reports concluding that there is a relationship between CYP2E1 gene polymorphism and the incidence of NPC generally combining homozygote and heterozygote mutantion or calculating the frequency of c2 allele
- whereas if only looking at heterozygote mutantion, there are no reports that have a significant relationship with the incidence of NPC

Conclusions

- Our study reveals that there is no association of CYP2E1 gene polymorphism (rs2031920) with nasopharyngeal carcinoma in the Minangkabau ethnic group.

Thank tou

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