CHAPTER I

INTRODUCTION

Migraine is one of the most common conditions encountered both in the general neurology and special headache clinic. A survey in Chulalongkorn Headache Clinic revealed the prevalence of migraine to be 49.5% of the patients visiting the clinic (Srikiatkhachorn and Phunthumchinda, 1992). According to the International Headache Society criteria (1988), this condition can be classified to various subtypes depending on their clinical features. There are two main types of migraine. The first, migraine without aura (previously called common migraine), is characterized by headache attacks lasting 4-72 hours. The headache is usually severe, unilateral pulsating, and accompanied by nausea, vomiting, photophobia and phonophobia. In the second type, migraine with aura (previously know as classical migraine) is characterized by the presence of transient neurological deficits preceding the phase of headache. Its gradual course of progression and the distribution of neurological deficits do not support the hypothesis that the primary cause resides in the vascular component.

In 1944, Leao reported his observation concerning a specific pattern of change of the electroencephalogram (EEG) which can be triggered by non-noxious stimulation. This electrophysiologic phenomenon is characterized by an increase in EEG activity of focal cortical areas usually occipital lobe. This excitation-depression wave gradually expands forward and normally disappears at the central sulcus. Base on the similarity in time course and pattern of spreading, Leao proposed that this electrophysiologic phenomenon, which was later

termed cortical spreading depression (CSD), might be the mechanism underlying the aura phase of migraine (Lauritzen, 1994).

Though CSD correlated well with the clinical features of neurological deficits, occurring during the aura phase, the relationship between this phenomenon and the generation of headache is still inadequately explained. Base on the vascular theory of migraine, a number of studies have documented an increase in cerebral blood flow during the headache phase of migraine (Wolff, 1987; Lance, 1981). As previously experiments demonstrated the increasing of regional cerebral blood flow (rCBF) in cortical areas during CSD (Piper et al., 1991). Furthermore, the microdialysis experiment showed the release of various neurotransmitters in brain tissue during CSD, such as glutamate and glycine (Frabicius et al., 1993). More recently, Read and Parsons (2000) measured the changes of nitric oxide (NO) level in parietal surface and demonstrated an increase in NO during CSD. Interestingly, some of released chemical, such as glutamate and NO, are known to be able to activate or sensitize the nociceptor and NO is a vasodilator which was considered to be the important mediator in the headache of migraine (Iversen et al., 1989a). Possibly, NO may plays roles in the mechanism of CSD-evoked cerebral hyperemia and pathophysiology of migraine with aura.

Several results indicated that serotonin (5-HT) play an important role in the pathogenesis of migraine (Raskin, 1991). Urinary excretion of 5-hydroxyindole-3-acetic acid, the metabolite of 5-HT, has been reported to increase during the headache phase whereas platelet 5-HT level decrease (Sicuteri et al., 1961; Anthony et al., 1969). Intravenous administration of 5-HT can alleviate migraine symptoms elicited by 5-HT depleting agents (Kimball et al., 1960). Recently, $5\text{-HT}_{1B/1D}$ receptor

agonist was used for migraine treatment because it can reduce the neuropeptide release which cause of vasoconstriction and decrease neuronal activity of trigeminal nerve. Interestingly, Read and Parsons (2000) demonstrated that 5-$HT_{1B/1D}$ receptor agonist, sumatriptan, could decrease the increasing of NO level evoked by CSD.

As previously mentioned, NO and 5-HT may involve in the mechanism of rCBF changes evoked by CSD and pathophysiology of migraine with aura. However, the relation of NO and 5-HT is unclear as well as their roles in the cerebral vascular changes evoked by CSD. Therefore, we design to study the effect of NO and 5-HT in CSD-evoked cerebral hyperemia.