# CHAPTER 5

## DISCUSSION AND CONCLUSION

The results of this study demonstrate the demographic characteristics in Table 4.1, which is similar to previous studies [3-8]. The proportion of females was higher than males (84.4 % and 15.6 %, respectively). The most common age group was between 18 – 31 years old, and migraine without aura was more common than migraine with aura. Aggravating factors in Table 4.4 including physical activity (60%) and bending over (77.8%) were more commonly seen, as previously reported [19], but in this study, menstruation was relevant among only 39.4% of female patients. Precipitating factors such as stress, lack of sleep, smell and food were less frequent among this study population, when compared with the study of Spierings et al. [19], and about half of them were triggered by weather and alcohol. Only 17.8% of respondents were affected by long travel ≥ 6 hours.

In general, the results of this study showed significant mean differences in the number of days with migraine attacks, total intensity scores, total severity scores and total duration scores per month between baseline and the hand-free use and non hand-free use group, but there was no a significant mean difference in the number of migraine attacks per month, even after adjusting the covariate factors such as anxiety scores, depression scores and smell stimulation over the past month, as shown in Table 4.10 and 4.14. This would support the hypothesis that exposure to electromagnetic radiofrequency (EMF) may have an effect on health [46]. However, this is still a controversial issue. Hocking [23] carried out a preliminary report of

symptoms associated with mobile phone use, which often began minutes after beginning a call, but could come on later during the day. These usually ceased within one hour after the call, but could last a lot longer. Another case report revealed neurological abnormalities associated with radiofrequency radiation (RFR) by an accidental exposure to RFR. This case reported a feeling of warmth over the abdomen, thirst, the onset of headache on the left-side, and sharp constant pain. These symptoms of migraine attack continued for long periods and were relieved by paracetamol [103]. The overall mean percentage of clinical findings from mobile phone use was 21.65% for headache [28]. However, all of these studies were only observational, observing general symptoms from EMF exposure, and it was therefore difficult to confirm that RF radiation from mobile phone use could really affect people's health, especially regarding headache. This study had a more specific objective and study design for migraine headache, according to the pathophysiology of migraine, and it aimed to ascertain whether EMF exposure would be able to affect the pattern of migraine headache [1, 24, 35, 37, 38].

Moreover, the neurobehavioral effects among inhabitants living near mobile phone base stations were reported to have a higher prevalence of headache among exposed persons than in controls [97]. However, a double blind randomized provocation study among people who were sensitive to mobile phone signals indicated no difference in severity of headache between GSM and sham exposure [95]. As in a recent study, there was no indication that radiofrequency (RF) exposure caused pain in the head of GSM 900 MHz users. This lack of effect was apparent among mobile phone users and controls [33]. A provocation study on the effect of EMF exposure, conducted by both open and double-blind tests, exhibited sham exposures

that caused significantly fewer symptoms than real exposure conditions, but not in the double-blind tests [98]. Findings from the above studies showed the weakness of intervention study regarding the awareness of patients on the issue of experimenting without a double-blind controlled trial. On the other hand, the experimental conditions were not natural for human habits, and studies were done in healthy subjects with short term exposure to EMF. A low level of radiofrequency radiation may take affect in long term exposure, as in the study of Finnie et al. [62] whose results showed leakage from very many blood vessels present in the three coronal brain sections. This study was designed for intervention in hypersensitive subjects (Migraineurs) and to keep to natural conditions for RF exposure according to their habits, but with an open-label. This method ensured that this study could not avoid a bias from patients' awareness of experimental conditions.

The main results of this study revealed that the number of days with migraine attack had a lower significant mean in the hand-free use group than baseline with 95% CI: 0.23; 3.63 (P=0.02), but not between the non hand-free use group and baseline. Furthermore, total intensity scores and total severity scores displayed a far lower significant mean in the hand-free use group than in the non hand-free use group when compared to the baseline with 95% CI: 1.71; 7.84 vs. 0.58; 7.15 (P = 0.001 vs. P = 0.016), and 27; 98.15 vs. 5.56; 86.65 (P = 0.001 vs. P = 0.021). On the other hand, total duration scores among the hand-free use group had a lower significant mean than baseline with 95% CI: 12.18; 60.88 (P=0.002), but not between the non hand-free use group and baseline, as was the case with the number of days with migraine attack (see Table 4.10 and 4.11). Even so, the outcomes of this study could be interfered with by these factors after adjusting the covariate factors for migraine (see Table 4.13). The

results still demonstrated a significant mean difference between the hands-free use group and baseline, and non hands-free use group and baseline, as shown in Table 4.14 and 4.15. The findings above showed a possible prophylaxis treatment effect on the outcomes of this study; because there was a lower significant mean in both pairs when comparing between the hands-free use and non hands-free use group with baseline. However, the significance levels of primary outcomes were greater among the hands-free use group than in the non hands-free use group when compared with baseline. In consequence, there was no significant mean difference of primary outcomes between the hands-free use and non hands-free use group, and relevant data is not shown in Table 4.11 and 4.15. These findings would indicate that Migraineurs could have more effective prophylaxis treatment. When patients avoided exposure to RF emitted from a mobile phone, it was better than receiving medication alone while using hand-free equipment with a cellular telephone by habit. Furthermore, Migraineurs could decrease duration of calls and frequency of calls per day in order to reduce the effective level of RF exposure from a mobile phone. These results are in accordance with Chia et al.'s findings from a cross-sectional study [29]. They reported that a significant increase in the prevalence of headache occurred with increasing duration of mobile phone use by minutes per day. In contrast, the prevalence of headache was reduced by more than 20% among those who used hands-free equipment for their cellular telephone, as compared to those who never used hands-free kits. As in the study of Oftedal et al [96], results indicated that headache typically appeared during or within 30 minutes after a call, and most people's symptoms continued for up to 2 to 6 hours after the call. Nearly 40% of headache patients experienced symptoms that were ipsilaterally relative to the side of the head where the

mobile phone was held. Headaches were most commonly connected to mobile phone use with significant probability. Interestingly, about 45% of people with symptoms, who attributed them to mobile phone use, had taken steps to reduce the symptoms by decreasing calling time and using hands-free equipment, and most of those people reported a reduction of symptoms. The results of this study revealed that patients held the phone mostly on the right side (66.7%), with fewer using the left or both sides (28.9% and 4.4%, respectively). However, headaches were more commonly presented on both and changed sides (40% and 46.7%, respectively), with only a few on the left and right side (8.9% and 4.4%, respectively). This contradicted a previous study [96].

Some experimental studies confirmed a reduction of RF exposure from a mobile phone by using hands-free accessories [30, 31, 101]. Bit-Babik et al. [30] demonstrated a significant impact of RF energy coupled into the leads of hands-free accessories, and this was strongly attenuated by the body. SAR to the user's head was substantially reduced by the use of a wired ''hands free'' earphone-microphone extension. The results from appropriate tests showed that these devices, "hands-free kits", were effective in reducing RF to the head [31]. With a personal hands-free (PHF) kit in use, the maximum body absorption depended on where the mobile phone was placed. If it was in the hand, the situation was similar to normal use of the phone against the ear. If it was in a pocket, then the body absorption was expected to depend on which way round the phone was placed. Personal hands-free kits offered very substantial reductions in SAR compared to the normal use of a mobile phone held against the ear [101]. A case report by Hocking and Westerman [104] demonstrated that the patient's symptoms such as brief sensations on the right side of the scalp, but not the left, after mobile phone use were worsened by exposure to the sun or wind, and

there was no effect from the use of an ordinary telephone. Symptoms seemed to decrease after patients avoided using a mobile phone directly, while preferring to use substituted materials such as hands-free equipment [54]. Personal hands-free (PHF) kit use would have greater benefit for decreasing RF exposure and could reduce the temperature effect to the head from RF emitted from cellular telephones [73, 74, 75, 76].

Indeed, the results of this study also revealed a significant correlation in duration grading of calls and number of migraine attacks in the non hands-free use group (see Table 4.18 and Figure 4.11). Similarly, the calling time on a mobile phone had a significant correlation with the number of migraine attacks in the baseline period in the non hands-free use group (see Table 4.20 and Figure 4.14, 4.15). On the contrary, a significant correlation of frequency of calls per day with the number of migraine attacks and number of days with migraine attack in the hands-free use group is shown in Table 4.19 and Figure 4.12, 4.13. Previous studies displayed the dose response and time effect from RF exposure on the biological changes of human cells [64, 65, 68, 69, 105]. Thus, it was possible that exposure to RFR from cellular telephones could cause a transient localized change in blood flow, pinocytosis, or permeability of the blood-brain-barrier. These effects could lead to local changes in brain functions [54, 56-63]. However, there were several studies showing that repeated exposure at relatively low SARs caused morphological changes in the central nervous system [80, 81, 82]. Radiation at very low power densities could affect the ion channels associated with transmitter receptors and it was also likely to be influenced by temperature changes in calcium efflux [83, 84, 85, 86]. Changes in neuronal electrophysiology, evoked potentials, and EEGs have been reported [77, 78, 79].

In contrast, exposure of the inner thighs to pulsing electromagnetic fields for at least 3 weeks was reported as an effective short term intervention for treating chronic migraine [106, 107]. The data on biological effects of EMF on human cells in the available literature are contradictory. Most probably because the experimental conditions were quite different for frequencies, intensity, exposure duration, positions, etc.

The strength of this study is its design, which is appropriate to the disease and intervention conditions. Both cases and controls could be subjects in the study through different periods of time. Hence, there was a comparison of outcomes within-subjects. Subsequently, this would increase the power of the study and decrease the sample size. Nevertheless, patients had to stay in the study for a long time, and some of them dropped out. Data analysis and interpretation in this study would be difficult if patients dropped out in sequence 1. However, the primary outcomes had a significant mean difference only when compared with baseline and the hands-free use group, and baseline and the non hands-free use group, but there was no a significant difference between the hands-free use and non hands-free use group. This would affect the size of difference, due to the intervention being too small, and detection could not occur because of possible prophylaxis treatment effect. When comparing the outcomes in only sequence 1 between the hands-free use and non hands-free use group with baseline, and between the hands-free use and non hands-free use group, a significant mean difference was still shown only in comparison between the baseline hands-free use and non hands-free use group, but not between groups. Another reason was the treatment effect for migraine while the patients participated in the study, which would affect the clinical improvement in both groups almost equally, and both

groups received similar treatment regimens according to the standard treatment for migraine. However, the size of difference seemed to be greater among the hands-free use group than in the non hands-free use group when compared to the baseline data. Moreover, a significant correlation between duration grading of mobile phone use, duration of calls and number of migraine attacks per month was observed in this study.

Other covariate factors including number of cups of coffee, number of glasses of alcohol, hours using a microwave, hours watching TV, hours listening on an MP3, hours using a computer, anxiety status, depression status, past month's food stimulation, past month's stress stimulation, past month's lack of sleep stimulation, past month's long travel > 6hr stimulation, past month's smell stimulation, and past month's hot weather stimulation; stimulated migraine attacks during the past month's exposure. Thus, these factors tested the difference between baseline to sequence 1, and sequence 1 to sequence 2 in both groups. The results showed that there was no significant difference of some of those factors between each period. Some differences were adjusted with the outcomes between each period. This could reduce the confounding factors in the study after adjusting the covariate factors, which were expected to have an effect on the outcomes of this study.



However, there were limitations in this study. Because the study had an open level design, the patients were aware of using hands-free kits for their mobile phone. Therefore, the intervention that patients received during the study period could not avoid bias. Another limitation was no run-in period in order to evaluate the compliance of the patients with intervention before enrolling them into the study. In addition, the study had a lack of standard intervention because there were not enough

budgets to apply the same brand and model of mobile phone and hands-free equipment for the patients. Different brands and models of mobile phone may have varied the radiofrequency radiation exposure to patients. Thus, patients could have a different specific absorption rate (SAR) from a cellular telephone, which could affect the patients at many levels. This could also bring bias into the study. Even so, the last experimental study showed no difference in reduction level of RF exposure from various hands-free set accessories [101].

In conclusion, mobile phone use with hands-free kits may decrease the level of radiofrequency exposure emitted from a mobile phone. Hence, this would reduce the degree of severity during migraine attacks. Direct mobile phone use would not be a precipitating factor; however it could be an aggravating factor for migraine headache. The use of substituted materials with mobile phones, such as hands-free kits and speaker phones, may reduce the level of exposure to pulse modulation from a mobile phone. This would help people to avoid the effects of EMF exposure to some degree. Again, patients would have greater benefit from prophylaxis treatment together with avoidance or reduction of mobile phone exposure during a current migraine attack than receiving medication alone. Further study in order to investigate the effects of mobile phone use with hands-free kits in a clinical study would need to identify more specific inclusion and exclusion criteria to test the hypothesis of whether EMF exposure can aggravate migraine severity. It would be important to have a run-in period in the study in order to decrease the bias. There should also be matched age groups and selected education level of the target population. In other cases, investigators should take back hands-free kits from the patients after finishing the intervention period and give them back to the study. Condition of experiments should

involve the same brand and model of mobile phone for the patients. In addition, it would be possible to perform a cross over design parallel with one group receiving medication for migraine treatment alone without hands-free kit use in order to evaluate the regression of outcomes. This effect really occurs in the intervention or in the treatment for migraine alone.