CHAPTER I

INTRODUCTION

Rationale of the study

Cadmium (Cd) is a toxic heavy metal posing severe risks to human health (Godt, et al. 2006). It can distribute in the environment as an inorganic salt. The major source of Cd contaminated environment coming from human activities (4,000 to 13,000 tons per year) such as mining and the burning of fossil fuels (ATSDR, 1999). A significant source of Cd exposure is occupational exposure, active and passive cigarette smoke (ATSDR, 2008). It can remain in the body for decades (Sugita, et al., 1995). Cd levels in the environment are depended on the appearance of industrial places or extensive of agricultural activity places. The environmental Cd is able to contaminate into the food chain and human can uptake Cd by inhalation and ingestion (diet and drinking water) (Martelli, et al., 2006). Previous study reported that Cd is found in environment in local areas including Mae Ku, Mae Tao and Pratat Pha Daeng of Mae Sot District, Tak Province, Northwestern Thailand. In addition, Cd has > 90% of the rice grain samples is collected from these contaminated areas (Simmons, et al., 2005; Swaddiwudhipong, et al., 2007). Other studies showed that environmentally expose to Cd increases maternal blood Cd and cord blood Cd levels and it is also induce low birth weight (< 2,500 g.) of their baby (Tian, et al., 2009). And, smoker pregnant women also show a low birth weight of their babies and histopathological changes in placenta including a decreased of a number of villi and syncytial knot. Placenta is a barrier protecting the fetus from toxic metals such as Cd. Toxic metals accumulation in placental tissue may involve in abnormal placental function which leading to impaired nutrient transport and fetal growth restriction (Osman, et al., 2000; Norberg, et al., 1998; Zadorozhnaja, et al., 2000). Divalent metal transporter-1 (DMT-1) plays a vital role in transporting multiple divalent metals; Fe^{2+}, Mn^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Pb^{2+}, Zn^{2+}, and Cd^{2+} (Garrick, et al., 2003). In human, DMT-1 has found in cytoplasm and basal membrane of syncytiotrophoblast cell of placental tissues which appears to be associated either with the absorptive or excretory functions in this tissue (Georgieff, et al. 2000; Chong, et al. 2005). The synthesis of DMT-1 protein is

significantly higher in cerebellum cortex and hippocampus of Cd and Pb treated rat brain than in control rat brain (Chengwu, et al., 2009). The expression of DMT-1 mRNA is increased in iron deficiency wild-type mice, resulting in up-regulation of Cd intake in the intestine (Suzuki, et al., 2008). DMT-1 is suggested to play an important role in Cd absorption in rat duodenum (Ryu, et al., 2004).

However, the information regarding association between Cd and DMT1 expressions in term human placenta is very little. Thus, this study is the first one that investigates differential DMT-1 mRNA and protein expression in term human placentas exposed to environment of Cd contamination.

Objectives of the study

1. To localize the DMT-1 protein in term human placenta.
2. To determine the DMT-1 mRNA and protein expressions in term human placenta of pregnant women living in Cd contaminated area comparing to those in non-Cd contaminated area, Mae Sot, Tak.

The scope of the study

In this study, the subjects were pregnant women living in Cd and non-Cd contaminated areas in Mae Sot, Tak, Thailand. The maternal blood, urine and placentas obtained from pregnancies living in Cd contaminated area were used as the experimental group compared with the control group taken from pregnancies living in non-Cd contaminated area, Mae Sot, Tak. We determined the levels of Cd in maternal blood on alteration of iron levels in their body. The DMT-1 localization and its protein expression were studied by immunohistochemistry staining and western blotting technique expression, respectively. In addition, the DMT-1 mRNA expression was analyzed by conventional PCR technique.

Hypothesis

1. DMT-1 protein is localized in the placental barrier of term human placenta
2. DMT-1 mRNA and protein are differential expressed in term placentas of pregnancies living in Cd contaminated area compared with those in non-Cd contaminated area.

The importance of the study

A basic knowledge:

The DMT-1 localization in term human placenta. And, the differential DMT-1 protein and mRNA expressions in term human placentas taken from pregnancies living in Cd contaminated area compared with those in non-Cd contaminated area. Also, the relationship between Cd accumulation and DMT-1 expression in placental tissues.

An applied knowledge:

According to the information above, it will be a useful knowledge to conduct the deeply future research. Moreover, it can be applied as healths index to aware the health risk for population, especially the pregnancies who exposed to the environment of Cd contamination.