

CHAPTER I

INTRODUCTION

Rationale and significance of the study

Methamphetamine (METH) is an illegal psychostimulant drug that rapidly increased use in recent years (Barr, et al., 2006). The National Survey on Drug Use and Health (2003) has reported that METH was used at least once in a lifetime in 5.3% of the United States people. The most METH users during 2002 are people age between 26-34 years (6.7%) and 18-25 years (5.7%), respectively (Sommers, Baskin and Baskin-Sommers, 2006). In Thailand, METH is an abuse drug that the most used in secondary school students age between 13-18 years (Sherman, et al., 2008).

METH acts as a stimulation on the central nervous system (CNS). It can induce alertness and euphoria. Moreover, the toxic doses of METH can induce delirium (Derlet and Heischouer, 1990), depression (Sommers, Baskin and Baskin-Sommers, 2006), anxiety, hallucination (Albertson, Derlet and Van Hoozen, 1999, Barr, et al., 2006; Sommers, Baskin and Baskin-Sommers, 2006) and paranoia (Barr, et al., 2006, Sommers, Baskin and Baskin-Sommers, 2006). Furthermore, METH has also been reported as a cause of violence in the family and associate relationship together with social problems (Sommers, Baskin and Baskin-Sommers, 2006). These may lead to be the national problem.

Sperm motility, sperm morphology and sperm concentration are sperm quality parameters (Seed, et al., 1996; Lee, et al., 2002). These methods are used to predict the fertilizing ability (Hirano, et al., 2001), pregnancy rate (WHO, 2010) and assess the reproductive toxicity (Seed, et al., 1996). Decreasing of sperm motility, sperm concentration and increasing of abnormal sperm morphology are related to change of fertilizing ability (El-Demerdash, et al., 2004).

Androgen, mainly testosterone, is a steroid hormone which necessary for initiation and maintenance for spermatogenesis (Collins, et al., 2003; Holdcraft and Braun, 2004). It is produced by Leydig cell and signal via androgen receptor (AR) (Collins, et al., 2003). AR expression is presented in Sertoli cell, Leydig cell,

peritubular myoid cell (Wang, et al., 2006; Xu, et al., 2007). Besides, the recent study shows that AR expression is presented in spermatogonia, spermatocyte and elongated spermatid at stage XI (Collins, et al., 2003) but AR expressions in germ cell are still in debate (Wang, et al., 2006). AR is also important for normal spermatogenesis. Androgen receptor knockout (ARKO) male mice showed lack of germ cells in seminiferous tubule (Collins, et al., 2003). Leydig cell-specific AR knockout mice showed an absence of epididymal sperm, maturation arrest at round spermatid and a decrease of serum testosterone level (Xu, et al., 2007).

METH has not only been reported as a CNS stimulant but also reproductive toxicity. The previous studies showed that METH administration in male rats can induce apoptosis in the seminiferous tubules in testis, abnormal sperm morphology and low sperm count (Nudmamud-Thanoi and Thanoi, 2011). In male mice testis, METH at least 5 mg/kg can induce apoptotic cells in the seminiferous tubules (Yamamoto, et al., 2002). In addition, male mice were treated with METH at 15 mg/kg showed a decrease of sperm motility and fluctuation of serum testosterone concentration (Yamamoto, Yamamoto and Hayase, 1999). Alteration of sperm motility, sperm morphology, sperm concentration and testosterone level may relate to change of AR expression after treat with METH. Therefore, the present study has investigated whether the effect of METH dependence on alteration of sperm quality, AR expression and plasma testosterone level.

Purpose of the study

A general experiment objective

This experiment is designed to evaluate the effect of METH administration that imitates human addiction on sperm quality, androgen receptor (AR) expression and plasma testosterone level in male rat with METH administration.

Specific objectives

1. To determine alteration of sperm quality consist of sperm motility, sperm morphology and sperm concentration in animals with METH dependence.
2. To determine alteration of AR expression in Leydig cells, Sertoli cells and germ cells in animals with METH dependence.

3. To determine alteration of plasma testosterone levels in animals with METH dependence.

Hypothesis

METH can induce alteration of sperm quality, AR expression in Leydig cells, Sertoli cells and germ cells and plasma testosterone levels.

Scope of this study

This study investigated the effect of METH that imitates human addiction in male rat on alteration of sperm quality. Variations of AR expression in testis after treated with METH was examined using immunohistochemistry technique as well as variation of plasma testosterone levels were examined in animals with METH dependence using electrochemiluminescence immunoassay.

Keywords

Methamphetamine, sperm quality, seminiferous tubules, androgen receptor, plasma testosterone.

Outcome expectations

1. To provide an information about the alteration of sperm quality, AR expression in Leydig cells, Sertoli cells and germ cells and plasma testosterone levels with METH dependence.

2. To provide more information about toxicity of METH on male reproductive system.

Conceptual framework

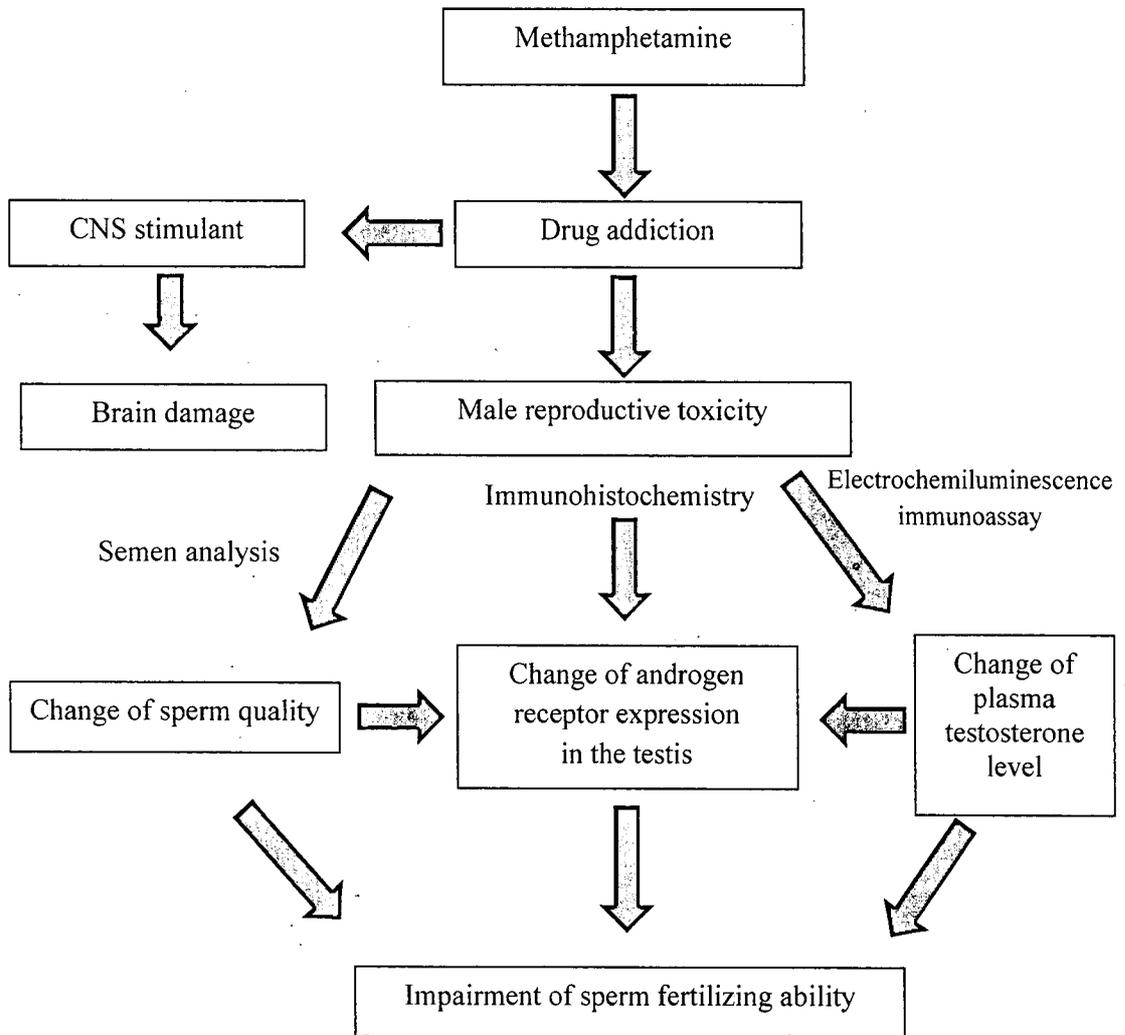


Figure 1 Conceptual framework of this study