J. Perinat. Med.
18 (1990) 479

Maternal kinetics of morphine during labour

Eva Gerdin[1], Tomas Salmonson[2], Bo Lindberg[1], and Anders Rane[2]

[1]Department of Obstetrics and Gynecology, Akademiska Hospital, Uppsala University and [2]Medical Products Agency, Uppsala, Sweden

1 Introduction

Morphine has been used for relief of labour pain since the early twentieth century [32]. After World War II the synthetic opioid meperidine, which was believed to cause less neonatal depression than morphine [16] came into use and morphine fell into disrepute as an obstetric analgesic. While the kinetics of morphine in human pregnancy have apparently never been studied, several investigations have been performed on the disposition of meperidine [15, 26, 31] and other new obstetric analgesics such as meptazinol [11] in the pregnant woman and in the neonate. It has been demonstrated that meperidine is slowly eliminated from the neonate [5, 7, 15] and the presence of the drug for several days in the neonatal urine indicates a potential for pharmacological effects during that period [15]. This drawback of meperidine as an obstetric analgesic agent was the basis of our renewed interest in morphine as a reliever of labour pain. Furthermore, in investigations on systemic analgesia during labour, morphine remains the standard with which other analgesics are compared [6].

Morphine is primarily eliminated by conjugation in the liver. Morphine-3-glucuronide (M3G), its major metabolite, lacks an analgesic effect [25] and is highly water soluble and excreted via the kidneys [3].

The pharmacokinetic properties of morphine have been characterized in studies on patients with chronic pain [20, 23] and undergoing surgery [2, 9, 22, 27]. Data from these studies cannot a priori be transferred to the pregnant woman, as the considerable physiological changes that occur during pregnancy may lead to important alterations in the absorption, distribution and elimination of drugs [10, 14].

The purpose of this study was to determine the disposition of morphine in human pregnancy, especially during labour, compared with that in female non-pregnant volunteers of child-bearing age.

2 Subjects and methods

2.1 Volunteers

The study was carried out on two groups of women.

1) A group of six non-pregnant female medical students, aged 24 to 32 years, with body weights ranging from 59 to 73 kg (64.2 $\pm$ 5.3 kg; table I). All of them were considered to be medically fit and denied taking birth control pills or any other medication. They were not addicted to or sensitive to opioid analgesics.

2) A group of 13 healthy nulliparous parturients, aged 16 to 35 years, with body weights ranging from 60 to 106 kg (80.5 $\pm$ 13.5 kg; table I). They had normal pregnancies and delivered at term (38–42 completed weeks of gestation). They were admitted to the obstetric department of the University Hospital of Uppsala and examined by the attending midwife and by the principal author. The decision to use systemic analgesia was made by the attending obstetrician on strictly therapeutic grounds. Oxytocin was administered intravenously in six cases because of uterine inertia and local anaesthetics were given for regional or local anaesthesia in seven cases. No other drugs were given. All of the infants were delivered vaginally in the vertex position. Their birth weight ranged between 3280 and 4200 g. The Apgar score was recorded at 1, 5