Abstract # 86

Effect of OPRM1 and COMT Genotypes on Response to Intravenous Followed by Intrathecal Fentanyl During Labor Analgesia

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Introduction: The analgesic response to intrathecal (IT) fentanyl during labor is affected by polymorphisms of the µ-opioid receptor gene (OPRM1) (1). The combined effect of A118G polymorphism of OPRM1 and that of Val158Met of COMT gene on labor analgesia has not been examined. We evaluated the response to intravenous (IV) and IT fentanyl according to OPRM1 and COMT genotypes in women requesting early labor analgesia.

Methods: Labor analgesia was initiated with IV fentanyl 1.5mcg/kg. Primary outcome was 'IV analgesic success' determined 15 min after IV dose and was defined by NVPS ≤10/100. Women requesting additional analgesia after receiving IV fentanyl were offered a CSE with 20mcg IT fentanyl. Secondary analgesic outcome was 'IT analgesic success' defined as NVPS ≤10/100 at 30 and 60 min post-IT fentanyl. Analgesic and side-effect outcomes were compared according to OPRM1 and COMT genotypes.

Results: 106 women were enrolled and received IV fentanyl. IV analgesic success rate was 20%. Homozygosity for Met158 of COMT (MM, N=34) predicted a lower IV analgesic success (9% vs 25%; OR 3.54, 95% CI 0.9-13.1). Overall, OPRM1 genotype did not influence IV fentanyl response, although it failed to provide successful analgesia in all G118 homozygotes (n=5). IT analgesic success rate was not significantly affected by OPRM1 or COMT genotypes in the 73 women that went on to receive a CSE. However, the IT fentanyl analgesic effect was inferior in women A118 homozygous for OPRM1 (AA, N=59) with significantly higher pain scores at 10, 20 and 25 min post-IT dose (Figure). Lower maternal age, prior IV analgesic success and ‘MM not AA’ predicted a lower pain score after IT-dose (R2=0.017; p=006).

Discussion: OPRM1 and COMT genotypes appear to influence the effect of labor analgesia with IV and IT fentanyl. The allelic combination with the weakest response to IV fentanyl was AAMM (18% of women in this cohort). Our findings that IT analgesia was superior in women with the G118 allele of OPRM1 supports previous work. In addition this study demonstrates for the first time that the response to IT fentanyl is best in women ‘MM not AA’ (14% of women in this cohort). Further studies in larger cohorts are needed to confirm these Results that have potentially useful clinical implications, such as not offering IV fentanyl in early labor to women who will most likely not benefit from it.

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Figure. NVPS after IT fentanyl according to OPRM1 genotype

Box-plots of number represent NPVS at each measuring points after starting IT fentanyl administration. Median presented as solid line, with box representing 25th and 75th and whiskers representing lower of minimum value and greater of maximum value.

* p < 0.05.

NVPS: numerical verbal pain score (0=no pain, 100=worse pain imaginable)

OPRM1: A118G polymorphism (A=A118; G=G118)