Prenatal Exposure to Buprenorphine or Methadone: Effects on Physical Growth, Neurological Development and Temperament in Early Childhood

Volume One

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Abstract

Pharmaceutical maintenance with methadone is the current gold standard for pregnant women with opioid-dependence. While there are many benefits of methadone, its use during pregnancy is associated with high rates of neonatal abstinence syndrome, and long term developmental and behavioural deficits in exposed infants and children. Buprenorphine is increasingly being prescribed as pharmaceutical treatment for opioid dependence due to its milder withdrawal effects, longer duration of action, and improved safety profile, compared with methadone. Although there is a growing body of research supporting the safety and efficacy of buprenorphine during pregnancy and the early neonatal period, studies of the longer term development of children exposed to buprenorphine are scarce.

This is the first study to provide comprehensive, longitudinal information about the physical growth, neurological and psychological development of Australian children prenatally exposed to buprenorphine or methadone. Participants were 30 women maintained on buprenorphine, 24 women maintained on methadone, and 33 women who were not opioid-dependent, and their children. Women were enrolled during pregnancy as part of an open-label non-randomised flexible-dosing longitudinal study, and children were assessed at four, 12 and 24 months post partum. Physical development was monitored in terms of weight, length and head circumference (HC) at each follow-up assessment. Neurological development was assessed by measuring latency of Visual Evoked Potentials (VEP) at four months of age and the Bayley Scales of Infant Development (2nd ed.) at 12 and 24 months. Care-giver ratings of child temperament were used as a measure of psychological development, and were collected at each follow-up assessment. Assessment of social, environmental and family risk factors was also undertaken.

Results showed that children prenatally exposed to buprenorphine did not differ from a non-exposed control group in their physical growth, neurological development, or temperament over the first two years of life. However, results indicated that prenatal exposure to methadone may have a pervasive influence on weight in early childhood, with children prenatally exposed to methadone continuing to have significantly lower weight, compared with non-exposed children, until two years of age. Additionally, it appears that prenatal exposure to methadone may result in significant delays to visual maturation in infancy. At four months of age, VEP latencies of infants prenatally exposed to methadone were found to be prolonged compared with those of both infants prenatally exposed to buprenorphine, and those of non-exposed infants. Scores on the Bayley Scales at 12 and 24 months of age, and caregiver-rated infant temperament at 4-, 12- and 24-months, did not differ between children prenatally exposed to methadone, buprenorphine, or non-exposed controls. Finally, regardless of substance-exposure, the quality of a child's care-giving environment was shown to have a strong influence over infant cognitive, motor and behavioural development, while maternal-infant attachment was found to be an important predictor of child temperament.

Overall, the findings of this study suggest that maternal use of buprenorphine in pregnancy appears to be as safe as methadone in terms of early child developmental outcomes. The benefits of buprenorphine, in terms of early neurodevelopment and healthy weight gain, suggest that it should be considered as a first line treatment for opioid dependence in pregnant women. Moreover, results from this study highlight the importance of a child's care-giving environment, and of early maternal mental health, over and above prenatal substance exposure, in shaping future developmental outcomes.

Declaration

I, Justine Nikola Whitham, certify that this work contains no material which has been accepted for the award of any other degree of diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Statement of Authorship

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List of Abbreviations and symbols

ACh	acetylcholine
AIDS	acquired immune deficiency syndrome
ANOVA	analyses of variance
AIHW	Australian Institute of Health and Welfare
BF	Breast Feeding
BISQ	Brief Infant Sleep Questionnaire
BM	buprenorphine-maintenance
BRS	Behavior Rating Scale
BSID-II	Bayley Scales of Infant Development- Second Edition
CA	corrected age
cc	cubic centimetres
CDI-III	Communicative Development Inventory: Level III
CI	confidence interval
CNS	central nervous system
cm	centimetre
CYWHS	Children Youth and Women's Health Service
δ	delta
DASSA	Drug and Alcohol Services South Australia
EDS	Easy/Difficult (temperament) Score
EPDS	The Edinburgh Postnatal Depression Scale
FMC	Flinders Medical Centre
gm	gram
GA	Gestational Age
GHQ-28	General Health Questionnaire

HOME	Home Observation for Measurement of the Environment
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IGR	intrauterine growth restriction
ISSI-SF	Interview Schedule for Social Interaction - Short Form
κ	kappa
LAAM	ι-α-acetylmethadol
M	mean
MDI	Mental Developmental Index
MGP	Midwifery Group Practice
MM	methadone-maintenance
MRI	magnetic resonance imaging
η^2	eta squared
NAS	Neonatal Abstinence Syndrome
NHMRC	National Health and Medical Research Council
NDSHS	National Drug Strategy Household Survey
NBAS	Brazelton Neonatal Behavioral Assessment Scale
NYLS	New York Longitudinal Study
PDI	Psychomotor Developmental Index
PND	postnatal depression
PSI	The Parenting Stress Index
RA	Research Assistant
RAKIT	Revision of the Amsterdam Children's Intelligence Test
SD	standard deviations
SGA	small for gestational age
SON	Snijders-Oomen Nonverbal intelligence test

STSI	Short Temperament Scale for Infants
STST	Short Temperament Scale for Toddlers
TGA	Therapeutic Goods Association
VEP	Visual Evoked Potential
WCH	Women's and Children's Hospital
WHO	World Health Organisation
WPPSI-R	Wechsler Preschool and Primary Scales of Intelligence – Revised
WISC-R	Wechsler Intelligence Scale for Children - Revised
μ	mu
ζ	zeta

Glossary

Apgar score	A standardised measure of a baby's condition at birth
Gravida	The total number of previous pregnancies
Primigravida	A woman pregnant for the first time.
Multigravida	A woman who has been pregnant more than once.
Parity	The total number of previous pregnancies resulting in live births or stillbirths.
Primipara	Pregnant woman who has had no previous pregnancy resulting in a live birth or stillbirth.

48' arc or 48 min arc = 48 minutes of the retinal arc. A minute of retinal arc is a unit of angular distance with one minute of arc equal to one sixtieth of a degree.

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