Opioid exposure in utero and the developing visual system

We will discuss the visual system consequences of exposure to opioids in utero. While the long-term effects of opioid exposure in utero on developing children have been recognised for decades, for the most part it has been assumed that effects were minimal. The experience of the authors is that opioids do in fact have profound and permanent effects on the developing visual system and brain.

There has been a five-fold increase in the number of babies born in the United States who are addicted to opioids, between 2000 and 2012. This experience has been mirrored in other countries. There has been a parallel rise in the numbers of babies with opioid related problems presenting to pediatric ophthalmologists. Clinicians in the United Kingdom and many other countries have been dealing with large numbers of opioid exposed children for many years and will share their experiences.

The workshop will describe the presentation, examination findings and long-term visual consequences of opioids on unborn children. Dr Hamilton will discuss the profound electrophysiological changes observed in these neonates, confirming that a real physical insult occurs in these children.

The long-term effects of in utero opioid exposure on the developing system and brain are not yet fully understood but are common and often profound. These effects include those on the visual system, problems in the neonatal period and, developmental as well as neuro-developmental problems persisting into childhood and beyond.

Different opioids prescribed as part of replacement programmes cause differing degrees of neonatal abstinence syndrome (NAS). Methadone likely causes more severe NAS than buprenorphine or naltrexone but the quality of evidence is not great.

**Mechanism:** Animal studies (rat model) have found that opioids may affect the developing brain. Both buprenorphine and methadone may affect oligodendrocyte development and the timing of myelination thus potentially interfering with brain maturation at critical stages.

**Presentation:** Some infants are referred by paediatricians or neonatologists specifically because they have had NAS. More commonly however, babies are referred due to concerns about visual development, early onset nystagmus or less commonly strabismus. The referral often omits any mention of NAS or pre-natal drug exposure.

**Consider pre-natal opioid exposure:** In infants referred with delayed onset of vision and/or nystagmus; especially if born prematurely (<36 weeks gestation); microcephaly; low birth weight; attending with grandparents or foster parents. Need to ask specific / leading questions about drug use in pregnancy.

**Examination:** These infants are often fractious and irritable.

- **Vision:** Some infants demonstrate no visual function in first few months of life with visual function developing later. In older infants and children, monocular and binocular visual acuities can vary greatly from normal to severe sight impairment (1.0 LogMAR; 6/60; 20/200). Vision improves relatively little, if at all, as children grow.
- **Nystagmus:** INS (?) which may be rapid and jerk type or slow pendular type. CHP common – usually face turn. Nystagmus sometimes very subtle and only visible on slit lamp examination or fundoscopy.
- **Strabismus** in approx. 50% - usually esotropia.
- **Binocularity:** Around 40% lack BSV.
- **Refraction:** normal for age and ethnicity.
• **Anterior segment:** Exam normal. Lens clear.
• **Posterior segment:** Usually normal though a small minority have optic nerve hypoplasia. Cause of ONH: May be due to associated alcohol use or perhaps secondary to brain insult from opioids?

**Management:**

• Correct any refractive error as appropriate.
• Strabismus surgery as indicated.
• Inform and involve visual impairment team / paediatricians / teachers.
• Long-term intellectual and behavioural outcomes uncertain.

**Ophthalmic manifestations of cocaine exposure**

Dominguez et al reported a case series of children with developmental delay and congenital cerebral anomalies following in utero exposure to cocaine and other drugs. Ophthalmic manifestations included strabismus, nystagmus and optic disc anomalies associated with brain anomalies postulated to be caused by the vasoactive effects of cocaine 21.

Significant fears over long-term effects of in utero cocaine exposure in the 1980s and 1990s do not seem to have been born out in the long-term, for the most part. Original fears that a generation of “crack babies” were going to put severe strain on society failed to materialise. Early studies were methodologically flawed (e.g. small sample sizes and other confounding factors) and overstated the potential effects. Most people exposed to cocaine in utero do not have disabilities or have relatively mild behavioural problems 22.

**References:**