

PROPYLENE GLYCOL: ARE LEVELS OBSERVED IN BRAIN MRS SOLELY RELATED TO DOSING?

Robert Johnstone^{1,2}, Katalin Povázai³, Jonathan Ashmore⁴, Nicholas Byrne^{2,3}, Sarah Peel^{2,3}, Ata Siddiqui³, Jean-Marie U-King-Im³, Denis Azzopardi², Andrew Kapetanakis³, and Geoff Charles-Edwards^{1,2}

¹Guy's & St Thomas' NHS Foundation Trust, London, London, United Kingdom, ²King's College London, London, United Kingdom, ³Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, ⁴King's College Hospital NHS Foundation Trust, London, United Kingdom

Target audience:

Physicists and clinicians involved with MRS of neonates for the assessment of hypoxic-ischaemic injury.

Purpose:

MRS is routinely used to assess elevated lactate levels in neonates following hypoxic ischaemic injury. The appearance of a doublet at 1.1 ppm in some spectra (e.g. fig. 1) is generally attributed to propylene glycol (PG) [1], a widely used excipient for various pharmaceutical preparations such as phenobarbital and phenytoin that are used to control seizures. However, to our knowledge the relationship between administered PG and observed PG levels in MRS has not been fully investigated, and it is not clear whether different dosing patterns are sufficient to explain the range of observed PG levels and the lack of any observable PG in the majority of neonatal MRS studies. The aim of this work was to compare PG levels observed in MRS with administered PG to investigate the relationship between these two variables.

Methods:

Radiology records between July 2010 and Aug 2013 were reviewed retrospectively to identify all hypoxic-ischaemic neonates from whom MRS had been acquired for the detection of lactate (PRESS sequence, TE = 288 ms). Clinical details for these patients were obtained, including dates and times of phenobarbital and phenytoin administrations. All MR spectra were reviewed by an MR physicist with 15 years experience of MRS. Cases with an observable doublet at 1.1 ppm were reprocessed with Tarquin [2] version 4.3.2 using a simulated basis set that included propylene glycol (PG) [3] and referenced to the unsuppressed water signal to obtain institutional units of concentration. All other cases, including one with an apparent doublet at 1.1 ppm but where the model fit for PG had a standard deviation of > 20%, were considered to have zero PG levels on MRS. Administered doses of PG were corrected using a biological half life of 8.8 hours, previously reported for neonates [4], to calculate an expected cumulative total PG level at the time of MRS. The Spearman's rank correlation coefficient for these two parameters was calculated in SPSS (IBM) version 22.

Results:

30 cases with sufficient quality MRS were found. Of these, 8 cases had an observed doublet at 1.1 ppm to which a fit of PG was obtained with a standard deviation < 20%. Little correlation was observed between PG levels observed in MRS and estimated levels of PG from administered doses of phenobarbital and phenytoin, as shown in figure 2. Two cases with relatively high estimated PG levels reveal little or no PG on brain MRS. Similarly most MRS cases with observable PG had almost no expected PG levels. The Spearman rank correlation coefficient was 0.318 ($p=0.087$).

Discussion:

Although the presence of PG in MRS has been described previously, the varying levels of PG observed in MRS have received little attention. The poor correlation between PG levels observed in MRS and expected from drug administration records in these data suggests other factors may influence the levels of PG observed in MRS.

Conclusion:

The presence and intensity of a PG doublet in MRS may not be explained solely by levels of PG administered as part of pharmaceutical preparations. Consequently, further investigations are warranted to establish the reasons for variable PG levels in MRS and any potentially clinical relevant information they may provide.

References:

[1] Cady *et al.* MRM 1994;32(6):764. [2] Wilson *et al.* MRM 2011;65(1):1. [3] Iltis *et al.* MRM 2008;59(3):631. [4] Kulo *et al.* Daru. 2012;20(1):5.

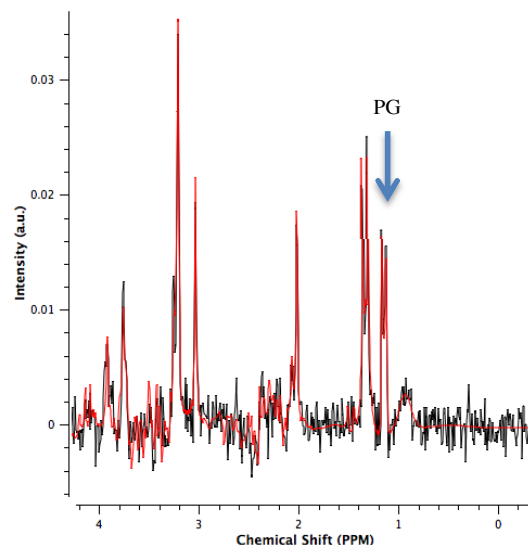


Figure 1. Example of neonatal MRS (red line = model fit) highlighting large doublet at 1.1 ppm attributed to PG

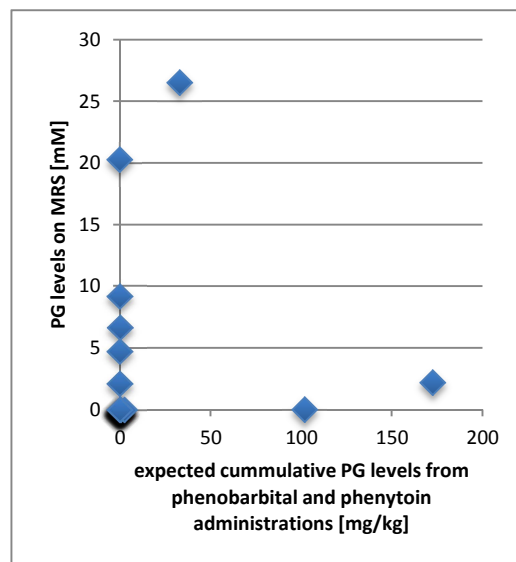


Figure 2. Comparison of expected cumulative PG levels from drug administrations versus PG levels observed on MRS.