Fentanyl for pain management in cancer patients – Population PK design

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Background: Transdermal fentanyl is used to control severe pain in cancer patients. Similarly to other opioids, there is a narrow therapeutic window between pain control and toxicity and a substantial potential for side-effects. Many factors including age, gender, dose, genetic variations, kidney and liver function, and plasma protein binding, influence how opioids are processed by the body. Another important consideration with transdermal fentanyl is that the extent of adhesion of a transdermal patch to a patients’ skin is directly related to the therapeutic efficacy of the medicine. A better understanding of these factors will allow us to improve the way we manage cancer pain with fentanyl.

Aims: To investigate the influence of demographic and clinical factors that have the potential to influence the pharmacokinetics (PK) of transdermal fentanyl and to describe any relationship between saliva and plasma concentrations, patient pain and degree of patch adhesion. This information is crucial in determining whether patients will benefit from individualised dosing regimens.

Methods: Paired saliva and plasma samples of in-patients and out-patients of an oncology/palliative care service are currently being collected for patients receiving fentanyl for cancer pain via a transdermal patch. The team has also validated a tool for scoring the degree of adhesion of fentanyl patches, which is recorded at the time of saliva and blood sampling. Pain scores are also recorded at the time of sampling and over the preceding 24 hours. Pharmacogenetic analysis will include the following SNPs: CYP2B6*6, OPRM1 A118G, ABCB1, ARB2, and DRD2 and any newly-identified gene polymorphisms describing variation in fentanyl/opioid metabolism. NONMEM will be used to obtain estimates of PK parameters and associated intra- and inter-individual variability and to identify factors that influence the PK behaviour of the drug.

Results and Conclusions: A suitable HPLC-MS/MS assay has been developed. Plasma protein binding (PPB) has been investigated, where human serum albumin (ALB) was shown to be the main binding protein and α-1 acid glycoprotein (AAG) showed a relatively small contribution in binding to fentanyl in phosphate buffered saline solution. Total PPB of fentanyl in human plasma was found to be slightly higher (89%) than that reported in the literature (80-85%). No significant binding with nor-fentanyl was observed with any of the plasma proteins. To date, 52 paired plasma and saliva samples from 29 patients have been collected and analysed. Relationships between saliva and plasma concentrations, patient pain and degree of patch adhesion will be presented.

http://www.paganz.org/abstracts/fentanyl-for-pain-management-in-cancer-patients-population-pk-design/