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Assessment of burden of illness due to herpes zoster and predictors of outcomes in Taiwan: a prospective observational study

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Background: Herpes zoster (HZ) is caused by the re-activation of latent varicella-zoster virus and is characterized by unilateral, vesicular cutaneous eruptions. Acute neuritis and post-herpetic neuralgia (PHN) are frequently debilitating, resulting in reduced quality of life (QoL). This study assesses the burden of illness associated with HZ in Taiwan in a real-life clinical setting.

Methods: This was a prospective, observational, single-cohort study. Patients were enrolled at various time points during the course of a zoster episode and were followed for ≤6 months. HZ-associated pain (ZAP) was assessed with the Initial Zoster Impact Questionnaire and the Zoster Brief Pain Inventory. QoL was assessed with the EQ-5D instrument using the Japan preference weights.

Results: The cohort comprised 150 HZ patients with a mean (SD) age of 64.9 (9.2) years and equal gender distribution. At baseline, mean (SD) time since rash onset was 18.8 (78.3) days. At the prodrome phase, a significant proportion (63.9%) of patients experienced a worst pain score of ≥5. ZAP was reported by 147 (98%) patients at baseline. Mean (SD) worst pain score decreased from 6.0 (3.1) at baseline to 2.7 (3.0) at 30 days and 0.3 (0.8) at 180 days. PHN (worst pain ≥3 after ≥90 days since rash onset) was experienced by 28 (18.7%) patients. The mean (SD) EQ-5D score significantly decreased (P<0.001) from 0.91 (0.16) before rash onset to 0.67 (0.18) after rash onset, increasing thereafter, showing significant (P<0.05) QoL deterioration up to 60 days post-rash onset. Acute pain severity (worst pain) and days of pain at rash onset were significant predictors (P<0.001) of poorer QoL at follow-up upon adjusting for QoL before rash onset. Furthermore, acute pain severity and duration interfered significantly (P<0.05) with all EQ-5D health domains –mobility, self-care, usual activities, pain/discomfort, anxiety/depression.

Conclusion: HZ pain can significantly reduce QoL and ability to perform daily activities of people living in Taiwan. Severity and duration of acute pain at rash onset were identified as robust predictors of poor patient QoL. These findings are consistent with observational studies in other countries.

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Xenobiotical virology: novel mechanistic concept of hazardous human viruses upregulation by body burden level of dioxins via AhR-mediated transcriptional pathway

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Background: Earlier we discovered transactivation of the HIV-1 and hepatitis B virus (HBV) in human cells by 30-300 ppt dioxin, a xenobiotic with extremely long serum half-life in humans. Also, upregulation of cytomegalovirus (HCMV) in human cells was shown by 10 ppq dioxin whereas current its background level in general population is ~4 ppt. So, human viruses were suggested novel target genes of cellular dioxin receptor (AhR/Arnt) complex. The complex was known as binding to dioxin-responsive elements (DRE) within mammalian genes, and amount of DREs determine level of target gene activation.

Methods: Productions of infectious HIV-1 in MT4 cells, HCMV in THP-1 cells, and HBV in HepG2 cells were determined using plaque assay. Viral *DNAs were determined* by hybridization and PCR. A computational search for viral DRE was performed by SITECON, a tool for detecting transcription factor binding site alignments/site recognition.

Results: A total of 13 bona fide DRE, all including the substitution intolerant core sequence (5'-GCGTG-3') and SITECON-selected adjacent variable sequences were used here to detect the above properties for the DRE site, and conformational similarity score threshold of 0.95 was utilized to rank identified DRE. It was found that regulatory region of HCMV genes encoding IE gp/UL37 has 5 DRE, 1.65 kb/UL36 – 6 DRE, pp65 – 7 DRE, pp71 – 7 DRE, and pp150 –10 DRE. Wile juxtaposing DRE contents with experimental results, the most susceptible candidate virus to be augmented with body burden dioxin is that one possessing at least similar to HCMV amount of DRE. SITECON recognized several cancer-associated human viruses possessing multiple DREs in their promoters. Thus Epstein-Barr virus (EBV) promoters L1A and L1 each contain 16 DRE, and gene of EBV R1 145K - 11 DRE. Genes encoding some major proteins of herpes simplex virus (HSV) type 1 have from 7 to 8 promoter DRE.

Conclusion: The above support the concept, and provide evidence that sub-nanomolar dioxin is able to activate DRE-containing viruses. Mechanistic data obtained allow searching for inhibitors of viremia and virally-driven malignancies among antagonist ligands of cytosolic Ah receptor, and modifiers of AhR/Arnt complex binding to viral DRE.

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