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Two banned sunscreen ingredients and their impact on human health: A systematic review

Susie Suh, BA, University of California, Irvine; Christine Pham, Janellen Smith, Natasha Atanaskova Mesinkovska

Background: Recent evidence of high systemic absorption of sunscreen ingredients has raised concerns regarding the safety of sunscreen products. Oxybenzone (BP-3) and octinoxate (OMC) are two common sunscreen ingredients, which have recently been banned in Key West and Hawaii due to their toxicity to aquatic species, but whether the systemic absorption of these ingredients poses risks to human health remains unclear.

Methods: We conducted a primary literature search in the PubMed database on February 2019 according to the PRISMA guideline.

Results: 29 studies met the inclusion criteria. Studies showed that elevated systemic levels of BP-3 had no adverse effect on fertility, female reproductive hormone level, adiposity, fetal and neonatal development, child's neurodevelopment and sexual maturation. However, BP-3 impact on the thyroid and male reproductive hormone levels, pubertal development, kidney function, the immune system and the risk of birth defect need further investigations as some evidence exists for an association between systemic BP-3 level and these health outcomes. Two studies on the health impact of the elevated systemic level of OMC demonstrated no clinically significant effects on the level of thyroid and reproductive hormones.

Conclusions: Current evidence is not sufficient to support the causal relationship between the elevated systemic level of BP-3 or OMC and adverse health outcomes. There are either contradictory findings among studies or an insufficient number of studies to corroborate the observed association. To evaluate the long-term risk of exposure to BP-3 and OMC from sunscreen, a longitudinal randomized controlled trial needs to be conducted.

Commercial disclosure: None identified.

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Primary Tumor location predicts survival in melanoma: A retrospective cohort study of 239,257 cases

Jeffrey Rajkumar, BS, Carolina Puyana MSPH, College of Medicine, University of Illinois, Chicago; Maria Tsoukas

Background: The link between primary tumor location and overall survival in melanoma has been studied in the past, but its associated populations and prognostic significance is less understood.

Objective: The purpose of this study is to characterize melanoma demographics and disease specific survival (DSS) in relation to primary tumor site.

Methods: Data from the SEER program was retrospectively analyzed. Patients diagnosed with cutaneous melanoma from the years 1973-2015 were included in the study. Cases were separated into three cohorts based on primary tumor site. The effect of primary location on melanoma survival was evaluated using cox proportional hazards models.

Results: Of the 239,257 subjects included, the majority were male, self-identified as white and of non-Hispanic origin, and married or in a domestic partnership. Tumors were predominantly localized and had a depth of 1 mm. Patients diagnosed with tumors originating in the upper and lower extremities had significantly increased DSS probability compared with those of head and neck. Characteristics including female sex, married or widowed status, treated in the pacific coast, and increasing year of diagnosis were associated with greater DSS. On the contraryConversely, being non-white or of Hispanic origin, increasing age at diagnosis, or tumors with increaseding depth, or nodular or acral melanoma histology were associated with lower DSS.

Conclusions: Primary tumor site is a significant predictive factor for DSS in cutaneous melanoma along with additional characteristics supported in our study.

Commercial disclosure: None identified.

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Systemic therapies for toxic epidermal necrolysis and Stevens-Johnson syndrome: A SCORTEN-based systematic review and meta-analysis

Ignacio Torres Navarro, MD, Dermatology Department, La Fe University Hospital; Álvaro Briz-Redón, Statistics and Operations Research, University of València; Antonio Sahuquillo-Torralba, Juncal Roca-Ginés, MD, Hospital Universitario y Politécnico La Fe Javier Sánchez-Arráez; Rafael Botella-Estrada

The SCORTEN score is a specific predictor of death for patients with Stevens Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN). Despite of the widely-extended use of systemic immunomodulating therapies for SJS/TEN, there is scarce evidence about. Medline, The Cochrane Library, Embase, Scopus, and Web of Knowledge were searched for original studies on the use of SCORTEN (PROSPERO, CRD42019123002). The standardized mortality ratio (SMR), was taken as the measurement of analysis. Random-effects meta-analyses were computed for each treatment (only supportive treatment, corticosteroids, cyclosporine, etanercept, immunoglobulins and combination of corticosteroids and immunoglobulins). Moreover, a multivariate meta-regression analysis was conducted. Finally, a random-effects network meta-analysis was performed. Of 3893 identified studies, fifty-two involving 3614 patients with SJS/TEN were selected. Data of 1827 patients was pooled, results [log(SMR)] for cyclosporine [−0.88 (95% CI −1.47 to −0.29])], etanercept [−0.95 (95% CI [−1.82 to −0.07)], and the combination of immunoglobulins with corticosteroid (−0.56 [95% CI (−0.94 to −0.19)] suggested a reduction of the number of deaths that SCORTEN predicts when using any of them. The meta-regression estimated for the combination of immunoglobulins and corticosteroid and cyclosporine implied a reduction of observed deaths than those expected by SCORTEN. A total of 19 direct comparisons were available for executing the network meta-analysis, which results do not allow us to conclude that any of the treatments presented a significant reduction on log(SMR). Although the suggestion of our results, the systematic use of any active treatment for SJS/TEN cannot be recommended due to the lack of strong evidence. Randomized controlled trials are needed.

Commercial disclosure: None identified.

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Elucidating the role of innate immunity involving interleukin-1 cytokines and inflammasome signaling pathways in the pathogenesis of psoriasis

Sophie Carrie Shan Cai, MD, Kim Robinson, PhD, SIRS, Eugene Sern-Ting Tan, MBBS, Hong Liang Tey, MBBS, FRCP, Bruno Reversade, PhD, National Skin Centre, Singapore; Franklin Zhong, Nanyang Technological University

Interleukin-1 family cytokines, as the central mediators of innate and adaptive immunity, are important in the pathogenesis of psoriasis. The inflammasome is a multiprotein complex that assembles the adaptor protein, apoptosis-associated speck-like protein with caspase activation and recruitment domain (ASC) to activate procaspase-1 to release mature IL-1β. However, the mechanistic steps governing inflammasome activation in keratinocytes in inflammatory conditions have not been studied in detail. Skin biopsies and serum samples were obtained from 6 psoriatic and 6 control patients. Using immunohistochemistry to examine the sub-cellular localization of ASC in psoriatic inflammation, we showed ASC was notably cytoplasmic in psoriatic lesional skin, but nuclear in normal and psoriatic non-lesional skin. This cytoplasmic translocation of ASC was similarly demonstrated in murine skin treated with topical imiquimod to induce psoriasis-like inflammation versus petrolatum-treated murine skin. Furthermore, pro-inflammatory cytokines of TNF-α and IL-17 acted together to directly cause ASC translocation in-vitro using ASC-GFP expressing immortalized keratinocytes and immunofluorescence. ELISA measurements of cytokines revealed a trend towards higher IL-1β within the sera of psoriatic patients and cultured keratinocytes derived from psoriatic lesional skin, compared with healthy controls. In contrast, IL-1α levels tended to be decreased. Our study highlights a link between innate and acquired immunity in plaque psoriasis, where the T_H17-dominant pro-inflammatory milieu may prime the inflammasome complex in lesional keratinocytes—using ASC cytosolic translocation as a novel regulatory mechanism—thereby, triggering the release of IL-1 cytokines, which act synergistically with the T_H17 downstream pathway, to drive psoriasis inflammation.

Commercial disclosure: None identified.