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Effect of Topical Corticosteroids on the Antiviral Inhibitory Activity of Topical (S)-HPMPC in the AD5/NZ Rabbit Ocular Model. YJ Gordon, EG Romanowski, & T Araullo-Cruz, University of Pittsburgh, Pittsburgh PA., USA

The antiviral efficacy of topical (S)-HPMPC against AD5 replication in the NZ rabbit eye has been established (YJ Gordon IOVS 1994, 35:4135-43). In the same model, topical steroids alone were effective anti-inflammatory agents, but significantly prolonged AD5 shedding (EG Romanowski, ARVO '94). This study determined how the addition of topical steroids would affect the anti-adenoviral inhibitory activity of topical (S)-HPMPC. In two experiments (Two-Eye Design), AD5-inoculated rabbits (10^6 PFU/eye) were treated with one of 3 regimens:(Grp I 1% Pred Forte (PF)QID X 14D + 1% (S)-HPMPC BID X 3D); Grp II Comfort Tears QID X 14d + 1% (S)-HPMPC BID X 3D); & Grp III Comfort Tears QID X 14d + Drug Vehicle BID X 3D). All eyes were evaluated for 21 days by serial eye titers, % viral-positive eyes, & duration of AD5 shedding. Compared to control eyes (Grp III), (S)-HPMPC alone (Grp II) demonstrated a significant antiviral effect: (reduced titers P <.01, fewer viral-positive eyes; 36% vs 49%, P<.000001, & fewer shedding days; 6.0 ± 3.7 vs 9.4 ± 3.9, P <.03). However, the addition of 1% PF to (S)-HPMPC (Grp I) nullified the antiviral inhibitory activity:(increased titers P <.01, increased viral-positive eyes 74% vs 36%, P <.000001, & increased number of shedding days 16.1 ± 5.7 vs 6.0 ± 3.7, P <.01). Concurrent therapy of EKC with topical (S)-HPMPC and steroids will not be advised.

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INDUCIBILITY OF SQUAMOUS DIFFERENTIATION BY INTERFERONS DETERMINES ANTIGEN PRESENTATION IN HPV NEGATIVE AND POSITIVE KERATINOCYTES IN VIVO AND IN VITRO. Stephen K. Tyring[1,2], Istvan Arany[1] and Miriam M. Brysk[1,2] [1]Department of Microbiology and Immunology and [2]Department of Dermatology, The University of Texas Medical Branch, Galveston, Texas.

An appropriate antigen presentation by APCs or cells which inducibly express MHC molecules (e.g.keratinocytes) can be greatly influenced by the presence of different endogenous or exogenous factors (viruses, etc.). A number of studies have demonstrated different alterations leading to insufficient immune response in various HPV lesions. The aim of the present study was to investigate the role of HPV infection and expression of different viral genes on the levels of various genes participating in antigen presentation and immune response. Also, we wanted to study the role of this altered antigen presentation in interferon (IFN) resistance. Using reverse-transcription PCR (RT-PCR), mRNA levels of various genes playing a role in antigen presentation, such as HLA-DR, HLA-B7, β2-microglobulin and CD1a (Langerhans cell marker) were determined in condylomas and normal skin biopsies. Also, mRNA levels of different cytokines (GM-CSF, IL-1α, IL-1β, IL-2, IFNγ, IL4, IL5), T-cell markers (CD4, CD8) and viral genes (E7 and L1) were measured by the same method. Our results demonstrate a negative effect of HPV infection on antigen presentation in skin lesions. On the basis of these results we extended our studies to different in vitro cultures of normal skin or oral keratinocytes, immortalized skin keratinocytes, different HPV negative oral squamous carcinoma cell lines and established HPV positive cell lines. Using RT-PCR method, we determined the inducibility of HLA-DR upon IFNγ treatment in these cell lines and correlated the results with changes in WAF-1, p53, RB and K10 mRNA levels caused by IFNγ. These changes showed a positive correlation between K10 inducibility (squamous differentiation marker) and extent of changes in tumor suppressor genes (p53,RB, WAF-1) and antigen presentation (HLA-DR) in which inducibility depends upon the cell type, state of transformation and presence or absence of HPV.