Phytotherapy Research

Study Summary September 2009

Echinacea – a natural anti-inflammatory[1]

Aim of the study

Although the clinical efficacy of Echinacea preparations has been demonstrated in numerous studies[2], many pharmacological aspects relating to the use of this medicinal herb still remain unresolved (e.g. regarding pharmacodynamics or mechanisms of action). An experimental *in vitro* common cold model was used to answer important questions about the natural history of the disease following rhinovirus infection as well as the prophylactic and therapeutic potential of a standardised *Echinacea purpurea* extract.

Researchers involved

Dr. *James B. Hudson* and Dr. *Manju Sharma*, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada.

Plant extract used

A standardised alcoholic extract of the fresh herb (95%) and roots (5%) of the medicinal plant *Echinacea purpurea* (L.) Moench (Echinaforce®, A.Vogel Bioforce AG, Switzerland).

Test material/study procedure

Human epithelial cell lines from the respiratory tract - firstly from bronchial mucosa (BEAS-2B), and secondly from pulmonary alveoli (A549) - were used as the infection model. Contiguous cell monolayers were cultured from these materials in various culture media. The tested viruses comprised two common rhinovirus subtypes (RV1A and RV14). The infections were performed in the plaque assay with increasing virus amounts up to 1 infectious unit per cell. The signal proteins produced by the investigated cell cultures (interleukin-6 and interleukin-8) were measured in an immunological ELISA assay.

Results

Kinetics of proinflammatory cytokine secretion

One-hour rhinovirus exposure and infection of the respiratory tract cells induced a substantial increase in cellular IL-6 and IL-8 4 hours later. Interleukin secretion continued to increase during the further course, reaching a maximum 24–96 hours later and then receding. In non-infected control cultures, either without or with addition of Echinacea, cytokine secretion hardly increased. On simultaneous incubation of the infected airway cells with the Echinacea extract, cytokine release was almost completely reversed regardless of the rhinovirus type.

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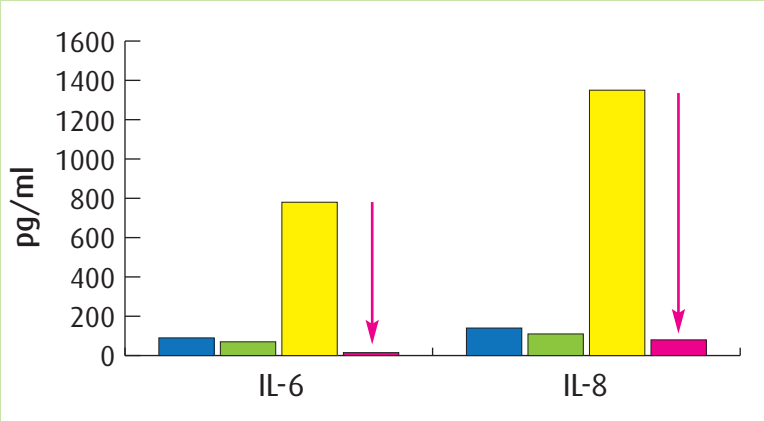
[1] Sharma M, Schoop R, Hudson JB: Echinacea as an antiinflammatory agent: the influence of physiologically relevant parameters. Phytother Res. 2009 Jun;23(6):863-7.
[2] Sha SA, Sander S, White M, Rinaldi M, Coleman C. 2007 Evaluation of Echinacea for the prevention and treatment of the common cold: a meta analyses. Lancet Infect Dis 7 :473-480

The standardised Echinacea plant extract studied corresponds in terms of raw materials used, manufacture and composition to the product Echinaforce® (A.Vogel Bioforce AG, Roggwil, Switzerland).



Normalisation of virus induced cytokine release (interleukin-6, interleukin-8) in human bronchial mucosa cells by Echinacea (after 48 hours).

Time of administration
Virally induced cytokine secretion was also blocked when the Echinacea was added 4, 24 or 48 hours post infectionem (acute use) and Echinacea exposure was continued for 24 hours. If the cells were already incubated with Echinacea 24 hours before the infection (corresponding to prophylactic use), the virally induced increase in cytokine secretion was also absent.

Dose
Cytokine modulation was seen at Echinacea dosages relevant to therapeutic practice (160 µg/ml, equivalent to an extract dilution of 1:100), but also at higher dilutions (up to 1:800). A definite dose-response relationship was observed. None of the Echinacea dosages tested had any adverse effects on the studied cell lines.

Virus concentration
The experimental increase in the virus amount used for infection dose-dependently induced increased secretion of IL-6 and IL-8. In every case, Echinacea reversed these responses and normalised the cytokine secretion to levels resembling those of the non-infected control cells.

Exposure period
The period for which the mucosal cells were exposed to Echinacea in a dilution of 1:100 before washing out from the cell culture was varied from 5 minutes to 48 hours. While a short Echinacea exposure period of 5 minutes did not yet show any definite effects on cytokine release, these effects became increasingly evident from 30 minutes' exposure onwards. The most potent inhibition was seen after 48 hours' exposure.

Conclusion

The results presented show how dramatically the cellular secretion of inflammation promoting cytokines can increase during an infection with rhinoviruses ("cytokine storm"). This in turn, according to our modern understanding, causes typical clinical symptoms with a natural disease history. Not least in infections caused by rhinoviruses which show only limited viral replication and only mild cytopathic effects.

The Echinacea extract (Echinaforce®) studied was able to modulate the virally induced increase in inflammation promoting signal proteins such that the cytokine hypersecretion normalised and decreased to levels resembling those of non-infected cells. Moreover, Echinacea was effective regardless of the time of use. In the clinical context, this means that immunomodulating effects occur both in prophylactic use and in therapeutic administration.
Echinacea exerted with low dilutions already anti-inflammatory effects *in vitro*.