Modulation of Cytokine Synthesis in Human Leukocytes by Individual Components of a Combination Homeopathic Nasal Spray

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Abstract

Using whole blood cultures, the individual components of the antihomotoxic preparation *Euphorbium compositum nasal spray* were studied with regard to their ability to influence responses of human immune-system cells. There was considerable variation in the modifying effects of the different samples on the release of mediators by leukocytes.

From tests performed on the blood of three different donors, it was apparent that pronounced donor-specific modulation was another essential factor influencing the effects of individual test substances. It can be assumed, however, that part of the good clinical efficacy of this combination preparation is based on its components' effects on the immune system.

Introduction

An integral component of treatment with homeopathic medications is the choice of substances individually suited to each patient. This stands in obvious contrast to conventional trends in therapy, which prescribe the same medication for the overwhelming majority of patients with the same basic illness and neglect individual differences among patients with regard to degree of illness or immune status for the sake of simplifying therapy.

In cases of diseases that come about or persist because of dysregulation of the immune system, it is often overlooked that each individual patient's immune system has its own very specific prerequisites that determine not only the degree of success of a particular therapy but probably also what its side effects will be. Allopathic medications that affect the immune system are especially known for undesired side effects. Some examples are methotrexate, glucocorticoids, normally administered in cases of chronic inflammatory illness; and the somewhat gentler anti-inflammatories that suppress specific metabolic processes such as cell division or the formation of mediators such as cytokines or prostaglandins. Because these processes are important in activating immune responses to microorganisms, the danger exists that infections appearing during treatment with such medications can no longer be optimally eliminated by the immune system.

In homeopathic therapy, on the other hand, the therapeutic substance that promises

the greatest results is chosen on the basis of experience. In arriving at this choice, the practitioner considers many different criteria that take the patient's idiosyncrasies into account. Furthermore, the actual quantities of substance administered are small enough that side effects can be avoided to the greatest extent possible.

Methods

The data presented below demonstrate not only that homeopathically potentized substances can have obvious effects on the human immune system but also that by using substances of this sort, important adjustments can be made in action of the medication to adapt it to the individually specific situation of each donor (Tables 1-8). This is also the reason why, in presenting our data, calculating average values for the effects of the test substances on all three subjects would not reflect the reality of the situation. It is more important to determine the specific effect a substance develops in relationship to the immune system of each individual donor. This is the only way in which it is possible to assess the ability of such preparations to adapt to individual needs.

{Captions for Tables 1-8:}
Tab. 1: Mediator synthesis in cultures of whole blood from three different donors, using the test substance *Euphorbium*; the results are expressed as enhancement or inhibition of mediator release as compared to solvent controls (control = 100%).

{The captions of the remaining tables are identical to that of Table 1 with the exception of the name of the test substance. Please make the following substitutions: Tab.2: *Pulsatilla*; Tab. 3: *Mercurius bijodatus*; Tab. 4: *Hepar sulfuris*; Tab. 5: *Luffa operculata*; Tab. 6: *Argentum nitricum*; Tab. 7: *Mucosa nasalis suis*; Tab. 8: *Sinusitis nosode*.}

According to the rules of homeopathy, it should also be expected that dosage-effect relationships do not remain constant within a dilution series, since individual potencies always prove to be especially effective. In this regard, too, our data provide clear indications about the individual test substances. Selecting the exceptionally effective dilution is normally accomplished by administering increasingly high potencies directly to the patient on a trial basis, but procedures such as Voll's electroacupuncture are also available for this purpose.[1]

The human immune system's regulatory network is the most complex feedback system we know of today.[2] The immune system not only mounts adequate defenses against infection-causing germs that appear in great quantity but also recognizes harmful substances that appear in extremely low concentrations and responds to them before illness can come about.

All adaptive processes are based on the ability of different types of immune-system cells to communicate with each other. On the cellular level, this takes place through messenger substances known as mediators (cytokines), of which we now recognize more than a hundred different types. Depending on the composition of the mediator

cocktail in which the cells are constantly swimming, cellular activity can be very finely adapted to actual needs.
Furthermore, the immune system of each individual has its own very personal developmental history, which is determined by the person's genes, eating habits, and psychological constitution, the infections that have appeared in the course of his or her life, and many other factors. For these reasons, we came to the insight that the immune system might be the ideal target structure for determining the effects of homeopathic medications.

In order to assess the variation in immuno-pharmacological effects among different individuals, each substance was tested on the cells of three donors. For purposes of this study, three different cytokines were selected as representative of the many different mediators of the immuno-regulatory network – two stimulant types (interferon gamma: IFN-γ; tumor necrosis factor alpha: TNF-α) and one inhibiting mediator (interleukin 10: IL-10). Because of the type of stimulation that occurs and because of what is known about the origin of mediators, it was possible to make relatively unequivocal statements about which leukocyte types were influenced by the activity of the test substances. Thus IFN-γ, a mediator that activates monocytes and macrophages, comes from T-lymphocytes, while TNF-α, and IL-10 are released primarily by monocytes.

The samples were studied in whole blood cultures. In comparison to standard test systems using isolated leukocytes, this system permits incubation of test substances with target cells in an approximation of *in vivo* conditions.[3, 4] The data presented in Tables 1-8 can be taken as clear indications of the validity of considering individual therapeutic factors in homeopathy. The donor-depended differences in reactions to the test substances also makes it clear why allopathic, highly concentrated medications can again and again provoke isolated and often unexpected side effects.

The values presented in the tables were obtained from so-called „co-stimulated" cultures, which received a preliminary stimulus that imitated the pathophysiological cellular change occurring during inflammatory diseases. The strength of the effects were calculated as percentages of increase or reduction of the release rates for immuno-regulatory factors compared directly to co-stimulated controls, which were incubated with solvent alone. In our experience with the whole blood system, effects differing from the control by more than 20% can be considered true pharmacological effects, while changes of less than 15% must be seen as values falling within the test system's range of biological fluctuation.

Explanation of Results

Even under the restrictive conditions of whole blood culture, the test substances were clearly active enough to permit the assumption that at least part of the observed effects would also come into play *in vivo* (see Tables), even if expectations would have to be reduced with respect to how these effects would develop *in vivo*. Especially with regard to the samples tested here, the probability is relatively high that a significant portion of

their effective principles would also be active *in vivo*, because the homeopathic single remedies in question are administered as a combination remedy in the form of a nasal spray. When such substances are applied directly to the nasal mucosa, where immune-system cells are located only a few layers deep, the medication contacts the immune cells very easily and without any pharmaco-kinetic detours worth mentioning. This is especially true during inflammatory reactions, when the mucosae demonstrate increased permeability.

The complete spectrum of pharmacological activities of the substances investigated here may extend well beyond the parameters tested. Thus, the results presented here clearly show that even homeopathically potentized substances are capable of exerting a variety of effects on immuno-regulatory mechanisms and that the effects are not limited to a single leukocyte type. Both the release of mediators by the antigen-*un*specific part of the immune system (TNF-α, IL-10) and IFN-γ synthesis by antigen-specific lymphocytes are influenced.

Stimulation seems to have a „priming" effect, which means, for example, that the effect of enhancing a cell's release of mediators is such that secretion does not come about immediately, as a direct result of administering the medication, but becomes noticeable only when the cells are subsequently triggered by a relevant pathophysiological stimulus.

Discussion

The results presented here clearly demonstrate the possibility of recording pharmacological effects of homeopathic dilutions in whole blood assay and also clearly show the extent of inter-individual differences in the reactivity of the human immune system, which in turn determine to a significant extent the pathogenesis of many acute and chronic inflammatory diseases. These differences apparently apply not only to immune response to germs but also to how medications take effect. We may speculate that the presence of a number of active ingredients, each in low concentration, is a basic prerequisite for individualizing the expression of effects in human immune systems. If this proves to be the case, then homeopathic and antihomotoxic remedies are certainly exceptionally well suited to correcting immune system dysbalances, because the effects of these substances seem not to be imposed on the leukocytes, as occurs when relatively high doses of glucocorticoids are administered. Instead, these remedies work in ways that offer a spectrum of possibilities from which the immune system selects the ones that apply to the individual's situation.

Although the variability of effects among individual donors makes it difficult to predict *clinical* efficacy, our results clearly demonstrate both the pharmacological potency of these homeopathic preparations and their adaptability to individual immune status.

Inadequate activating processes of the immune system are to be seen not only as consequences of chronic inflammatory diseases but also as important primary and/or secondary *causes* of these syndromes, which are among the most important areas of

applicability for homeopathic therapy. This study has demonstrated the great diversity of immuno-modulatory processes induced by substances in low concentrations; these processes may prove very helpful in correcting immuno-regulatory failures in such diseases, without having to reckon with massive side effects.

The human immune system constitutes an ideal model for investigating the effects of homeopathic and antihomotoxic remedies in the low and middle potency ranges. Furthermore, studies involving whole blood cultures may constitute a valuable complement to classical provings performed on healthy subjects, which were introduced by Hahnemann[5] and can now, following Riley's suggestions,[6] be conducted according to the modern standards of the EU Good Clinical Practice Guidelines.[7]

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Tab 1

Substance: Euphorbium									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Euphorbium D4	47%	50%	13%	5%	3%	-18%	0%	-15%	1%
Euphorbium D6	47%	33%	-52%	3%	4%	-8%	31%	--8%	-8%
Euphorbium D8	7%	34%	-27%	-1%	15%	0%	11%	-13%	-23%

Tab 2

Substance: Pulsatilla									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Pulsatilla D3	0%	-13%	-67%	4%	3%	18%	17%	-25%	-8%
Pulsatilla D8	46%	40%	-15%	4%	4%	-8%	35%	-24%	31%
Pulsatilla C30	8%	15%	-6%	1%	9%	7%	8%	-19%	8%

Tab 3

Substance: Mercurius bijodatus									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Mercurius D5	52%	-7%	-1%	-23%	-6%	-1%	-5%	34%	8%
Mercurius D6	-5%	-50%	-11%	47%	74%	73%	-14%	-3%	-10%
Mercurius D8	0%	-37%	18%	-11%	-6%	2%	-6%	49%	7%

Tab 4

Substance: Hepar sulfuris									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Hepar D6	47%	13%	13%	5%	-11%	-13%	10%	89%	-57%
Hepar D8	20%	-9%	43%	-14%	-1%	3%	-1%	-9%	2%
Hepar D10	32%	8%	34%	1%	-11%	-17%	-13%	98%	-51%

Tab 5

Substance: Luffa operculata									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Luffa D4	-11%	34%	-55%	5%	-8%	14%	27%	3%	29%
Luffa D6	3%	54%	-54%	4%	-6%	-9%	37%	13%	29%
Luffa D8	2%	-28%	-9%	-7%	-16%	3%	25%	-14%	42%

Tab 6

Substance: Argentum nitricum									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Argentum D4	-7%	27%	-46%	-3%	-7%	-8%	23%	38%	9%
Argentum D6	1%	-42%	-36%	-2%	-7%	-14%	17%	41%	1%
Argentum D8	-2%	-57%	-8%	-4%	-1%	10%	50%	21%	4%
Argentum D10	47%	-42%	-51%	5%	-12%	-2%	46%	34%	-12%

Tab 7

Substance: Mucosa nasalis suis									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Mucosa D5	-4%	-20%	-14%	-6%	-7%	28%	32%	11%	10%
Mucosa D6	-12%	-37%	-34%	-19%	-11%	28%	48%	26%	10%
Mucosa D7	-4%	-22%	-30%	-8%	-13%	6%	32%	7%	19%
Mucosa D8	7%	-25%	-2%	-3%	-10%	22%	4%	9%	6%

Tab 8

Substance: Sinusitis Nosode									
Cytokine	IFN-γ			TNF-α			IL-10		
Donator	A	B	C	A	B	C	A	B	C
Sinusitis D4	-4%	-27%	-24%	-3%	6%	2%	65%	41%	0%
Sinusitis D6	10%	-21%	-19%	-10%	-10%	-1%	63%	26%	-10%
Sinusitis D7	-19%	-58%	-21%	0%	-6%	3%	45%	18%	-1%
Sinusitis D8	-3%	-35%	-21%	13%	-2%	-5%	42%	24%	-6%
Sinusitis D13	34%	-14%	-33%	-8%	2%	0%	46%	19%	-4%