

Symptom Picture of Homeopathic Medicine
Aspergillus niger
in Healthy Participants:
A Randomized, Double-blind,
Placebo-controlled Study

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INTRODUCTION

Rationale

The homeopathic drug proving was carried out according to the directives as they are laid down in the consensus HDP of the German central association of homeopathic doctors (DZVHÄ) as well as in the Homeopathic Drug Proving Guidelines by the European Committee for Homeopathy (ECH) (see References).

The HDP is based on the Guidelines for Good Clinical Practice (GCP) which are described in the documents by the International Conference on Harmonization (ICH) and the European Central Council of Homeopaths (ECCH Guidelines for Homeopathic Proving).

The Study Protocol was approved by the Ethics Committee in St. Petersburg on February 24, 2014.

Objective of the study

The objective of the study is to record all physical and psychological reactions (symptoms) of healthy participants induced by the use of the homeopathic medicine *Aspergillus niger* and a placebo, and to compare them with their baseline picture reaction pattern as well as their symptoms recollected from the period before the baseline recording of symptoms.

Sponsor, principal investigator

Sponsor:

Pharmaceutical Manufacturing Company SANUM-Kehlbeck GmbH & Co. KG,
Hoya, Germany

Principal Investigator:

Rolik, I., MD, PhD, professor
Institute of Regenerative Medicine of the Russian Academy of Natural Sciences,
Moscow, Russia

METHODS

Blinding

The trial was double-blind, randomized, and placebo-controlled.

The principal investigator, the research physician and study coordinator as well as the study supervisors were blinded. The only non-blinded investigator was the independent research physician.

Recruitment of participants

During the trial 12 voluntary persons took part as participants. Two of the 12 volunteers received a placebo. The principal investigator, study coordinator and study supervisors did not know which substance was applied to which participant.

All symptoms were described by the provers in their own words. At the beginning of the proving, the participants were thoroughly advised by the study coordinator to pay close attention to each occurring symptom during the drug trial to avoid any kind of negligence in this regard. The participants described the occurring symptoms in writing at the moment of the manifestation. Besides, the principal investigator and the study coordinator determined the modalities of the appearing symptoms, which also reflect in the trial documents.

The test persons were unaware of the substances and of the sample number of the substances applied to them. Only the independent research physician had this information.

Inclusion criteria

- Age of participants: 18 to 70 years

All persons were advised of the diary keeping in all phases of the homoeopathic drug proving.

Exclusion criteria

- General mental-emotional disorders;
- Planned allopathic medical treatment;
- Allopathic medicine;
- Pregnancy or lactation;
- Drug addiction;
- Participation in another trial within 3 months prior to the study.

PHASES OF THE TRIAL

The homeopathic drug proving was divided into the following phases:

Run-in period:

Preliminary observation during one week prior to the proving.

Immediately before the beginning of the proving a special telephone line was installed to ensure that the study coordinator and the study supervisors were accessible to all participants day and night.

Before the trial all participants were examined clinically by the research physician. Additionally they were questioned according to the "head-to-toe-scheme" by the independent research physician, an experienced homeopathic professional, to establish the baseline picture reaction patterns of the provers.

All applicants were admitted to the proving, as they did not have any severe physical or psychic symptoms, did not need any medical assistance, were under no medical treatment before or during the trial, took no allopathic or homeopathic drugs.

Each participant signed the consent form of the voluntary participation in the trial after detailed instruction by the study coordinator with regard to the realization and the conditions of the proving.

Test period phase 1

Day of application of the homeopathic remedy and the day after.

All participants had sufficient homeopathic experiences to properly judge the occurrence of symptoms during the trial.

Test period phase 2 (until 6 weeks after start of the HDP)

The completion of the diaries and the description of the occurring symptoms were carried out by the provers personally.

Observation time during week 1 after application: daily contact 1-2 hours.

Observation time during weeks 2 and 3 after application: three times a week or more.

Observation time during weeks 4-6 after application: 1-2 times a week.

Follow-up (3 months after start of the HDP)

After the end of the trial, the study coordinator and the study supervisors discussed the symptomatology with the participants either in a personal meeting, by telephone or by e-mail. As a result, specifications of the symptomatology were stipulated with approval of the participants. All anamneses, introspection protocols, and exam protocols are in the care of the sponsor, Sanum-Kehlbeck GmbH & Co. KG, and can be viewed upon request.

No rejections and adverse reactions were observed in the course of the trial and none of the provers discontinued the test.

INTERVENTION

Homeopathic medicine

This proving substance has not been subject to any proving before.

The proving substances were produced and packed, according to GMP and GCP requirements, by the sponsor.

Placebo

The placebo, which was also manufactured and packed by the sponsor, did not differ from the proving substance in smell, color or viscosity.

Dosage

Dosage form and potency of the homeopathic substance for proving:

Globuli C12. 9 globuli, every 2 hours, up to 6 times per day, oral application.

No further application after appearance of the first symptoms.

30 minutes prior and after application: No smoking, no eating, no drinking, no conventional toothpaste.

RESULTS

Symptom list

The symptoms of the HDP in the "head-to-toe-scheme"

Mental/Emotional:

Hypersensitivity, wanted to cry while watching a movie. Mental activity during the day when remedy was taken. Anxiety at night next day after taking. Feeling of helplessness after first taking. Weakness from mental exertion. Feel more impressionable. Desire to be useful. Desire for fast driving. Feeling affectionate. Feel offended easily. Woke up at night with feeling of despair. Feeling of melancholy. Increased irritability. Fear of death. Doubtfulness. Feel serenity at the day of taking. After third taking everything seemed strange in a minute. Sensitive to reproaches. Wish to jesting. Woke up in the morning in euphoria. Emotions excited easily. Lowered mental energy. Causeless anxiety. Apprehension of insanity.

Head:

Tingling in the head at morning. Heaviness in the head. Pulsating in the forehead. Numbness of the left temple. Tension in the right side. Sense of lightness in occiput. Headache in rainy weather. Hair painful when touch. Headache from eyes moving. Headache after taking coffee. Headache after smoking. Headache before menses.

Sleep:

Moaning during sleep. Restless sleep after midnight. Sleeplessness. Feeling more easy to fall asleep. Feeling sleepy at the next day. Interrupted sleep with vivid dreams. Difficult waking at the next morning. Feel energy and freshness after sleep. Too late falling asleep. Shallow sleep, wakening with anxiety. Nightmares with perspiration.

Vertigo:

Feeling unsteady. Vertigo on rising. Dizziness on looking upwards. Sudden fear and vertigo when driving. Vertigo with sensation of heat in the body. Feel like swinging on closing eyes. Dizziness in the dark. Vertigo when look on moving things. Feel vertigo from noise on the street at the evening.

Eye:

Slight pain in the eyes after waking. Burning in the eyes after driving. Itching in the eyes the next morning after taking. Twitching of the right eye. Feeling exertion in the eyes. Swollen eyelids. Irritation from light. Lachrymation. Tired sensation in the eyes after working.

Nose:

Nasal discharge. Nasal congestion on waking. Feeling smells less. Increased sensitivity to cold air. Feel dryness inside nose. Sneezing after first taking.

Ear:

Pain in the right ear during cough. Ears more sensitive to cold. Feeling of congestion during swallowing. Sensitivity to loud sounds. Itching in the left ear. Feeling formication behind the ears. Numbness of the earlobes. Tingling in the right ear on turning head. Feeling pulsation in the left ear on waking. Lowered hearing during the next day.

Face:

Dryness of the lips. Greasy skin of the face on the next day. Slight eruption on the cheeks. Acne appeared in the forehead. Feeling that face skin got rough. Itching in the forehead. Desquamation of skin in the chin region.

Mouth:

Sensitiveness of gums. Burning sensation in the tongue. Feel dryness of palate. Unpleasant taste in mouth after meal. Bitter taste in the mouth after waking. Bitter taste in the mouth after meal. Dryness and bitter taste in the mouth at night. Acid taste in the mouth after meal. Increased salivation before meal.

Teeth:

Slight toothache after third taking. Increased sensitivity to cold and acid food. High sensitivity of teeth during brushing.

Throat:

Dryness in the throat causing cough. Throat more sensitive to cold air. Collar causes discomfort. Light pain in the throat at morning. Sensation of sore throat during the night. Pain in the throat on swallowing. Feeling that clothes are strangling. Slight pain in the throat on inspiration, during some minutes. Pain in the throat on coughing. Difficult swallowing and dryness in the throat at night. Feeling lump in the throat.

Larynx and trachea:

Pain behind breastbone on coughing. Feeling that voice got rough at the next morning. Weakened voice on cold air. Feeling of hoarseness during some minutes after first taking. Tiredness of voice comes quickly on talking. Nasal tone of voice. Hoarseness in the evening. Feeling that voice breaks when worried. Barking cough at night. Feeling tension and numbness in the larynx.

Stomach and intestines:

Sensation of heat in the upper abdomen after dinner. Eructation after first taking. Increased flatulence at night. Heaviness in the stomach afternoon. Increased appetite on the next morning. Rumbling in the stomach before breakfast. Lowered appetite on the next day. Unclear abdominal pain after breakfast. Slight pain in the right side of the abdomen after lunch. Feeling thirst during next night. Flushes of heat in the stomach after meal. Heartburn after drinking cold water.

Rectum / Stool:

Feeling itching in the rectum after third taking. Increased flatulence during stool. Slight diarrhea at the next morning. Constipation during next two days. Anal burning after stool.

Female genitals:

The feeling of heat in the genital area. Menstruation began three days earlier. Did not want sexual contact with husband. Sudden urge to urinate. It seemed that the orgasm was more vivid. Back pain in the middle of the menstrual cycle. Slight numbness and coldness in the genital area. Unusual pain in the lower abdomen during menstruation. Suddenly felt sexual arousal. Pain in the right inguinal area in the evening. There were all sorts of depraved thoughts. A tugging feeling in the right lower abdomen. Menstruation began two days later than usual.

Male genitals/ Sexual potency:

As if an erection has become weak. Pulling sensation in right testicle. Suddenly felt sexual arousal. Aching pain in the left groin. Noticed some decrease in libido. The feeling of heat in the genital area. A small difficulty urinating. It seemed that the orgasm was more vivid. Aching pain in the testes. Obscene thoughts come to mind. Slight numbness and coldness in the genital area. Noted improved erection.

Chest / Mammary:

Shortness of breath when going outside. Feeling that the breasts are swollen. The feeling of shortness of breath and anxiety with large crowds of people on the subway. Intermittent shooting pain in chest when tilted. The feeling of lack of air when excited. Short-term pain in the breast. Woke up with a sense of fear and lack of air.

Back/ Backbone:

Tension and stiffness between the shoulder blades. In the morning increased crunch in the neck. Heaviness and tension in the lower back. For a moment it seemed that the neck feels nothing. Quivering in cervical region. Tension and slight pain in lower back at the evening. Numbness and stiffness in lower back after waking. Feeling of crunch and light pain in dorsal region. Sensation of

trembling between shoulder blades on anxiety. Lower back pain after sleeping on hard bed.

Extremities:

Crunch in the right shoulder joint on movements. The feeling of vibration in the arms in the evening when tired. Legs and arms heavy, as if paralyzed. Moderate pain and crunching in the knees. The evening after the working day tingling in the legs. Stiffness and crunching in the joints of the hands in the morning. Feeling of stiffness and numbness in shoulders. Shooting pain along the right arm with a sharp turn of the head. Lightness in the legs like can fly. Sensation of restless legs in the night. Pain and stiffness in the left elbow. Slight pain in the right hip joint. Feeling of numbness and tingling in the feet.

Skin:

Redness of the skin in a stuffy room. Skin like someone else's, not mine. Sensation that skin on the feet is chapping. Increased sensitivity of the skin of the scalp. Skin is very sensitive to the cold air. Irritation and redness of the skin from cold water. Light dryness and burning of skin after hot shower. Feeling that skin peels off. Itching of the skin between the shoulder blades in the night. Redness of the skin on the open air.

Cold / Fever:

Sweating in the night and woke up with anxiety. As if the whole body became numb and cold. Perspiration with nausea and languor while awaking. Heat and sweat at first day of menses. Increased perspiration on exertion. Intermittent chill the next morning after waking up. Feeling heat with chillness before menses. Coldness in general during emotional stress. Sudden chill at night followed by sweat. Heat of the whole body after breakfast. Weakness and perspiration after waking. Increased perspiration during anxiety. Short-time coldness with shivering after cough.

General symptoms:

Suddenly it seemed that all colors become brighter. Suddenly felt sorry for myself. While riding in the car suddenly lost orientation. Feel unconcern about past. Had a dream that drowns and suffocates. Suddenly felt lightness in the whole body. The whole evening felt sorrow remembering the dead parents. Sensation of carelessness about future. All the smells became sharper for a few minutes. The mood changed frequently throughout the day. Wanted to cry when remembered the first love.

Table 1.***Evaluation of symptoms***

Attribute	Globuli C12 (<i>Aspergillus niger</i>)	Placebo
No. of provers	10	2
Gender ratio	7F/3M	1F/1M
Age (years)	21-65	30-48
Average age	43.6	39.0
Total of symptoms	211	19
Average symptoms per prover	21.1	9.5

Table 2.**Allocation of the symptoms (number, %):**

Region	Number of symptoms	
	Globuli C12 (<i>Aspergillus niger</i>)	Placebo
Mental/Emotional	26 (12.3 %)	1 (5.3 %)
Head	12 (5.7 %)	1 (5.3 %)
Sleep	10 (4.7 %)	1 (5.3 %)
Vertigo	9 (4.3 %)	-
Eye	7 (3.3 %)	1 (5.3 %)
Nose	6 (2.8 %)	1 (5.3 %)
Ear	9 (4.3 %)	1 (5.3 %)
Face	6 (2.8 %)	1 (5.3 %)
Mouth	8 (3.4 %)	1 (5.3 %)
Teeth	2 (0.9 %)	1 (5.3 %)
Throat	11 (5.2 %)	1 (5.3 %)
Larynx/Trachea	9 (4.3 %)	-
Stomach/Intestines	10 (4.7 %)	2 (10.5 %)
Rectum/Stool	4 (1.9 %)	1 (5.3 %)
Female genitals	12 (5.7 %)	1 (5.3 %)
Male genitals/Sex. Potency	12 (5.7 %)	-
Chest/Mammae	6 (2.8 %)	1 (5.3 %)
Back/Backbone	8 (3.4 %)	1 (5.3 %)
Extremities	13 (6.2 %)	-
Skin	9 (4.3 %)	1 (5.3 %)
Cold/Fever	13 (6.2 %)	-
General symptoms	9 (4.3 %)	2 (10.5 %)
Total (100 %)	211	19

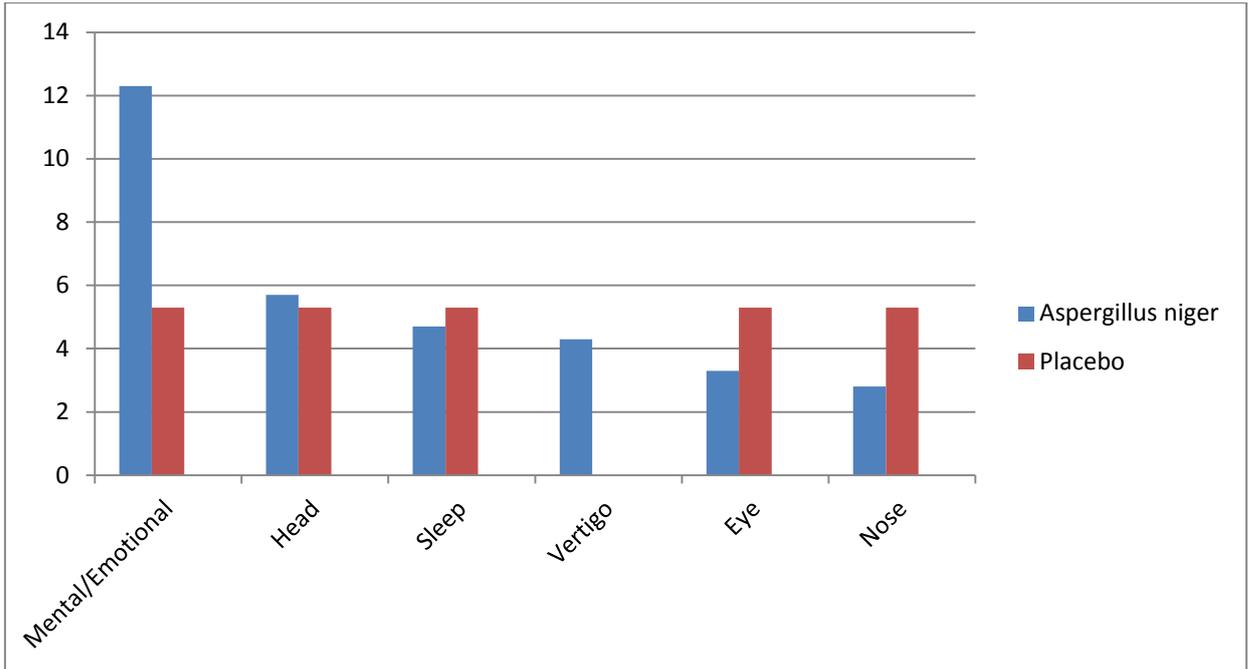


Figure 1. Occurrence of symptoms (%) in regions.

1 – Mental/Emotional;

2 – Head;

3 – Sleep;

4 – Vertigo;

5 – Eye;

6 – Nose.

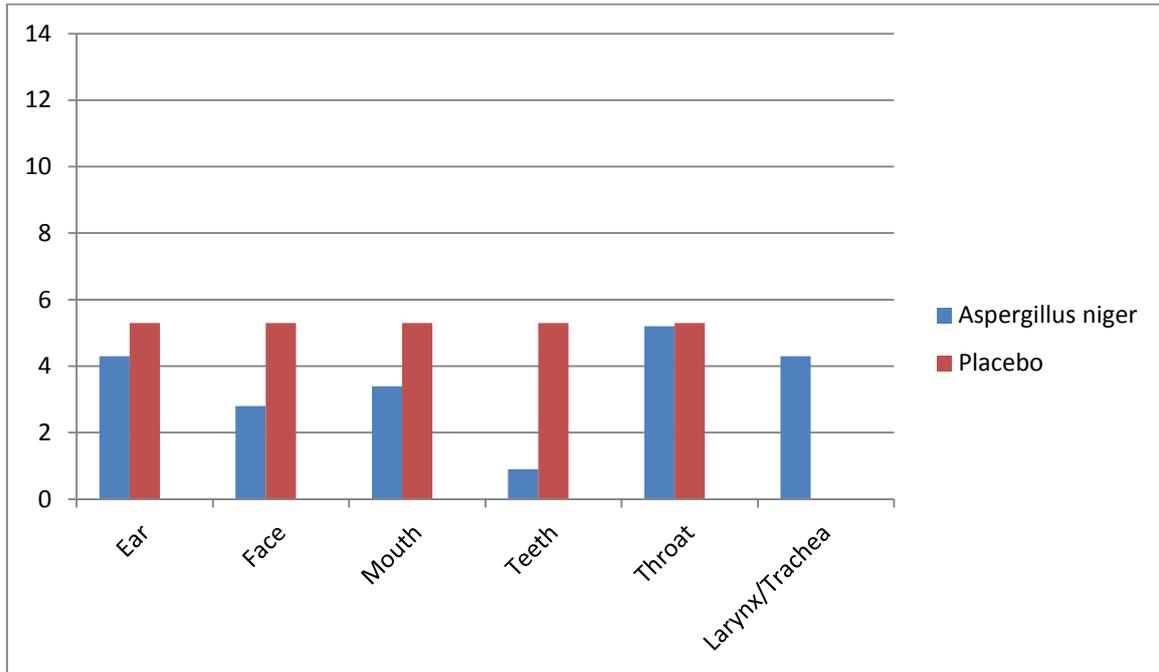


Figure 2. Occurrence of symptoms (%) in regions.

7 – Ear;

8 – Face;

9 – Mouth;

10 – Teeth;

11 – Throat;

12 – Larynx and Trachea.

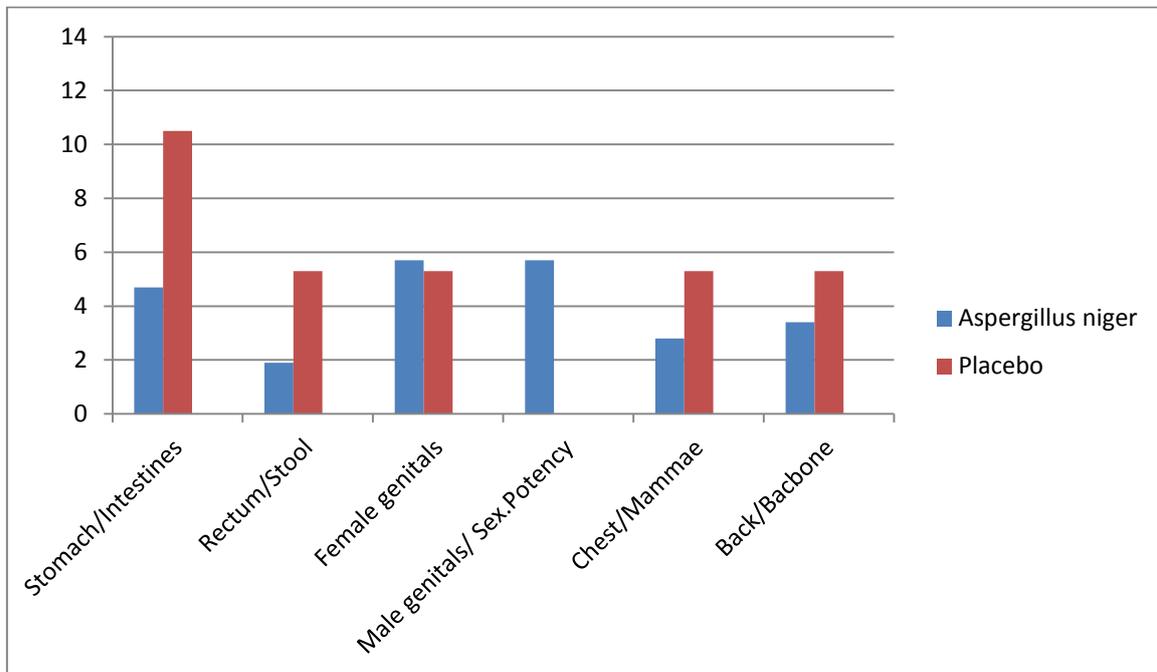


Figure 3. Occurrence of symptoms (%) in regions.

- 13 – Stomach and Intestines;
- 14 – Rectum/Stool;
- 15 – Female genitals;
- 16 – Male genitals / Sex. Potency;
- 17 – Chest and Mammae;
- 18 – Back and Backbone.

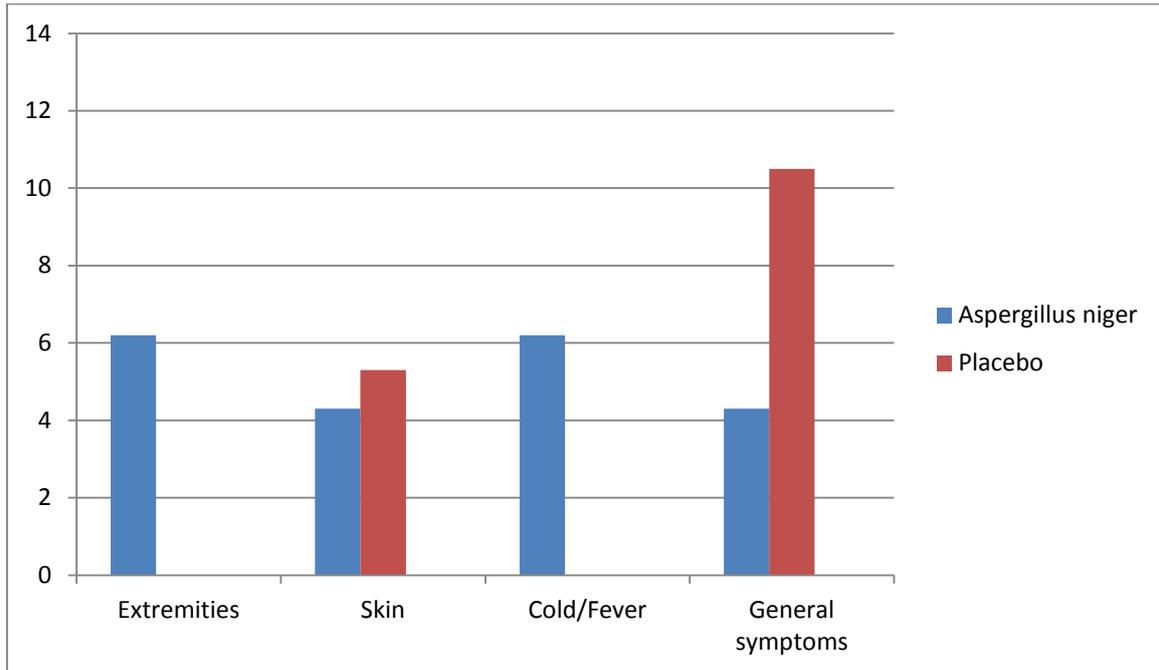


Figure 4. Occurrence of symptoms (%) in regions.

19 – Extremities;

20 – Skin;

21 – Cold/Fever;

22 – General symptoms.

SUMMARY

This report presents the results of the proving of the homoeopathic medicine *Aspergillus niger* with the participation of 12 volunteers, two of whom received a placebo. The study provided some data characterizing the homoeopathic picture of this substance.

Many symptoms concerning different organs and body systems were observed in the process of careful questioning, observation and examination of the provers. Observed symptoms and manifestations were unusual patterns of reactions for them. At first glance some symptoms may be considered quite nonspecific. Manifestations matching with those ones from the placebo group were excluded after the final analysis.

In the analysis according to the "head-to-toe-scheme" frequent manifestations concerning mental/emotional (12.3 %), respiratory (12.3 %) and reproductive systems (11.4 %) were observed. Also symptoms concerning backbone and extremities were frequent (9.6 %).

DISCUSSION

Describing the homeopathic picture of the drug it is common to use the traditional "Head-to-toe" scheme. According to this scheme some symptoms were observed not so often.

But some manifestations concerning different regions (head, vertigo, larynx/trachea, stomach/intestines, rectum/stool, chest/mammae, back/backbone, cold/fever, general symptoms, skin) resembled phenomena of autonomic nervous system imbalance.

These vegetative dysfunction symptoms distinctively often combined with manifestations concerning mental/emotional sphere and reproductive systems. For now we know enough about unity of nervous and endocrine regulations of the body.

The role of stress factors in the genesis of endocrine disorders is also well known. Symptoms of disorders are often nonspecific and difficult to interpret in this challenging regulating region.

Of course, it is difficult to identify the symptoms of influence on the endocrine glands in healthy volunteers using the "testing" dosage form of the homeopathic substance C12.

However indirectly, the frequent symptoms concerning genitals (because generally these symptoms manifest in the clearest way) confirm this influence. So it is possible to assume that this drug influences on the nervous system and endocrine regulation, because the combination of these groups of symptoms was frequently observed among provers.

The manifestations concerning the respiratory system also are frequently reminiscent of the autonomic nervous system imbalance. This is understandable because respiratory disorders are closely connected with the emotional sphere (fear, anxiety). In this case the high frequency of respiratory symptoms may speak of a principle of similarity. It is well known that human aspergillosis is mainly striking in the lungs, especially in conditions of immunodeficiency.

Also it should be noted that the symptoms concerning head, vertigo, extremities regions can be regarded as cardiovascular and neurological. But these symptoms are almost always combined with the manifestations of the backbone and

extremities. Therefore, it is more likely that the drug influences exactly on the musculoskeletal system.

In general this combination of symptoms of the musculoskeletal system and neuro-endocrine regulation suggest the drug influence on the structural and organizational sphere of the body.

GENERAL REMARKS

The occurring symptoms were slight and all symptoms were reversible and decreased within 24 hours. All manifestations disappeared in the period from 1 to 7 days.

No severe adverse reactions were observed during the study, no intercurrent diseases were diagnosed.

None of the participants discontinued the trial after accepting the consent form of participation and nobody was excluded.

Within 4 weeks after the study, there were no symptoms that could be associated with the application of the study remedy.

QUALITIES

Thus, on the basis of these findings it is possible to specify the following directions of *Aspergillus niger e volumine cellulae (lyophil., steril.)* C12 action:

- Disorders of the autonomic nervous system and neurological abnormalities in the area of mental-emotional sphere;
- Pathology of the endocrine system, especially reproductive system;
- Pathology of the respiratory tract;
- Problems of musculoskeletal system, mostly degenerative-dystrophic by nature.

INFORMATION ON THE INVESTIGATIONAL MEDICINAL PRODUCT (IMP)

Proving substance

Aspergillus niger e volumine cellulae (lyophil. steril.) C12, globuli
[HAB methods 5a, 6, 10]

Starting culture

Aspergillus niger DSM 6563

Raw material and production

Biotechnological biomass production, separation from culture medium, cell mill treatment and further special manufacturing steps according to the master file of Sanum-Kehlbeck.

Homeopathic starting material

Aspergillus niger e volumine cellulae (lyophil. steril.), synonym Aspergillus niger e volumine mycelii (lyophil. steril.), as used for dilutions and triturations to produce several dosage forms of the Nigersan® line (Sanum-Kehlbeck).

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