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Placebo: Therapy at its Best?

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Abstract

Despite much scientific evidence of the effectiveness of placebo therapy, it is still insufficiently introduced into routine medical practice. In Western countries, there is constant discussion in the mass media and in politics about banning homeopathic treatments, which have been condemned as placebo. However, there are a number of

known oaths and declarations by physicians that harming a patient's health is unethical. What are known side effects of chemical remedies other? In truth, the use of placebo's could be the basis of medical healing art. The death of patients by relentless use of harsh chemical agents could be avoided.

Keywords: Placebo Effect, Medical Side Effects, Medical Healing Art, Gentle Therapy

Introduction

Placebo's do not have a good image. They are generally regarded as ineffective and useless. They are used in randomized, placebo-controlled, double-blind studies - the pinnacle of pharmaceutical science - to assess the effect of the drug under test. The assumption is that there is no effect in the placebo group and that no effect can be detectable in the placebo group. A significant difference between the verum and the placebo group is then considered as proof that the agent under test is effective. Can we therefore assume that placebo drugs (such as capsules without active substance) are indeed ineffective? On the other hand do drugs with chemical active substances have to show side effects? Is it possible that there are no main effects without side effects?

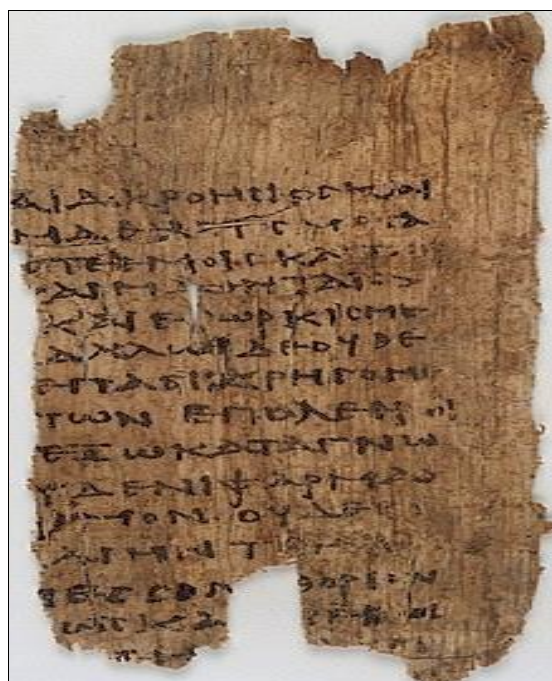


Fig 1: Fragment of the Hippocratic oath, Papyrus Oxyrhynchus XXXI 2547, 3rd century

Hippocrates

Let us go back to Hippocrates (Fig.1) ^[1]. His short, summarizing sentence "Primum nihil nocere" is famous. Primum non nocere, primum nihil nocere and primum nil nocere (Latin, German 'first do no harm'; ancient Greek μή βλάπτειν mē blaptain, English 'do no harm'), is a principle that the Hippocratic tradition places at the center of its notion of morally required medical action. The quote reads in full "primum non nocere, secundum cavere, tertium sanare" (English: "first do no harm, second be careful, third heal").

Does this still apply today? Like other contents of Hippocrates' oath ^[2], this has been forgotten. No future doctor still swears.

Therefore, no doctor who takes the oath seriously should perform an abortion. Because also becoming life is life, and a killing is the largest possible damage which can be caused to a patient - even if not yet visible in the outside.

The so-called Oath of Hippocrates (or Hippocratic Oath, also Oath of Hippocrates), named after the Greek physician Hippocrates of Kos (c. 460 to 370 BC), is a physician's vow originally written in Greek and is considered the first fundamental formulation of medical ethics. However, the authorship of the oath is unclear. First attested in the 1st century under the Latin title Iusiurandum, ^[1] the code of duties was handed down as part of the Corpus Hippocraticum, a collection of medical texts, as Ὁρκός (Horkos, "oath"), and assigned to Hippocrates.

Nuremberg Medical Trial

Another subject that is affected by the "do not harm" is eugenics ^[3, 4], which is unfortunately no longer frowned upon today, possibly combined with euthanasia. In the war crimes tribunal 1946/1947 in Nuremberg it was expressly forbidden. The Nuremberg medical trial led to a return from a collective to an individual medical ethic ^[5]. Typical components of the collectivist medicine of National Socialism, such as Nazi racial hygiene, were at best touched upon in the margins of the trial. The verdict established a framework for future medical (and psychological) human experimentation that is still valid today as the Nuremberg Code ^[6, 7].

In 1996, the IPPNW (International Physicians for the Prevention of Nuclear War/Physicians in Social Responsibility) organized an international conference on the 50th anniversary of the Nuremberg Medical Trial, with a congress volume entitled Medicine and Conscience. On the basis of the results of this congress, it decided to reaffirm the Nuremberg Code in a renewed form (Nuremberg Code 1997). Important points of the Nuremberg Code (Opinion of the I American Military Tribunal on "Permissible Medical Experiments") are:

«The voluntary consent of the subject is essential. This means that the subject must be capable, in the legal sense, of giving consent; that he must be able, uninfluenced by force, fraud, deception, coercion, pretense, or any other form of restraint or coercion, to exercise his freedom of choice; that he must have sufficient knowledge and understanding of the field in question, in its details, to be able to make an understanding and informed decision.

This last condition makes it necessary that, before consent is obtained, the subject be made aware of the

nature, length, and purpose of the experiment; the method and means to be employed; all inconveniences and dangers which may reasonably be anticipated; and the consequences to his or her health or person which may result from participation. The duty and responsibility to determine the value of consent is incumbent upon anyone who orders, directs or conducts the experiment. This is a personal duty and responsibility that cannot be passed on to others with impunity.

The experiment shall be conducted in such a manner as to avoid all unnecessary physical and mental suffering and injury.

No experiment may be conducted if it can be reasonably assumed from the outset that it will result in death or permanent harm, except at most those experiments in which the experimenter also serves as the subject.»

Declaration of Geneva

The Nuremberg Code was followed by the Declaration of Geneva in 1948 ^[8]. The Geneva Declaration, authorized by the World Medical Association, as adopted by the 68th General Assembly of the World Medical Association in Chicago, United States of America in October 2017, reads as follows:

«The Physician's Pledge: As a member of the medical profession I solemnly vow to devote my life to the service of humanity. The health and welfare of my patient will be my primary concern.

I will respect the autonomy and dignity of my patient.

I will maintain the highest respect for human life.

I will not allow considerations of age, illness or disability, creed, ethnicity, gender, nationality, political affiliation, race, sexual orientation, social status, or any other factor to come between my duties and my patient.

I will maintain the secrets entrusted to me even after the death of the patient.

I will practice my profession to the best of my ability, with dignity and in accordance with good medical practice.

I will promote the honor and noble traditions of the medical profession.

I will show due respect and gratitude to my teachers, my colleagues, and my students.

I will share my medical knowledge for the benefit of the patient and for the improvement of health care.

I will take care of my own health, well-being, and abilities to provide the highest level of care.

I will not, even under threat, use my medical knowledge to violate human rights and civil liberties.

I do so solemnly, freely and on my honor.»

Medical Ethics

What conclusions can be drawn from all these vows and declarations? Is it therefore at all ethically acceptable for a doctor to use drugs that are known to have - possibly considerable - side effects? Is it acceptable for a physician to use drugs that achieve their main goal only inadequately or not at all? Is it acceptable when a doctor feels compelled - since this is the only thing the health insurance companies pay for - to use strongly effective chemical agents, although

there are gentle, herbal or orthomolecular agents that can achieve the goal of the therapy without side effects?

One example: until about 1970, the herbal cardiac remedy strophanthin (ouabain, a substance produced by the heart) was commonly used for heart failure. Since it was no longer profitable, the drug was banned and the glycoside digitalis (as digoxin, digitoxin, acetyl-digoxin, etc.) was introduced as the standard in cardiac therapy. One difference was that strophanthin is nontoxic and there is no poisoning, whereas digitalis is toxic in overdose. There have been many digitalis deaths. Nevertheless, it was used until the patents expired. Many cardiologists claim to this day that strophanthin is ineffective.

Placebo

Now we come to the gentlest treatment method of all, the placebo (fig. 2) [9]. Placebo effects are all positive psychological and physical reactions that are not due to the specific efficacy of a treatment but to the psychological, spiritual, and psychosocial context of the treatment. The placebo effect does not work for every patient. According to Beecher [9], 35% of people respond to the effect of a placebo treatment. Personality plays less of a role, but rather psychological factors that cause somatic changes. Placebo effects can be triggered by eliciting expectancies or by a conditioned stimulus. The triggered neuronal activations in the brain can influence the metabolism and thus cause physical reactions.

Individual conditioning

Classical conditioning is a response to a stimulus that is usually learned unconsciously, whereby this factor decisively influences the effect of placebos without the subject's knowledge.

Amanzio and Benedetti [10] were able to demonstrate in detail in a complex series of experiments that a pain-reducing placebo effect can be triggered by both cognitively induced expectancy and classical conditioning.

Classical conditioning states that a new conditioned reflex can be added to the natural, usually innate, reflex. Given an unconditioned stimulus (US), which triggers an unconditioned response (UR) as a reflex. If a previously neutral stimulus (NS) is presented several times before the US, the latter becomes a conditioned stimulus (CS). It now also elicits a reflex response (the conditioned response CR), which is usually very similar to the unconditioned response UR.

Placebo conditioning was demonstrated in animal experiments by Manfred Schedlowski in rats [11]. For this purpose, heart transplanted rats received in the first step a sweetener solution (saccharin) in combination with the drug cyclosporin A, which has an immunosuppressive effect. A control group received the drug in combination with normal water, which has no conditioning effect on the rats. Three days after surgery, the drug was discontinued. However, the effect persisted in the conditioned rats.

According to a recent study, these results are also applicable to humans [12]. In this study, the rats' saccharin was replaced with a green drink with a lavender scent and strawberry flavor. In a double-blind placebo-controlled study design, subjects were given the immunosuppressant cyclosporine A along with this drink during the first week of the trial. In the second week of the trial, the drink was administered along with placebo capsules. A markedly suppressed synthesis of

the relevant cytokines, interleukin-2 and interferon, was observed, similar to the specific cyclosporine A effect.

British rheumatologists analyzed 198 placebo-controlled trials involving osteoarthritis patients. Fourteen of these studies had an untreated control group. This allowed a meta-analytic comparison between placebo and non-treated patients, which in turn allowed conclusions to be drawn about the effect size of placebo [14]. The analyses show that placebo not only reduces pain, but also reduces self-perceived joint stiffness. The effects are both statistically significant and clinically relevant. The placebo effect was particularly evident when placebo therapy was administered by injections or acupuncture needles rather than oral medication [13,14].



Fig 2: Page from the Très Riches Heures for the Prayer for the Dead. Inscription in picture frame: Placebo, then follows verse 1 from Psalm 116

Placebo effects are all positive psychological and physical reactions that are not due to the specific efficacy of a treatment but to the psychosocial context of the treatment. Relative to the dangers, side effects and possible ineffectiveness of drug treatment, placebo's are thus an alternative worth discussing. They work together with the regulation and self-healing mechanisms and abilities of the patient. They stimulate these and do not suppress or manipulate. Thus they correspond to the ethical standards of all declarations and vows. They do not correspond to a material but to an information therapy of psycho-neuro-endocrino-immunology. Thus, in principle, they are the highest possible standard of a medical healing art. Their rejection is not acceptable.

Conclusions

The placebo effect has been known since the beginning of human medicine. In ancient times it was regularly used, e.g. in the healing temples of the physician god Asclepius. Remedies with known side effects were avoided. Today we have a completely different situation: the standard therapies contain far predominantly substances with side effects. When a patient asks a conventional doctor about a gentle remedy, he gets the answer: I can't prescribe that for you. Only a few health insurance companies pay for gentle therapeutics. In the statistics of the causes of death in the so-called 1st world, drug-related deaths appear as the 3rd cause of death. A return to the good traditions of the doctors of former times with inclusion of the placebo effect would be desirable.

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