

Review Article

Maximizing Drug Effect & Reducing Pain by Placebo Drug Therapy by Diminishing and Ending Use of Painkillers/ Anaesthesia in Chronic Painful Disorders

ABSTRACT

The placebo effect has shown prominent results with scientific evidence. It is the methodology of giving placebos raises questions. There is limited investigation/research in the placebo pain relieving effects. As the ethical concerns are contended. Many medical service providers use placebo habitually and patient are accepting these interventions. The positive patient-clinician outlook is very essential to develop clinically meaningful placebo effect in chronic pain patients. For clinical use of placebo, it is important to understand the placebo based clinical trials yields ethical possibility and boundaries. Since placebo effect contribute to active responses, so it is possible to enhance the positive placebo effect. Placebo is psycho-neurobiological responses capable of modulating pain and producing variable changes of different neurobiological body at emotive and analytic levels. This development can be achieved by different contextual factors (CFs) presented in the therapeutic encounter between patient and healthcare provider, such as healing rituals and sign. The CFs directly impact on the quality of the therapeutics outcome. When we say chronic pain, we know the patient is suffering from some condition from long period of time. In this scenario there are high chances of patient taking some pain management medication. Most of the chronic pain condition such as arthritis, osteoarthritis, IBS, fibromyalgia, etc. cannot be cured. Pain with time increases as patient gains tolerance to the medication therefore the doses of the medication is increased due to no effectivity or the drug is changed. This continues lifelong, due to these heavy pain medications given with the pain causative condition medication causes various negative effects on the body. In Clinical psychology placebo drug therapy can be very helpful in depression, anxiety disorders, mood disorders, psychotic disorders, etc. About clinical use of placebo effect very little known every year we learn new facts.

KEYWORDS- Placebo effect, Pain, ethical, ritual, patient-clinician, contextual factor

INTRODUCTION

In India 180 million Indians are suffering from ' ' ARTHRITIS ' . 80% urban Indians are vitamin D deficient which makes them prone to bone diseases. 95% population in India are taking NSAIDS. 90% headache with no underlying medical cause. India is second largest knee 'OSTEOARTHRITIS' suffers in the world, etc. (source: pain pract. 2014, prevalence of chronic pain. Impact on daily life & treatment practices in India by dureja GP et al ; PHD research Bureau,2015) [1].

Considering various facts form above survey, most of our population is suffering from chronic painful disorders. Currently most of the population is dependent on NSAIDS and other category of painkillers for the pain management. Most of these chemicals/medications are hazardous for the body. Prolong use or addiction of these painkillers leads to ADR (Adverse Drug Reaction) [2]. These NSAIDS mainly and other category of painkillers have numerous side effects they affect kidney, liver and can cause high blood pressure, etc. This can be very dangerous for patients suffering from painful disorders. As the patient is already on medication for those particular disorders and to manage pain these painkillers are given in such situations patient can acquire more problem related to kidney, liver and blood pressure, etc. [3]. So, considering all this situation a therapy can be developed using the placebo therapeutics. This therapy can include placebo pill triggering psychological placebo effect and pavlovian conditioning (In pavlovian conditioning the scientist experiment on dog and its food eating habit by ringing the bell while giving food to the dog. He continued this for some time later he observed that whenever the bell is rang dog starts salivation without food) likewise when patient is on painkillers we can add exotic looking sugar pills or use some placebo threptic so patient feels he is treated and develops psychological placebo effect [4]. Combining all this factors a 'PLACEBO DRUG THREAPY' can be developed. This therapy will not only help reducing pain but will also help maximizing the drug effect on the patient for that particular disorder the patient is suffering from. As this therapy can also help patient

to develop a positive psychological effect. Patients with defective genetic disorders, age related disorders or any chronic painful disorder can be benefitted with this therapy as this will help reducing pain positively and without exposing patient to continuous drug use.

OBJECTIVE

The purpose of this review article is to look for better way to manage pain of the patient without exposing the patient to harmful chemicals which can cause serious medical issues. So, the placebo drug therapy can be developed for patient suffering from chronic painful disorders and to reduce pain without any chemical exposure. Most of these painkillers are addictive. This therapy can be best alternative method in future for pain management with negligible side effects. It will help us to determine various essential factors that will help us to trigger psychological placebo effect. This is mostly based on patient-clinician relationship to maximize placebo drug effect. As majority of patient are layman. When they are admitted in hospital they believe in white coat the clinicians for their betterment. They trust clinician for the treatment. Therefore clinician can build a good relationship with patient using this trust and belief for the betterment of the patient [5]. Therefore high possibility of achieving psychological placebo effect.

METHODOLOGY

There are various possibilities and lot of unknown facts in placebo research. Clinical trials can be conducted using different therapeutic methods. The main obstacle in the placebo trials is ethics and deception. The placebo shows more positive results if given deceptively. Many clinicians practice and prescribe placebos in daily life. Previously placebo effect has been used against some disorders like irritable bowel syndrome (IBS). In which patients were given lidocaine to reduce pain while rectal examination. Placebo trails were conducted it significantly reduced pain levels compared to NH-Group [6]. Such trails can be conducted with various chronic painful disorders. Different facts and parameter of placebo therapeutic uses can be determined. Its fact that placebo effect exist can be used in medical practice. More research and scientific study is required. Due the ethical concerns and deceptively treating the patients is main obstacle. But this giving placebo threptic deceptively is also very

important to induce the placebo effect [7]. So, it's challenging to carry out trials and researches keeping the ethical boundaries in sight. A rational way must be found do trials.

DEVELOPING A PLACEBO THERAPY

Now-a-days pain management drugs are used in abundance without any prescription. It's a serious crisis, most of the pain management drugs are addictive and shows side effects after prolong use. Many patients in chronic painful disorder have no option but to be dependent on painkillers as some disorders like IBS, arthritis cannot be cured. Patient with time develop resistance to these pain medications. The dose required by the patient is increased this also multiplies the chances of developing adverse reaction with time. The patient after a point doesn't response well to the drugs and complaints of its inefficiency. So, the patient is than subjected to higher class of pain killers [8]. A placebo therapy can be developed by combination of pain killers and placebos therapeutic. This needs to be given deceptively with taking patient in trust and exaggerating the benefits of this placebo drug therapy [7]. With time the dose of pain killers can be reduced while increasing the placebo therapeutics. We need to investigate the results and determined till what limit the placebo can show effect, can the painkillers completely be replaced by the placebo therapeutics in chronic pain disorder patients? Or can placebo effect can be induced only in certain disease? All these question needs to answer. There is need of extensive research in this field. Placebo therapy can be a boon to many people. As we know majority of population is suffering from some pain related issues. Many of them are addicts to these drugs. In severe painful disorders most of the disease cannot be cured. Patients have to be on continues medication to manage this disorder. Along with this the patient has been on heavy pain medication to manage severe pain. If this therapy helps induce positive placebo effects in severe pain patients it will be a great achievement. Placebo effect till today is not well understood, as it involves the complex neurobiological reaction that includes the increase in feel-Good neuro transmitters, like endorphins and dopamine, to greater activity in certain brain regions [9]. Administering the placebo like normal drugs will not show effects. The proper ritual is required with some exotic looking drugs or therapeutics to administer to the patient. So, the patient feel psychologically that he is been treated and will self-induce the effect.

To understand how the placebo work we can compare it with the Pavlovian conditioning or experiment. In this experiment the Russian physiologist Ivan Pavlov experimented on his dog. In normal condition whenever the dog use to see the food the salivation occurred. Povlov than started ringing a bell when he use to feed the dog this continued for a period of

time. Then after some time he observed that whenever he rang bell the dog started salivation even no food was given.

From few researches carried out on specific disorders or conditions which have chronic pain has shown positive effect for example 66 patients suffering from migraine headaches a randomized trial were performed. They were classified into three groups “rizatriptan” group, “placebo” group, or “rizatriptan or placebo” group. Surprisingly the mislabelled placebo drug as rizatriptan reduced headache significantly [6].

Experimental research was carried out on 48 patients of chronic back pain and to improve the patient’s physical activity. They were given placebo tincture combined with the instruction that it is “highly effective opioids”. There was huge difference in the pain reduction. As average pain was 5.0 on the pain scale and after the placebo tincture it was reduced to 2.5 (0= no pain, 10= worst pain)[6] .

A brief understanding about the psychology and neurobiological reaction is necessary, every clinician knows that placebo effect is real and its works. How it works? We still are unable to answer this question due to limited researches. Due to ethical limitation intensive research in the field cannot be conducted. There is billion-dollar pharmaceutical business flourishing on these pain medications as these are addictive and easily available in developing countries [10]. This is like an endemic. People who truly are in pain can be helped with this therapy without exposing them to chemicals. Adaption of this therapy can very beneficial for masses.

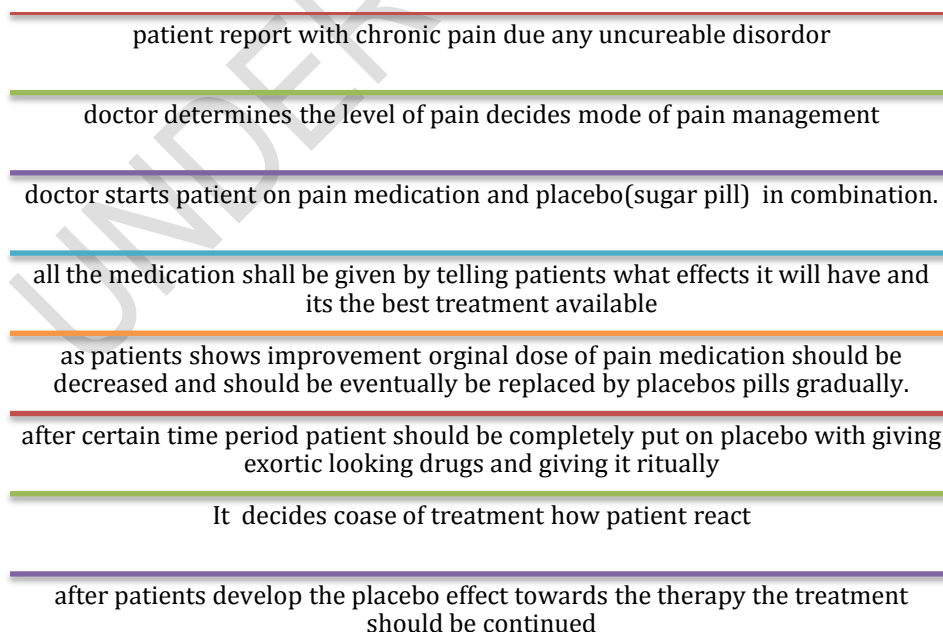


Fig 1.

OBSATLES IN PLACEBO RESEARH AND TRIALS

Placebo research has not much progressed because of the ethical boundaries. As the placebos has to be administered deceptively by building a trustful patient-clinician relationship [9-11]. Many factors have to be considered in placebo research as physical as well as psychological. A mirage has to be created by the clinician in the mind of patient about the placebo and its effects how it will affect him. A patient's positive outlook is also very much important. All these factors are needed to be considered to induce the psychological effect [12]. All these things are crucial as every patient is different and has different levels of pain. A standard guideline or understanding of the neurobiological reaction and certain psychological check point is essential. Suppose a group of people are suffering from same disorder and have different level of pain tolerance when placebo therapy is given to them every patient will have different levels of positive response. This can be challenging to determine as what amount of dose or therapeutic will trigger the positive response. If the trials are conducted by informing the patient about the placebo therapy the results may not be the same. Ethical design of these trails and research is also a challenge [13]. But this trail and research is need of an hour as the statistics show majority of the population are in pain. If these placebo drug therapies are ethically approved and researched, brought in daily practice can help the majority of people. Still today and every year we learn and discover new facts about human body and we will keep discovering the same in future as well. But due to the ethical reasons the development and research in the field is not progressing. World with information and knowledge about this field will be completely different because it has potential of changing the way the pain is perceived, studied and managed. We know placebo effect is real and is effective but the real challenge is practically and evidently proving the effect exists with scientific evidence with biological reactions. The reaction which is induced during placebo effect which reduces pain is unknown if known can be beneficial [14]. Certain techniques or therapeutics can be studied or researched so a meaningful positive placebo effect can be effectively induced. For this human experiment are required which is highly ethical. So, its huge obstacle in this therapy development. Various experiment done on animals can be referred or understood how this effect works such as Pavlovian conditioning. An ethical methodology is essential which does not violate any human right such method must be found and explored to learn about placebo and its medical use.

THE WORLD WITH PLACEBO DRUG THERAPY

After ethical approval and development of this therapy. It will benefit millions of people from harmful exposure and abuse of this pain management medications. The placebo drug therapy will make people more tolerant to pain. To induce these placebo effects in the patient both physically and psychologically is a skill. Clinicians will require more experience and training to induce these effects. All the pain management is done deceptively for the greater good of patient. Researchers also found that the placebo effect can ease pain, fatigue or depression with using non-active treatment. Long term use of pain medication has various side effects such as nausea, drowsiness, dizziness, itching or sweating, depression, tolerance as with time body needs more drug to produce same effect and eventually cause addiction [15]. Long term use of certain NSAIDS leads to side effects including stomach problems, kidney problems, high blood pressure, fluid retention, and allergic reactions [16-21]. All of these side-effects or ADRs can be prevented by placebo therapy. There are many disorders which cannot be cured and have high amount of pain. To manage the condition the patient is already on medications for pain management separate medications are given. So such conditions can be identified and researched in which placebo drug therapy can work. This will not expose the patients to more chemicals and helping with giving same pain relieving effects.

DISCUSSION

Placebo therapy can be developed is a possible goal. As the researchers are still discovering and investigating and learning new facts about how placebos work. Placebo can be given combined with pain management drugs and then consecutively decreasing its dose deceptively. Patient is unknown of these advances and thinks that he is taking the authentic pain medication this creates a psychological effect. Extensive researches are need to be done in which conditions the effect is possible? What are its enhancing effects? Does the placebo effect is positive for all the pain disorder or only works in some? How specifically or till what degree the patient will respond? All these questions need to be answered. There is need of extensive research in this field. Doctors around the world use placebos for clinical purposes due to their effects on a range of illnesses. A Danish study Trusted Source in 2008 found that 48 percent of doctors had prescribed placebos at least 10 times in the past year. Most often, these placebos were antibiotics for viral illnesses and vitamins for fatigue. A similar study of doctors in Israel found that 60 percent Trusted Source prescribed placebos to deter patients who wanted unjustified medication, or if a patient “needed calming” [9]. So, this shows for the good of the patient doctor prescribed placebos and it’s helpful. Ethical approval is important so, more people can be benefited if this placebo drugs and therapy is approved.

CONCLUSIONS

In clinical practice placebo effect can be very useful. Many patients come to clinic with complaints of fatigue or pain in various regions like head, back, legs etc. without any underlying pathology. Such patients can be helped with placebo drug therapies without exposing them to unwanted drugs. Wellness can be aroused in patients in the context of good patient-clinician relationship.

It is ideal that all the treatment should be specific in action and used only if necessary. But unfortunately, placebo works well deceptively and has no specific action or yet to be discovered. Doctor should not leave the patient in uncertainty about the treatment effects. Even if the doctor is not sure about the effects but patient must be told this is the best treatment to manage his pain. Doctor must guide patient to identify the positive improvement occurring in the patient. The hope of improvement and wellbeing must be induced in patient. Patient should be told what they should expect from the treatment how it will affect them.

REFERENCES

- 1) Dureja GP, Jain PN, Shetty N, Mandal SP, Prabhoo R, Joshi M, et al. Prevalence of chronic pain, impact on daily life, and treatment practices in India. *Pain Pract.* 2014;14(2):E51-62.
- 2) Non-steroidal anti-inflammatory drugs (NSAIDs). In: *Encyclopedic Reference of Immunotoxicology*. Berlin/Heidelberg: Springer-Verlag; 2006. p. 480–1.
- 3) Hörl WH. Nonsteroidal anti-inflammatory drugs and the kidney. *Pharmaceuticals (Basel)*. 2010;3(7):2291–321.
- 4) Babel P. Classical conditioning as a distinct mechanism of placebo effects. *Front Psychiatry*. 2019;10:449.

- 5) Ha JF, Longnecker N. Doctor-patient communication: a review. *Ochsner J.* 2010 Spring;10(1):38–43.
- 6) Klinger R, Stuhleyer J, Schwartz M, Schmitz J, Colloca L. Clinical use of placebo effects in patients with pain disorders. Colloca L, editor. *Int Rev Neurobiol.* 2018;139:107–28.
- 7) Colloca L, Howick J. Placebos without deception: Outcomes, mechanisms, and ethics. *Int Rev Neurobiol.* 2018;138:219–40.
- 8) Morrone L, Scuteri D, Rombola L, Mizoguchi H, Bagetta G. Opioids Resistance in Chronic Pain Management. *Curr Neuropharmacol.* 2017;15(3):444–56.
- 9) The power of the placebo effect [Internet]. Harvard.edu. 2017 [cited 2021 Oct 25]. Available from: <https://www.health.harvard.edu/mental-health/the-power-of-the-placebo-effect>
- 10) Taylor D. The pharmaceutical industry and the future of drug development. In: *Issues in Environmental Science and Technology.* Cambridge: Royal Society of Chemistry; 2015. p. 1–33.
- 11) Friesen P. Placebos as a source of agency: Evidence and implications. *Front Psychiatry.* 2019;10:721.
- 12) Horin AP, Lee KM, Colloca L. Placebo effects in therapeutic outcomes. *Curr Clin Pharmacol.* 2014;9(2):116–22.
- 13) Cherry K. How does the placebo effect work? [Internet]. Verywellmind.com. [cited 2021 Nov 15]. Available from: <https://www.verywellmind.com/what-is-the-placebo-effect-2795466>

- 14) Colloca L. The placebo effect in pain therapies. *Annu Rev Pharmacol Toxicol.* 2019;59(1):191–211.
- 15) Common side effects of painkillers & OTC pain relievers [Internet]. Webmd.com. [cited 2021 Oct 25]. Available from: <https://www.webmd.com/pain-management/pain-medication-side-effects>
- 16) Marcum ZA, Hanlon JT. Recognizing the risks of chronic nonsteroidal anti-inflammatory drug use in older adults. *Ann Longterm Care.* 2010;18(9):24–7.
- 17) Bhokardankar, Prashant S., and Bharat Rathir. “Indigenous Wisdom of Ayurvedic Drugs to Treat Urinary Tract Infections.” *INTERNATIONAL JOURNAL OF AYURVEDIC MEDICINE* 11, no. 3 (September 2020): 370–77.
- 18) Gandhasiri, Diti, V, Tilak M. Dhamgaye, Ulhas Jadhav, and Babaji Ghewade. “A Case of Disseminated Extensively Drug Resistant Extrapulmonary Tuberculosis.” *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH* 14, no. 11 (November 2020): LD1–3. <https://doi.org/10.7860/JCDR/2020/44916.14183>.
- 19) Agrawal, Rajat Kumar, and Shailesh Nagpure. “A Study on Polypharmacy and Drug Interactions among Elderly Hypertensive Patients Admitted in a Tertiary Care Hospital.” *INTERNATIONAL JOURNAL OF HEALTH AND ALLIED SCIENCES* 7, no. 4 (December 2018): 222–27. https://doi.org/10.4103/ijhas.IJHAS_152_17.
- 20) Patel, Krupali, Sandul Yasobant, Jaykaran Charan, Mayur Chaudhari, Abhay Gaidhane, and Deepak Saxena. “Acceptability and Perceptions of Generic Drugs among Patients, Pharmacists, and Physicians.” *JOURNAL OF PHARMACEUTICAL RESEARCH INTERNATIONAL* 32, no. 33 (2020): 40–47. <https://doi.org/10.9734/JPRI/2020/v32i33330948>.
- 21) Patel, Mohan, Jitendra Goswami, Manish Balwani, and Manoj Gumber. “Prediction of Tacrolimus Drug Dosing and Metabolism Based on CYP3A5 Polymorphism in Indian Renal Transplant Recipients.” *TRANSPLANTATION* 102, no. 7 (July 2018): S92. <https://doi.org/10.1097/01.tp.0000542683.60190.23>.