



## **Ethically Leveraging the Placebo Effect to Reduce Pain Levels in Patients Experiencing Post-Extraction Pain**

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### **Abstract**

Dental procedures can frequently result in pain and discomfort, leading to anxiety and fear in patients. Following tooth extraction, mild to moderate discomfort is typical, along with issues such as swelling and bleeding. This has prompted researchers to investigate various approaches to improve patient comfort during and after dental procedures, including using placebo interventions. The placebo effect refers to the phenomenon where a patient's perception of pain or treatment outcome is influenced by their beliefs and expectations rather than specific properties. It entails a complex neurological response that involves heightened neurotransmitters such as dopamine and endorphins, an increased activity in certain brain regions associated with moods, emotional reactions, and self-awareness, amongst others.

As the anticipation of benefit from a placebo occurs at the administration time point there is an activation for dopamine receptors within reward-linked brain regions. This knowledge may be ethically utilized to enhance patient comfort during dental procedures. Methods like delivering detailed descriptions of treatments, highlighting positive results, and instilling confidence in the effectiveness of the treatment can foster constructive anticipation among patients, which might potentially strengthen the placebo effect, lessen perceived discomfort in the procedure, and reduce post-extraction painful sensation levels.

Keywords: placebo effect, pain perception, dental procedures, patient comfort, beliefs and expectations, dopamine receptors, ethical leverage, open-label placebo, NSAIDS

### **1. An Overview of Tooth Extraction**

The necessity for tooth extraction can stem from various reasons, including irreversible tooth damage, periodontal disease, teeth overcrowding, and impacted wisdom teeth. To alleviate pain during the tooth extraction process, dentists typically administer local anesthesia by applying a numbing agent to the area near the targeted tooth and delivering one or more injections in its vicinity. This action serves to inhibit nerve signals, thereby preventing the transmission of pain sensations to the brain. Utilizing instruments such as forceps, the dentist will dislodge the tooth root and extract it while avoiding contact with nerve endings. Following removal, dental personnel will apply gauze over the extraction site to manage bleeding and promote clotting. During recovery, patients may undergo significant discomfort around the extracted area for twenty-four to seventy-two hours post-procedure. The primary cause of post extraction discomfort is a dry socket condition that arises when the protective blood clot gets dislodged or fails to form within the socket. This pain is typically managed through pain medications, such as anti-inflammatory medications, as prescribed by the dentist.

## 2. The Side Effects of Pain-Relief Medications and the Importance of Effectively Leveraging the Placebo Effect

In the treatment of dental pain, patients were administered anti-inflammatory medications including Ibuprofen, Naproxen, and Diclofenac. Despite their widespread availability and proven safety record, these medications are commonly linked to adverse reactions such as abdominal pain, diarrhea, cardiovascular events, renal toxicity, and teratogenic effects. Notably, all NSAIDs inhibit COX-1 and COX-2 enzymes responsible for prostanoind formation in the inflammatory response pathway. This mechanism poses an elevated risk of gastrointestinal ulcers along with serious upper gastrointestinal complications like bleeding and perforation (Ong et al. 2007). Endoscopic studies have revealed that gastric ulcers develop in 15 to 30% of regular NSAID users (Laine et al. 1996). The accompanying Figure 1 showcases the comparative risk of gastrointestinal complications associated with NSAID usage versus non-use with a 95% confidence interval.

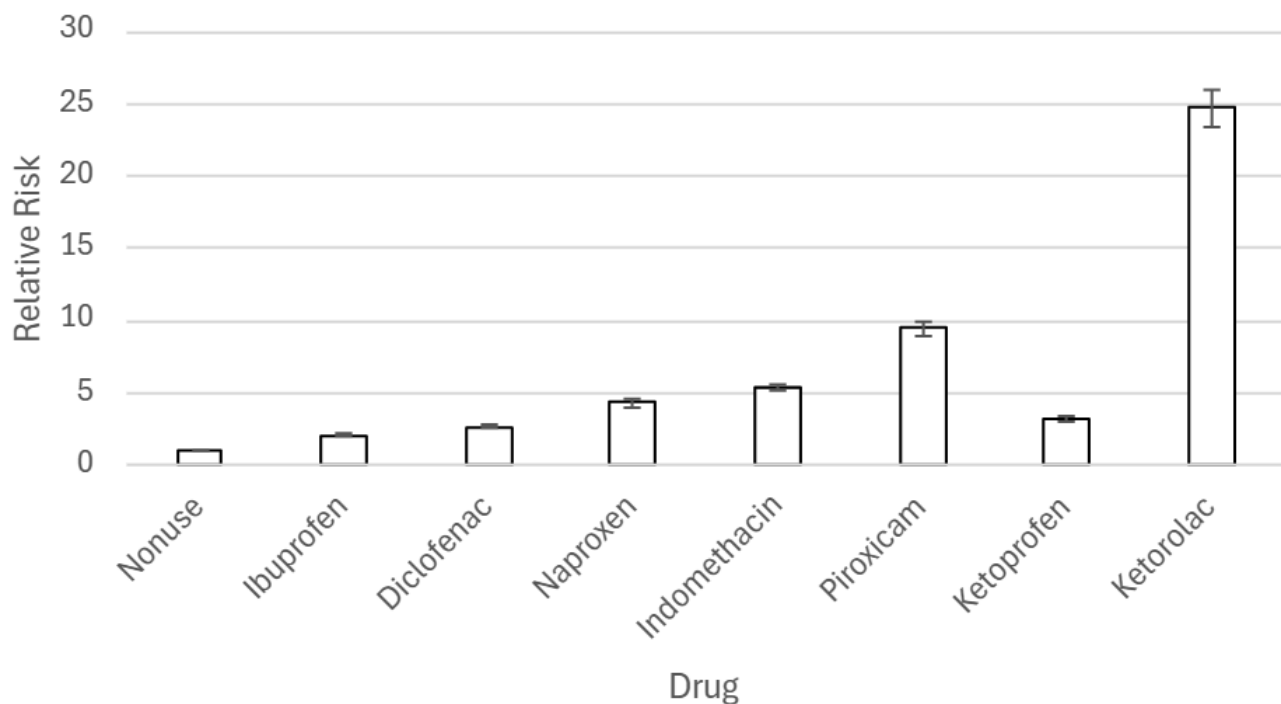


Figure 1: Adapted from Rodriguez et al. (<https://pubmed.nlm.nih.gov/9437376/>)

In addition to potential side effects, patients may inadvertently consume more than the recommended doses of anti-inflammatory medications. A study monitoring the Ibuprofen usage of 1,326 patients revealed that over one-third had taken a second NSAID medication, with fewer than half recognizing that both medications were in the same class. Furthermore, up to 15% exceeded the recommended dosage (Kaufman et al. 2018). While NSAIDs can effectively alleviate pain, exceeding recommended dosages or combining multiple NSAID medications increases the risk of serious side effects such as heart attack, stroke, and gastrointestinal bleeding (Wongrakpanich et al. 2018). Prolonged use among patients experiencing chronic

dental pain also raises their risk of developing complications like peptic ulcers, renal failure, and cardiovascular issues (Marcum et al. 2010). Given these risks associated with traditional pain management approaches, it is imperative to explore alternative strategies for enhancing patient comfort following dental procedures.

### **3. Analyzing the Placebo Effect: Pain Relief in Dentistry**

Effectively leveraging the placebo effect can be a powerful tool in enhancing patient comfort without relying solely on medication. In dental practice, placebos such as nonactive medications, mechanical procedures, psychological interventions, and therapeutic environmental adjustments have been demonstrated to positively impact patient outcomes.

#### **3.1. Nonactive Medications and Psychological Responses**

Nonpharmacological interventions such as inert substances or saline solutions can have a significant impact on the perception of pain when patients believe they are receiving an active pharmaceutical intervention. This effect is governed by the physiological process of classical conditioning. Through repeated pairings of the inert substance with relief from pain, patients may develop a conditioned response in which the placebo itself triggers the release of endogenous opioids or other neurotransmitters that diminish pain perception. A study comparing preoperative medications and placebos for alleviating pain in patients with irreversible pulpitis found that the success rate for the placebo group (40%) was comparable to that of groups receiving ibuprofen (55%), aceclofenac with paracetamol (55%), and etodolac with paracetamol (50%) (Jena et al. 2013). This indicates that nonpharmacological interventions can elicit a similar level of pain relief in dental patients compared to active NSAID medications.

#### **3.2. Performing Mechanical Procedures**

Mechanical procedures such as simulating acupuncture with non-penetrating needles or applying pressure without needle insertion have been supported by various studies as effective in reducing pain levels in dental patients. The effectiveness of this method was demonstrated in a study to assess if dry needling at a specific acupoint can reduce the dental pulp sensory threshold produced by electrical stimulation of incisor teeth. A total of 40 healthy adults were given real or sham acupuncture (non-penetrating blunt needle), and the results showed insignificant differences in pain reduction between volunteers who received real acupuncture and those who received the placebo intervention (Goddard et al. 2009).

#### **3.3. Psychological Interventions for Pain Relief**

Psychological interventions, such as providing thorough explanations of the procedure and instilling confidence in its effectiveness, can also enhance the placebo effect and reduce pain perception during dental procedures. The use of positive communication, reassurance, and empathy from dental providers has been shown to improve patient outcomes and reduce pain perception. Patient's conscious and subconscious reactions to signs and actions in the clinical environment can cause expectancies leading to the placebo effect. According to research done on the role patient-practitioner relationships have on the placebo phenomenon, practitioner

characteristics such as empathy, friendliness, and competence favor the formation of positive expectancies (Maxie et al. 2018). The engagement of emotional resonance in the form of empathy can help regulate the patient's autonomic arousal and decrease the allostatic load (McEwen et al. 1998), thus promoting physiological homeostasis (Adler et al. 2007). A study by Gracely compared postoperative pain after dental surgery in a double-blind setting with 60 patients divided into a placebo-naloxone (PN) group and a placebo-naloxone-fentanyl (PNF) group. Results showed that pain levels in the placebo arm of the PNF group were significantly lower when compared to the placebo PN group (Gracely et al. 1985).

### **3.4. Creating a Therapeutic Environment**

Research has shown that establishing a therapeutic environment tailored to the physical and emotional needs of the patient can enhance the patient's sense of well-being (Sarapultseva et al. 2022). Dental patients experiencing post-extraction pain may have their pain perception influenced by various factors, including anxiety levels, which can indirectly impact dental pain through salivary pH changes and increased sensitivity to pain (Lunde et al. 2020), as well as exacerbating gum disease. Anxiety reduces saliva production, causing alterations in pH balance and increasing mouth acidity, potentially leading to heightened tooth sensitivity and decay. A study involving 105 patients categorized into three groups based on their anxiety levels concluded that higher anxiety levels correlated with elevated saliva acidity; average resting salivary pH was found to be at 6.79, and in a state of anxiety, it dropped to 6.43 (Said et al. 2020). Furthermore, studies have indicated that stress significantly impacts immune system functioning, including inflammation and wound healing processes, which could result in inflamed gums and amplified perception of discomfort (Seiler et al. 2019). To alleviate patient stress levels and improve comfort during dental procedures, it is crucial to consider factors such as optimal temperature control, visual comfort, a serene atmosphere, and indoor air quality (Mewomo et al. 2023). These approaches may involve creating a soothing and inviting atmosphere within the dental office, tapping into relaxation techniques like deep breathing or aromatherapy, integrating calming music, and providing diversions, such as virtual reality experiences or tranquil visual stimuli. By implementing these strategies, dental professionals can create a therapeutic environment that reduces patient anxiety and mitigates the negative impact of stress on pain perception.

### **4. Ethical Considerations in Using Placebo in Dentistry**

Before utilizing placebo interventions in dentistry, it is crucial to consider the ethical implications and ensure that appropriate guidelines are followed. These guidelines should include obtaining informed consent from patients, clearly explaining the nature of the placebo treatment and its potential effects, and ensuring that patients have access to alternative treatments or interventions if desired. Additionally, dentists should prioritize the well-being and comfort of their patients by providing adequate pain management and ensuring that the placebo effect is used ethically as an adjunct to other evidence based treatments rather than as a standalone approach. Furthermore, it is essential for dental professionals to communicate openly and honestly with their patients about the use of placebos, addressing any concerns or questions they may have.



According to a study on US patients' attitudes on the use of placebos in medical care, most respondents (50-84%) judged it acceptable for doctors to use placebos in certain situations in which the physician is certain about the benefit and safety of treatment, the purpose of the treatment, and the transparency with which the treatment was described to the patients. Only 21.9% of the respondents claimed it to be never acceptable for doctors to recommend placebo treatments, underscoring the wide acceptance of placebo treatment, given that it is done in a fully transparent manner. The respondents valued honesty regarding placebo usage and believed that not doing so could undermine physician-patient relationships (Hull et al. 2013). The results of this study suggest the potential of ethically leveraging the placebo effect through open-label placebos with a high acceptance rate of transparent treatment among patients.

However, despite the positive attitude patients may have towards placebo treatments, a study by Fassler on the frequency and circumstances of placebo usage in clinical practice provided insights into the high prevalence but low frequency of placebo usage outside of clinical trials. Although 17 - 80% of physicians reported the appliance of 'pure' placebos during their professional lives, the actual frequency of such is low. In the two studies reviewing the medical records of hospital inpatients for various departments in a USA hospital, the incidence of the application of pure placebos was 0.3% for 6 months (Fassler et al. 2010). Comparing this result to the high acceptance of placebo treatment among patients, there is a disconnect between patients' acceptance of placebo treatments and the actual implementation of such interventions in dental practice.



Author year	Setting	Type	Placebo use	Definition of use	Frequency or other additional information
<b>Questionnaire- based quantitative surveys</b>					
<i>Physicians</i>					
Goodwin 1979 [19]	Hospital (house officers)	Pure*	78%	Ever use for pain relief	
Gray 1981 [20]	Hospital	Pure	80%	Ever use	
Classen 1985 [23]	Unclear	Pure	60%	Use 'sometimes'	About 30% less than once a month
Classen 1985 [23]	Unclear	Impure	54%	Use 'sometimes'	
Lynøe 1993 [26]	Unclear	Both	99%	Ever use	None very often, 1% often, 4% rather often, 26% quite rarely, 68% rarely/very rarely
Hrobjartsson 2003 [30]	General practice	Both	86%	During the last year	38% 1-10 times/year, 48% > 10 times/year
Hrobjartsson 2003 [30]	Hospital	Both	54%	During the last year	44% 1-10 times/year, 10% > 10 times/year
Hrobjartsson 2003 [30]	Specialist practice	Both	41%	During the last year	31% 1-10 times/year, 10% > 10 times/year
Nitzan 2004 [31]	Hospital/family practice	Pure*	53%	Use with a minimum frequency of once a year	37% once a month or more oftent
Sherman 2007 [33]	Medical school faculty	Both	45%	Ever use	15% 1-10x, 8% > 10x, 22% not at all during last year
Tilburt 2008 [34]	Specialist practice	Both	80%	Ever use	34% = once a month, 28% 2-3 times/month, 18% = once a week
Bernateck 2009 [35]	Hospital	Pure	52%	Use with a minimum frequency of once a year	40% 1-2 times/year, 9% 1-2 times/month, 4% more often
Fässler 2009 [37]	Primary care	Pure	17%	Ever use	93% once a month or less often
Fässler 2009 [37]	Primary care	Impure	57%	Ever use	
<i>Nurses</i>					
Goldberg 1979 [18]	Hospital	Pure	51%	Ever use	44% with current use or use in the last 6 months
Goodwin 1979 [19]	Hospital	Pure*	82%	Ever use for pain relief	
Gray 1981 (sample 1) [20]	Hospital	Pure	80%	Ever use	
Gray 1981 (sample 2) [20]	Hospital	Pure	89%	At least once during the last 5 years	63% during the last year
Saupe 1985 [24]	Hospital	Pure	100%	Ever use	79% once or less per month, 21% more often
Ernst 1997 [27]	Unclear	Pure	57%	Ever use	
Ernst 1997 [27]	Unclear	Both	68%	Ever use	12% during the last year
Nitzan 2004 [31]	Hospital	Pure*	71%	Use with a minimum frequency of once a year	37% once a month or more oftent
Bernateck 2009 [35]	Hospital	Pure	87%	Use with a minimum frequency of once a year	45% 1-2 times/year, 33% 1-2 times/month, 9% more often
<i>Interns</i>					
Berger 1999 [28]	Hospital	Pure	16%	Ever witnessed use	Only 2% (1/47) had actually given a placebo
<b>Substudies with prospective screening of medical records of hospital patients</b>					
Goodwin 1979 [19]	Hospital	Pure*	0.3%	During 6 months (prospective)	
Lange 1981 [21]	Psychiatric hospital	Pure	5.1%	During 12 months (prospective)	6.1% in women, 3.9% in men

\* Limitation to pure placebo not explicitly stated but questions/report with clear focus on pure placebo use.

† Numbers related to both physicians and nurses.

Table 1: Frequency of Placebo Use in Healthcare Settings. Reprinted from Fassler et al. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2837612/>)

When examining the circumstances under which placebos were employed, it was observed that placebo interventions were administered with an element of deception, often to 'problem patients' or those deemed 'questionable or unreliable' (Fassler et al. 2010). While it was traditionally believed that the placebo effect could only be achieved through deception, recent

research has shown that open-label placebos can also elicit significant therapeutic responses. In a comparative study on the use of open-label placebo versus no-treatment control in the treatment of irritable bowel syndrome (IBS), patients receiving treatment reported a significant score increase on the IBS Global Improvement Scale (IBS-GIS) compared to the control group with matched patient provider interactions (Kaptchuk et al. 2010). Given the effectiveness of open-label placebo treatments in relieving the symptoms of various health conditions without active medication intervention, it may be beneficial for dental professionals to increase their frequency of placebo usage after engaging in transparent discussions with patients about potential placebo interventions and gaining their informed consent for incorporating them into the treatment plan.

## **5. Discussion**

Considering the elevated risks for gastrointestinal complications and cardiovascular issues among others, conventional methods for pain alleviation such as NSAID medications may no longer be the optimal treatment. The efficacy of placebo interventions in managing post-operative pain has been demonstrated in various studies. To address the ethical implications surrounding placebo use in dental practice, it is crucial to promote transparency and open communication between dental professionals and patients regarding the use of placebo interventions. This can be achieved through the administration of open-label placebos and by obtaining informed consent from patients for placebo treatments. Some limitations of this study may include limited research on the prevalence of placebo usage among dentists and the effectiveness of open-label placebos in managing dental pain. While existing research on the prevalence of placebo usage among physicians provides insights into its frequency within dental clinics, there is a need for further investigation specifically focused on dental professionals and their attitudes and practices regarding placebo usage. Additionally, future research should explore the efficacy of open-label placebos in dental pain management and examine the possibility of transitioning to non-pharmacological interventions for pain relief.

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## **Conflicts of Interest**

The author declares no conflict of interest.

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