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Identifying perceptions and knowledge gaps among pre-clinical and clinical medical students regarding placebo therapy

Haseeba Mukhtar[1], Syeda Unzila[2], Taskeen Babar[3], Syeda Mahdokht Shah[4], Sujjad Khan[5] and Sidra Khan[6]

[1] Department of Community Medicine, Northwest School of Medicine,
[2,3,4,5,6] Department of Medicine and Surgery, Northwest School of Medicine

ABSTRACT

Background: Misleading definitions and perceptions of placebo and placebo effect result in fewer realizations on the subject, hence reducing its perceived importance and applications. This study aims to assess undergraduate medical students' perceptions and knowledge gaps regarding placebo therapy across different stages of their education.

Methods: A comparative cross-sectional study was conducted for six months, from December 2022 to May 2023, among 350 pre-clinical students (1st and 2nd year MBBS) and 526 clinical students (3rd, 4th, and Final-year MBBS) to assess their perceptions regarding placebo and placebo effect through a validated questionnaire. SPSS was used for analyses, and Pearson's Chi-square was applied, keeping the statistically significant value of <0.05.

Results: The study included 876 medical students, with 350 pre-clinical and 526 clinical participants. The mean age was 21.32 years (±1.606). A significant gender distribution was observed, with 45.5% males and 54.5% females. Clinical students demonstrated a greater acceptance of placebo use (68.3% vs. 62.3%, p=0.031) and were more likely to find placebo therapy ethical in psychological cases (70.3% vs. 60.3%, p=0.006). Knowledge assessment revealed that 65% had fair knowledge of placebo therapy, 31.8% had good knowledge, while only 3.2% were highly knowledgeable.

Conclusion: The study revealed that many pre-clinical and clinical students held misconceptions about placebo therapy, believing it permissible and beneficial in treating organic disorders. This highlights a significant knowledge gap, emphasizing the need for improved education on placebo use and ethics.

Key Words: Placebo therapy, Placebo effect, medical students, Perceptions, Knowledge gaps

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Introduction

The term "placebo" has been around for some time but is nothing short of a minefield filled with endless confusion attached to various definitions and perceptions. The term was initially generated from pharmacology, but later the concept entered the premises of almost every discipline. According to the Shorter Oxford Dictionary, the term placebo has been used since 1811 to refer to a treatment given to satisfy the patient more than to benefit the patient's condition. The concept is surrounded by misleading conceptual definitions and incoherent

perceptions, which has made the understanding and, ultimately, the utility of it a lot less than its true significance and application (1).

CORRESPONDENCE AUTHOR
Haseeba Mukhtar
Department of Community Medicine,
Northwest School of Medicine, Peshawar
Email: haseeba.mukhtar123@gmail.com

The simplest definition to get into clarify the concept is that a placebo can be labelled as any inert (inactive) substance that is given, though it is an active substance. Placebo, regarding clinical practice, is a therapy devoid of the active ingredient but still capable of producing a therapeutic outcome, whereas else, the research does not follow this aspect and takes placebo as an inert agent. Regarding its utility in clinical trials, it is a substance given to a control group to avoid bias and make scientific comparisons (2). The term's history can be traced back to the early 13th century when the Latin term "placebo domino" was used as a reference to the dead. Later through years of advancement, it ended up as the term we now know as the placebo (3). The placebo effect is an outcome of positive expectation of the consumer towards the state of their healthy, contrary to the nocebo effect that follows a negative expectation. The placebo effect is partly attributed to how the patients respond to the given substance. However, the frequency of the effect is technical to determine (4). Studies have shown the responses ranging from an effect as effective as the original treatment to the need for discontinuance owing to the intolerable side effects. These subjective outcomes affected by negativity, expectations, and interactions make the topic difficult to conceptualize. To focus on the effect despite the confounding concepts, we may define the placebo effect as the response that follows the placebo administration, e.g., the resultant analgesia in the pain study using a placebo will be labelled as the placebo effect/response. This effect is associated with stimulating the release of substances endogenously depending on the targeted system, including opioids, dopamine, cannabinoids, vasopressin, etc. (5). However, even in the scientific community, there are contrasting opinions regarding the utility and perceptions of placebos, especially their use in clinical practice. There are two contrasting frames of thought. One category believes that placebos are, without doubt, a significant part of clinical trials, but their effectiveness as a therapeutic option and the related ethical constraints are controversial and raise debate. The other category believes that placebos should also not be a part of clinical trials and those active medicines instead of placebos should be used as comparators (6).

The medical community starts in medical colleges from being medical students to become physicians and researchers; therefore, it is mandatory to assess the students' perceptions towards the placebo therapy to drive them in the right direction and impart the necessary knowledge after identifying the knowledge gaps. That will be the beginning of medical practitioners and researchers with significant knowledge that will lead to beneficial innovation and clinical practice. This study's main aim was to assess medical students' perceptions and knowledge regarding the placebo to understand their perspectives and figure out gaps in knowledge to act as a foundation for implementing study guidelines accordingly.

Methods

This study was designed as a comparative observational cross-sectional study,

conducted at the Northwest School of Medicine, Peshawar over six months, from December 2022 to May 2023. The study population consisted of 2000 consenting medical students from various public and private institutions of Peshawar. Non-random convenient sampling technique was used to select the study participants. The sample size was calculated using the Open Epi Sample Size Calculator with a confidence level of 99.99%, anticipated frequency (p) of 50%, and confidence limit (d) of 5%. The calculated sample size was 863, but for convenience, a total of 900 questionnaires were distributed among the participants, out of which 876 filled questionnaires were received back. Study participants included 350 pre-clinical medical students (students of 1st and 2nd year MBBS), and 526 clinical medical students (students of 3rd, 4th, and Final year MBBS). Before enrolment, all the participants were given information about the study's objectives. After obtaining verbal consent from each participant, data was collected with the help of a questionnaire. The study design was reviewed and approved by the medical research board and ethical committee of the affiliated institution (IRB&EC/2022-SM/052), dated: 19th December 2022. Undergraduate medical students from 1st to final year studying in various public and private medical colleges across Peshawar were included in the study and all medical students who were unwilling to participate were excluded from the study. The data was collected through a self-structured questionnaire that was constructed based on the basic concepts and confusion surrounding the placebo and placebo effects. The questionnaire design followed an extensive literature search and was finalized after validation by experts in the field and had a Cronbach's alpha value of > 0.9. The questionnaire consisted of 2 portions: the first included questions concerning demographic data, such as age, gender, institution, and education level. The second part of the questionnaire consisted of questions on placebo therapy. The questions focused on the definitions of placebo and placebo effects and the general concepts and confusions following the terms and their applications, including the definitions, acceptability of placebo therapy, the rationale and use of placebo and placebo effect in organic diseases, and perceptions regarding the actual utility and benefit of the placebo and the placebo effect. Questionnaires were filled out via direct interviews. SPSS was used to analyze the data (Version 26). The analysis of the variables included descriptive statistics such as means, frequencies, and percentages. The relationship between the responses of the pre-clinical group and the clinical group was ascertained using the chi-square test, which had an alpha level of 0.05.

Results

A total of 350 pre-clinical (1st and 2nd year MBBS) and 526 clinical (3rd, 4th, and Final year MBBS) participants participated in the study. The mean age of participants was 21.32 years $\pm$ 1.606. The pre-clinical participants included 157 males and 193 females (Total= 350), while the clinical participants included 242 males and 284 females (Total: 526) (Table 1).

Table 1: Demographics of the Participants.

Variables	Frequency (%)
Gender of Participants	
Males	399 (45.5%)
Female	477 (54.5%)
Institute of the Participants	
Public Institute	326 (37.2%)
Private Institute	550 (62.8%)

Table 2 presents the responses of pre-clinical and clinical medical students to various questions regarding placebo therapy. Statistical analysis shows significant differences in perceptions between pre-clinical and clinical groups, with p-values and $\chi 2$ values indicating the extent of these differences.

Table 2: Perceptions of placebo & placebo effect among pre-clinical & clinical medical participants

Study Variables	Pre-Clinical Group (n) (%)	Clinical Group (n) (%)	P Value	X^2 Value*
The use of placebos in treatment is permissible:				
Yes	218 (62.3)	359 (68.3)	*0.031*	*6.918*
No	83 (23.7)	87 (16.5)		
Not Sure	49 (14)	80 (15.2)		
Evidence suggests that placebo therapy is effective in treating organic diseases:				
Yes	141 (40.3)	164 (31.2)	*0.018*	*8.090*
No	109 (31.1)	199 (37.8)		
Not Sure	100 (28.6)	163 (31)		
Organic illnesses in which a suitable cure exists, prescribing placebo therapy is appropriate:				
Yes	81 (23.1)	87 (16.5)	*0.016*	*8.302*
No	211 (60.3)	365 (69.4)		
Not Sure	58 (16.6)	74 (14.1)		
Organic illnesses in which a suitable cure doesn't exists, prescribing placebo therapy is appropriate:				
Yes	115 (32.9)	112 (21.3)	*0.000*	*23.035*
No	195 (55.7)	376 (71.5)		
Not Sure	40 (11.4)	38 (7.2)		
In cases of purely psychological illness without an underlying organic disease, it is ethical to prescribe a placebo:				
Yes	211 (60.3)	370 (70.3)	*0.006*	*10.366*
No	83 (23.7)	85 (16.2)		
Not Sure	56 (16)	71 (13.5)		
Which of the following, in your opinion, could be a placebo's benefit:				
Mental Satisfaction	153 (43.7)	285 (54.2)	*0.002*	*14.704*
Decreases the side effects of the drug	111 (31.7)	110 (20.9)		
Don't Know	86 (24.6)	131 (25)		

* Pearson Chi-Square Value.

The findings revealed that there was a significant knowledge gap among medical students regarding placebo therapy. The majority (65%) of the 876 participants demonstrated fair understanding, meaning they correctly answered up to two of the five

questions. The remaining 31.8% demonstrated good knowledge by properly answering up to 4/5 questions. Only 3.2% were extremely knowledgeable about placebo therapy. (Table 3)

Table 3: Participants knowledge of placebo therapy

Knowledge	Frequency (%)
Fair Knowledge	569 (65%)
Good Knowledge	279 (31.8%)
Excellent Knowledge	28 (3.2%)

Discussion

The results of this study provide important clues into the perceptions and attitude of pre-clinical and clinical medical students regarding the use of placebos as a form of treatment. Of the two, high proportions of the participants considered the use of placebos acceptable. Indeed, 62.28% of the pre-clinical students and 68.2% of the clinical students indicated that using placebos was an acceptable treatment. Their results showed that most of the future professionals in health would not have a problem using placebos as treatment. This has supported the general conclusion from earlier research, through the investigation by Amanzio et al. that many medical students believed placebos, under certain conditions, could be both ethical and effective (7). The study also outlined differences in beliefs about the efficacy of placebos in the treatment of organically caused diseases. Only 40.28% of pre-clinical and 31.17% of clinical students believed in the effectiveness of placebos as a treatment for organically caused illnesses, which means relative skepticism about their potential to work in these contexts. However, the higher response was found in both the pre-clinical group and the clinical group by those believing that placebos could be used with organic disorders in which no organic treatments were available. On the other hand, a lower percentage of 23.14% of the pre-clinical group and 16.53% of the clinical responded that placebos could be used when there were effective medications against a disease. These data suggest that there might be greater receptiveness to the use of placebos where there is no alternative treatment (8).

Previous research also indicated that knowledge deficit existed with regard to placebo mechanisms and benefits among medical students. In a similar way, an assessment of the level of knowledge of medical students on placebo therapy showed that, overall, participants were not aware of the possible benefits and mechanisms of action of placebos. This knowledge deficit is not unique to the current study but represents a more pervasive problem in medical education (9). The results may be the effect of cultural differences, educational programs, and populations under study; for instance, the one done in Turkey that expressed a higher skepticism on the use of placebos among medical students in the country by Joyce et al. (10). A further descriptive study reported 70.9% of students who approved of placebo therapy with 33.3% of the respondents considering placebos to be effective for organic disorders. A minority 12.9% of the students felt that using placebos for organic disorders with known treatments was ethical, although a majority were in favor of using placebos for conditions without known treatments 64.4% and psychogenic conditions 81.6% (11). Another point that can be raised in the argument concerning the use of placebos is ethical considerations. The tendency for the bulk of the students to agree that it is ethical to administer a placebo in cases of organic disorder, 60.28% of pre-clinical and 70.34% of

clinical students, implies that a good number of future health professionals consider placebo usage in some settings to be morally justifiable. Howick et al. reported similar findings in which most medical students agreed that placebos were ethical under certain conditions (12).

Benefits of placebos were also explored, and mental satisfaction was identified as such by 43.71% of pre-clinical students and by 54.18% of clinical students. This agrees with the literature by Berrnstein et al., which evidenced that healthcare professionals realized how placebos could enhance patient satisfaction and give them a feeling of control (13). A repeat of this study in Switzerland by Fässler et al. found a significant proportion of medical students who believed placebos to be physiologically effective-such as pain relief-although they couldn't quite understand the underlying mechanisms (14). In the present study, both pre-clinical and clinical students mentioned that mental happiness might be a potential benefit (43.71% and 54.18%, respectively), and this is consistent with some findings from similar research in the UK (15). On the other side, a small portion (31.71% in the pre-clinical group and 20.9% in the clinical group) thought that placebos reduced the side effects of other medications. One more sizable number, 24.57% of the students in the pre-clinical and 24.90% in the clinical group, did not state an advantage resulting from taking placebos, thus still reflecting a knowledge gap. In the present study, 3.2% of undergraduate medical students showed outstanding knowledge in the domain of placebo therapy, whereas 31.8% of students showed good and 65% showed fair knowledge. In a comparative cross-sectional study by King Saud bin Abdul-Aziz University for Health Sciences assessing the level of understanding on placebo therapy among medical and nursing students, the average knowledge scores have been reported to be 7.68/15 and 2.07/15 respectively (11).

Study Limitations

Study limitations includes non-random convenient sampling, which is likely to be biased, and is likely to affect the generalizability or representativeness of the sample in this study. Also, the cross-sectional nature will allow for very few inferences to be made causally and not in a longitudinal manner.

Conclusion

This study found that a significant percentage of both pre-clinical and clinical group students believed that using a placebo as a treatment therapy is permissible. A smaller proportion considered placebos effective for organic disorders, with some believing placebos could be used with or without effective treatment available. Many participants viewed using placebos in organic illnesses as ethical, citing mental satisfaction and reduction of side effects as main benefits. However, some were unaware of the benefits of placebos, indicating a knowledge gap. The pre-clinical and clinical students often misunderstood the true concept of placebos, mistakenly believing they could produce therapeutic benefits as sole therapy. This underscores the need for improved education on the topic, given the ethical constraints and the importance of a proper understanding of placebos and the placebo effect.

Study Recommendations

Further research should be carried out on a sample of students from different areas,

which includes qualitative research in regard to placebo therapy and its effects. Placebo and its concept should at least form part of the topics covered in medical curricula. The knowledge gap that was identified is large, and therefore, the emphasis in education for students should be in terms of the core concepts and proper use of placebos because it will be the future specialists and researchers who must apply them.

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CONTRIBUTION OF AUTHORS	
AUTHOR	**CONTRIBUTION**
Haseeba Mukhtar	A,B,C
Syeda Unzila	A,B
Taskeen Babar	A,B
Syeda Mahdokht Shah	A,C
Sujjad Khan	B,C
Sidra Khan	B,C

KEY FOR CONTRIBUTION OF AUTHORS:

A. Conception/Study/Designing/Planning
B. Active Participation in Active Methodology
C. Interpretation/ Analysis and Discussion