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Placebo Use in Clinical Practice, Clinician's Perspectives.

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ABSTRACT

Use of placebo treatment in clinical medicine is controversial. Minimal information exists on use, beliefs and attitude about placebos in clinical practice by Nepalese clinicians. So the present study objectives are to assess the pattern of placebo use in clinical practice and explore believes experiences, attitudes and factors affecting it. A cross sectional study was performed from March, 2014 – September, 2014. One hundred thirty clinicians were invited, we measured patterns of placebo use along with believes, attitudes and factors affecting it. Result of the study shows that significant proportion clinicians have been using placebos in their practice. Clinicians have used placebo in 1-10% of their patients (average no of patients they consult is 80) in a week. The most common situation where placebo was used, reported to be nonspecific symptoms. Forty percent clinicians reported that efficacy was more than 5 on a scale of 1-10. Fifty-six percent of clinicians agreed to be psychological mechanism behind it. Placebo was reported to be more effective in female patients. Majority are not transparent to their patients about placebos. About 60% clinician said that "placebo could be allowed" if researches support the efficacy and safety. Multivitamins and over the counter analgesic are the most commonly prescribed placebos. Although the available evidence is incomplete, the prevalence of placebo used in clinical practice is considerably high. Views and attitude on placebo use differ considerably among clinicians. Further research at broader level is needed to address these issues.

Keywords: Clinical practice; Nepal; Placebo.

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INTRODUCTION

Placebos can be beneficial when they give rise placebo effect [1]. American Medical Association defines placebo as a substance that physician believes has no known specific pharmacological activity against the condition being treated [2]. A pure placebo is a substance with no pharmacologic potency, while an impure placebo has a pharmacologic effect or a different indication in larger dose (like antibiotics for viral illnesses).

Little data about clinicians view and thought about placebos exist. One review of clinical trials having placebo (no-treatment group) and an active treatment group found little evidence that placebo are effective [1]. Others however, have demonstrated significant placebo effects in conditions, like perception of pain with increased production of endogenous opiates [3].

Minimal data of placebo use by Nepalese clinicians exist. The purpose of the study was to assess the pattern of placebo use and explore believes and attitude of Nepalese clinicians about it.

METHODS

We considered impure placebo as placebo in our study. We developed a performa consisting of 20 questions related to use of placebos in routine clinical practice, including frequency of placebo use, types of treatments (including pharmacologically active medication for non-indicated purposes) used and their clinical scenario, information given to patients prior to use, perceived efficacy, adverse effects, if any, and perceived therapeutic mechanism of placebo. We also explored the underlying motivations, views, ethics, beliefs, and whether clinicians themselves would have gone for placebo treatments. Majority of the questions were multiple choices, the questions on the years of medical practice, efficacy of placebo on a scale of 1 to 10 and types of placebos prescribed and type of clinical practice included in an open-ended format. Several of the questions were adapted from other studies of placebo use [5-8]. The practicing clinicians in city of Pokhara were personally approached in an informal get together organized by Nepal medical Association, Gandaki branch, and requested to fill up the questionnaires, remaining clinicians were approached in their work places from March, 2014 – September, 2014. The clinicians were explained about the purpose of the study, those willing to participate were requested to fill up the questionnaire. Institutional ethical approval obtained.

Sample size calculation

In a study conducted prior to the original study with 10 subjects showed 80 percent use placebo. So, with 5% significance level, p=80%, Q=20% and allowable error =8[10% of P]. Required sample size was 96.

Data analysis

Our results consists frequency distributions of various responses. We classified substance such as analgesics, antibiotics and vitamins as placebos, if they were used for conditions, where efficacy not explained pharmacologically. We investigated associations between clinician's characteristics such as age, sex, clinical specialties, practice settings, highest degree obtained by clinicians, maximum number of patients consulted in a week and frequency of placebo use. We also investigated associations between age group of clinicians and beliefs regarding the therapeutic and ethical role of placebos in clinical practice. Descriptive statistics and testing of hypothesis used as statistical tools. A P value less than 0.05 considered as statistically significant. Collected data were analyzed using SPSS 16 software.

RESULTS

General description of study subjects

Out of 130 clinicians invited 100 responded, a response rate of 76.9 %, a summary of the demographic and other characteristics of study population is shown in Table 1.

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Table 1: **General description of study subjects.**

Gender	number	Percent, 95% Confidence Interval
Male	63	63, CI(53.54,72.46)
Female	37	37,CI(27.54, 46.46)
Age group		
<35 years	74	74, CI(65.4, 82.6)
>35 years	26	26, CI(17.4, 34.6)
Speciality		
Medicine and allied	45	45,CI (32.25, 54.75)
Surgery and allied	20	20, CI (12.16, 27.84)
Medical officers/house officers	28	28,CI(19.2, 36.8)
Others	7	7,CI (2, 12)
Practice setting:		
Medical college only	49	49.0, CI(39.2,58.8)
Government hospital only	1	1.0,CI(0.95, 2.95)
Private hospital only	2	2.0, CI (0.74, 4.74)
Medical college and private hospital	33	33.0, CI(23.78,42.22)
Government hospital and private hospital	13	13.0, CI(6.41,19.59)
Others (NGOs/UNICEF/WHO)	2	2.0, CI (0.74, 4.74)
No of patients seen/consulted in a week:		
<10	9	9.0,CI (3.39, 14.61)
10-30	14	14.0 CI(7.2,20.8)
30-50	14	14.0 CI(7.2,20.8)
50-100	28	28.0, CI(19.2, 36.8)
>100	35	35.0, CI (25.65,44.35)

Frequency of placebo use

More than 90% of the clinician used placebo in their clinical practice. (38% of them used in less than one percent of their patients, 45% about 1-10%, and eight percent in more than ten percent) nine percent reported they never use placebos(table 2). There was no significant difference in frequency of placebo use when we compared younger clinicians (<35 years old) with older clinicians (>35 years old) with p value 0.0104, neither with the years of clinical experience clinicians have with p value of 0.638. There were also no significant difference in frequency of placebo use and various clinical specialties (P = 0.2914), various practice settings, like working in medical colleges or government hospitals or private clinics (P = 0.0453), highest degree obtained by clinicians (P = 0.0149) and number of patients seen/consulted by clinicians in a week (P = 0.0737).

Table 2: Age group and believes/ attitude about placebos:

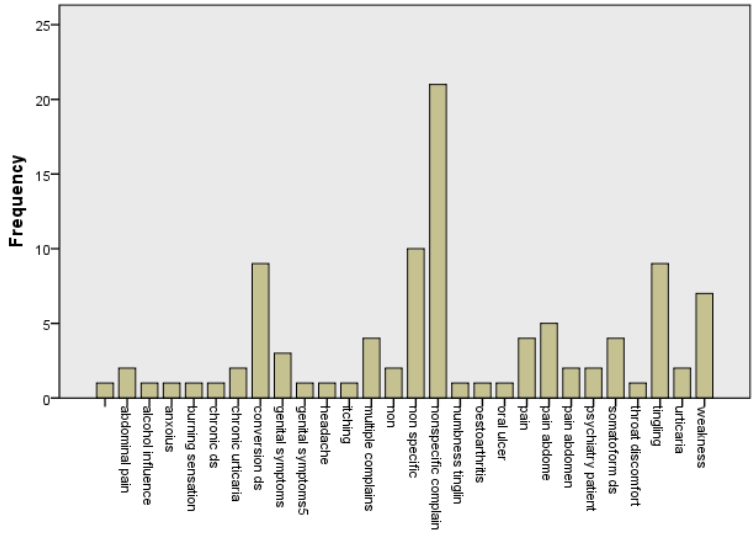
	Age<35 years	Age>35years	P value
Psychological effects behind the efficacy of placebo	43	13	0.00001*
Placebos should be permitted if research shows its efficacy and safety	48	12	0.00001*
No interference in decision of placebo use by colleagues	17	13	0.43
Placebo used to calm complaining pt	25	06	0.0002*

Statistically significant (p<0.05)

Clinical scenario where Placebos used

Clinicians used placebos in a variety of clinical conditions. The most common reason in our study was for nonspecific symptoms. (31% of total placebo use) followed by unexplained tingling sensation and conversion disorders nine percent of each. Additional reasons are mentioned in graph 1.

Graph 1: Clinical scenario where Placebos used.



Information given to Patients

About 25% of clinicians said to their patients “it is a medicine with no side effects”. 24 % said it’s an alternative medication, 24% said it is a medication with no specific effects, 21% said it is a medication with no side effects, 16% disclosed saying nothing to their patients. None of the clinicians mentioned “placebo” in prescription, however, one fourth used the term symptomatic management. There was no significant difference in age group of clinicians and information given to patients (p = 0.1710).

Perceived efficacy of placebo

On a efficacy scale of 1-10, fifty seven % of clinicians said its efficacy was 0-5, 34% said it was 5-8, while one percent said its efficacy was more than 8.

Circumstances of placebo use

About 31% of cases placebo was used to calm complaining patients, 29 % as a supplement of medications, 12 % in place of medication where medication use is not justified, 14 % used as diagnostic tool (table 3). Significant number of younger clinicians (<35 years old) used placebos to calm complaining patients with p value of 0.0004 (Table 2).

Adverse effects of placebo reported by clinicians

About 50% of the clinicians said they encounter adverse effects related to placebo in less than one percent of their patients, 37 % clinicians said it was in 1-10% of their patients, while 10 % said it was noticed in more than 10% of their patients.

Perceived therapeutic mechanism of placebo

Fifty six percent of clinician believed that psychological effect was the mechanism behind placebo effect, 15 % thought it was “feel good factor”, 12% thought it may be unexplained factors, ten percent thought

it may be pharmacological mechanism behind the therapeutic action. Significant number of younger clinicians (<35 years old) believe in psychological effects behind the efficacy of placebo with p value of 0.0000 (Table 2.)

Clinicians views regarding placebo Use

Only six percent of the studied clinicians said that placebo use should be banned. The rest said that placebos could be allowed in certain situations, like, if clinical research supports (60%), experience in the department shows its efficacy and safety (28%) and after notifying the patient that he/she is receiving a placebo (16%). Significant number of younger clinicians (<35 years old) supports that placebos should be permitted if research shows its efficacy and safety with p value of 0.00001 (Table 2).

Perceived patients disappointment on placebo use

While responding to the question, whether their patient would be disappointed, if they come to know that they are provided placebos, 31% said "I do not know", and 33% said "mostly no", 25% said "few of my patient" and 20% said "yes many of my patient"

Encouragement on use of placebo

Fifty percent of clinicians prefer not interfere their colleagues/students regarding this issue. 46% said they will encourage if scientifically justified only four percent prefer not to encourage. There was no significant difference in age group of clinicians and their views regarding encouragement of placebo use (P = 0.4932).

Effectiveness of placebo in different genders

Placebo was found to be effective in more than 83% of female patients, while only eight percent of male patients responded to it. There was no significant difference between sex of the patients and frequency of placebo use (P = 0.0105).

Clinicians' response to whether they themselves would have undergone a placebo if were aware of it

Half of the clinicians said they, themselves would have undergone a placebo, if were aware of it, while half of them said "No"

Types of treatment used as placebos

Clinicians used many substances as placebos. The most frequently used placebos were multivitamins for nonspecific complains and viral diagnoses (32%), analgesics for non-specific tingling /pain (27%), topical emollients/soothing agents for nonspecific pain/burning sensations (17%). Others were antibiotics for cold, multivitamins for unexplained weakness, some ayurvedic preparations for non- specific symptoms and so on.

DISCUSSION

The use of placebo treatment has received more attention in clinical trials; its use in clinical practice is ethically and legally controversial. Little is known about the pattern, frequencies, believes, experiences, attitudes and factors affecting placebo use in day to day practice of Nepalese clinicians. Our study shows that more than 90% of Nepalese clinicians prescribe placebos in routine patient care in a comparison to 2008 study of Chicago academic internists (45%) and the Tilbert study (46%–58%) [4, 5]. Historically placebos often were used to relieve pain or other symptoms that has no medical/scientific explanations [3]. The most common reason for placebo use in our study was nonspecific symptoms in almost one third of the cases compared to antibiotics for viral illness (40%) in study by Kermen R et al [8]. About three fourth of the clinicians told their patients that they are giving some kind of medication which will help in recovery. More than 50% of studied clinicians believed in therapeutic potential of placebos. About one third reported the efficacy of 5-8 on a scale of 0 to 10. In a systematic review Fassler et al reported that up to 50% of physicians and nurses (16-50%) believed that placebos are often or either or usually effective [9]. In one third of cases placebo was used to calm complaining patient and in one third as a supplement of medications compared to Kerman et al, where it was for unjustified demand for medication in 32% cases and to calm patients in 21% of cases [8]. Three fourth

of physician believe the psychological mechanism or feel good factor behind the efficacy. More than ninety percent supported the use of placebos in clinical practice, with the common consensus, if research or clinical experience in the department supports it, six percent of clinicians said it should be banned as it may be harmful to patient's health or may impair doctor patient's relationship. Placebo was found to be more effective in female patient as in other studies [4, 5, 8]. More than 90% clinicians prefer to use placebo over giving no treatment compared to 61% of physicians in a study by Kermen R et al [8]. Clinician's response to the question whether they themselves would have accepted placebo, if they knew it, was 50-50. The most common form of placebo treatment reported in our study is multivitamin followed by an antibiotic which raises ethical questions, although ethics of placebo in clinical practice has received less attention. Furthermore, overuse of medications can contribute to drug resistance and undesirable side effects like antibiotic associated diarrhea. In addition, according to Bjelakovic et al multivitamins and antioxidants can be harmful [10]. None of the clinicians use the word "placebo" in prescription or patient's record, compared to two percent physicians in Kermen study [8]. However, one fourth used the term symptomatic management. The deception with placebo use can conflict patients autonomy and loss of trust to clinicians with serious consequences. However, It has been said that sustained disclosure may lead to extinction of placebo effect, however if a patient is asking about the nature of treatment he is getting and how it is going to help him, clinicians should response honestly [11]. Bostick et al recommends that physicians may use placebos for diagnostic or treatment purposes only after notifying him and if he agrees to it [2]. It has been claimed that if properly handled placebos can be boon to busy clinicians and their patients [12]. The debate which surfaced the medical literature about ethics of placebo in clinical medicine, started in 19th century seems to continue. Our study describes the present reality of placebo use in clinical practice in a metropolitan city of Nepal.

LIMITATIONS

Structure of the questionnaire was mainly multiple choice and many were adopted from other studies of placebo use, which may not represent Nepalese clinicians beliefs/thoughts regarding placebo in details.

CONCLUSIONS

The extent of placebo uses and believes about it in clinical practice is not well known. In our study, more than 90% of studied clinicians use placebo in day to day clinical practice. Nepalese clinicians perceive placebos as therapeutic tool either as supplementary or a principal treatment modality and most of them support the use of placebo, if research or experiences in the department support the efficacy and safety. Clinicians are usually not transparent to their patients about placebo. A better understanding of the placebo is of importance, as it has great impact in clinical practice.

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