ETHICAL ASPECTS OF PLACEBO ("SHAM") SURGERY

OBJECTIVES:

- Understand the definition of placebo ("sham") surgery and its accepted indications
- Identify the major differences between medical placebos and sham surgical procedures
- Identify the ethical implications of sham surgery and the proposed benefits it may provide in orthopaedic research
- Understand the ethical criticisms against sham surgical procedures

The use of placebo or sham surgery controls in randomized trials of surgical interventions has been employed in a limited fashion in orthopaedic research but is not without controversy. The debate over sham surgery controls involves two predominant issues. The first is whether a randomized clinical trial with sham surgery control is a scientifically superior method to test either novel or questionably effective interventions for orthopaedic conditions. Secondly, one must ask whether the risks to subjects in randomized clinical trials with sham surgery controls is reasonable in relation to the potential benefit to the subjects and to society. Some ethicists believe that a placebo surgery should be used as a control condition specifically when testing a novel surgical intervention. Unlike the inert placebos used in pharmacological trials, sham operations involve cutting into the human body and the administration of active drugs such as antibiotics and anesthetics. As a consequence, a series of moral and ethical concerns have been raised, including the use of deception, the violation of the doctor-patient relationship and a deep seated cultural ‘distaste’ for conducting surgery for reasons other than essential treatment.

Slides 3-6: Case

Dr. Janus is an orthopaedic surgeon specializing in arthroscopic surgery. Lately, he has treated many older patients with osteoarthritis in their knees. Patients continue to request this procedure hoping to improve their mobility.
However, in reviewing the current literature, Dr. Janus learns that the type of arthroscopic knee surgery he has been performing routinely (arthroscopic lavage and debridement) has been shown to provide no benefit over placebo. In fact, a strong placebo effect has been suggested.

Mr. Jimson is a 70-year-old retiree living on his limited pension. He suffers from advanced osteoarthritis in his knees and would do anything to be able to walk more easily on his own. He enters Dr. Janus' office one day requesting arthroscopic surgery for the osteoarthritis in his knees. He says to Dr. Janus, “My best friend had this surgery last month, and he’s already getting around the golf course great! He says this surgery was the best thing he ever did for himself. I sure would love to be able to keep up with him now. What do you say doc, can you do this surgery for me?”

**Slides 7-14: Questions, Issues, and Topic to Consider**

What are the practical issues?
What are the financial issues?
What are the ethical issues?

The scenario described in this vignette is frequently seen by orthopaedic surgeons. Arthroscopy of the knee is one of the most common orthopaedic procedures performed in the United States and has resulted in significant reduction in patient pain and improvement in function. However, some conditions and symptoms, such as pain from osteoarthritis in the absence of mechanical symptoms such as locking, catching, and giving-way, have not been found to improve following arthroscopy. Most clinical series have shown success rates between 50 and 75 percent. It is this lack of success that prompted the Mosely study in 2002 at Houston Veteran’s Affairs Medical Center.

- Mosely et al. investigated the benefit of arthroscopic surgery in 180 older adults, with a mean age of 75 years, suffering from osteoarthritis of the knee. Patients were randomized to three study arms:
  - Arthroscopic debridement
  - Arthroscopic lavage
  - Sham operation consisting of three 1-cm portal incisions.

- The primary outcome measure was knee pain two years after surgery.
- The Mosely study found no significant difference between treatment arms of the study, thus concluding that routine arthroscopic lavage and/or debridement was no better than the sham procedure.
Do the results of the Mosely study change your opinion of the benefit of arthroscopic surgery of the osteoarthritic knee?
What other information would you need to know before recommending knee arthroscopy for a patient with osteoarthritis of the knee?

Critics of this study point out that:

- Flexion weight-bearing radiographs were apparently not done to fully discern the degree of cartilage wear.
- X-rays were not taken of the entire lower extremity to assess the mechanical axis of the limb.
- The study population was comprised largely of males which may not be representative of the general population.
- The degree to which the patients experienced mechanical knee symptoms was not well-described.
- The authors used the Knee-Specific Pain Scale as their primary end point despite the fact that this is a non-validated measurement that was “created for this study.”

Therefore, there was harsh criticism from many orthopaedic surgeons following the publication of this controversial study.

This study suggests that routine knee arthroscopy for osteoarthritis of the knee is not clinically beneficial to any significant degree in patients who resemble those who participated in the Mosely trial. Considering the financial burden this procedure puts on an already stressed U.S. medical system, unless other studies offer a contrary conclusion, orthopaedic surgeons should exhaust other, less expensive, less risky, and more effective treatment options for patients with osteoarthritis of the knee.

The methodological justification for a sham surgical control in this study was based on the fact that approximately 650,000 arthroscopic procedures for osteoarthritis of the knee were performed annually in the United States despite the fact that there was only inconclusive evidence available for the efficacy of the procedure. This is especially relevant considering that over $3 billion was spent annually to treat osteoarthritis with knee arthroscopy. The results of this randomized, controlled trial indicated that there were no statistically significant differences between the operated upon and placebo groups in terms of the outcome measures utilized. As a result, the authors concluded that arthroscopy was an ineffectual treatment for knee osteoarthritis.
**Slide 15: Questions**

*How do you define equipoise?*

*What is the role of equipoise in research involving placebo ("sham") surgery?*

This case raises questions about the potential clinical benefit and ethical ramifications of placebo-controlled trials in surgery. “Equipoise” is a central element when considering the use of placebo controls in a research protocol. Equipoise refers to that state of uncertainty about which component or “arm” of a research trial may have greater benefit or harm. Equipoise represents a state of genuine and credible doubt about the relative therapeutic merits of some sets of interventions that target a specific medical condition. The current gold standard of a medical intervention is the double-blind randomized-control trial where the therapy of interest is compared to the accepted treatment or to a placebo. It is widely accepted that the purpose of evidence-based medicine is to implement medical therapies as “proven” by multicenter randomized controlled trials (RCTs).

**Slide 16: Questions**

*How do you define placebo?*

*Under what circumstances is it allowable to use a placebo in a study?*

The term “placebo” is commonly used to describe any substance or procedure a patient accepts as therapy, but which has no known mechanism other than a patient’s belief in its value. The use of a placebo in a study is allowed under several circumstances:

1. There is no standard treatment.
2. New evidence has raised doubt regarding the benefits of standard therapy.
3. Effective treatment is not available because of cost or short supply.
4. The patient population is refractory to standard treatment.
5. An add-on treatment is being compared to standard therapy.
6. Patients provide informed refusal of standard therapy for a minor condition.

**Slide 17: Questions**

*Under what circumstances is it acceptable to use a placebo ("sham surgery") in a clinical trial?*

*Was it acceptable to use "sham surgery" in the Moseley osteoarthritis trial?*
The term “sham surgery” is often used when a placebo procedure is used in a surgical trial. The word “Sham” derives from a Middle English variant of the word “shame”. Sham surgery in clinical research should not be confused with sham surgery in clinical care, where it has no legitimate role. As the word suggests, sham surgery has historically been ethically controversial. There is an essential ethical requirement that the sham surgery must pose less risk to subjects than the procedure being tested, which eliminates certain groups from participation in sham-controlled surgical studies:

- The critically ill
- The acutely traumatized
- Patients whose conditions can be successfully resolved with a proven safe and effective procedure.

Patients may experience the benefits of the surgical process despite the lack of a therapeutic intervention resulting from:

- Hospitalization
- Increased pain management
- Ancillary treatment
- Increased sympathy that surgery elicits from all caregivers

These benefits have been shown to include improvement in pain and quality of life measurements. Subjective measures such as function and pain are frequently difficult to gauge objectively. The variable and subjective nature of pain and function lack the quantifiability of objective measurements such as grip strength or range of motion. Clearly, the sham procedure used in clinical research must pose less risk to subjects than the procedure being tested.

Sham surgery is considered acceptable in a clinical trial when:

1. There is skepticism regarding the therapeutic merits of a particular surgical treatment.
2. There are disagreements about the perceived benefits of a particular procedure.
3. The benefits of a procedure might be due to the “experience of surgery” and the postoperative care regimen.
4. The risks are reduced as far as possible in the sham surgery arm without compromising the trial design.
5. There is a lack of a superior alternative therapy.
The methodological reasons in favor of sham-controlled surgical trials are reinforced when there is no clear physiological basis for why a given surgical procedure might work, as in the Moseley osteoarthritis trial.\textsuperscript{1}

By definition, a placebo control means that the subjects who receive the placebo medication are receiving a substance with no known medical benefit. The so-called “sugar pill” carries no risk in and of itself. Placebo medications are also different from sham surgery in that they do not directly cause the subject to suffer pain. In contrast, any sham procedure carries risks such as bleeding, infection, and anesthesia complications, which are present in every surgical intervention whether it is for a therapeutic purpose or intended as a placebo. Unfortunately, sham operations need to cause some pain and to appear like the “real” operation or subjects will think they did not have the experimental intervention, and the concept of a placebo control will be lost. The surgeon who participates in a placebo-controlled surgical trial must also actively strive to deceive the subject. This calculated deception is the basis for the potential power of the sham operation to influence the subject’s condition.

Critics of sham surgery point out that the use of a procedure that could cause harm without offering a compensating physiologic benefit poses ethical problems and might violate the principle of non-maleficence. For example, the well-known ethicist Ruth Macklin concluded that “performing surgery in research subjects that has no potential of therapeutic benefit fails to minimize the risk of harm.”\textsuperscript{8} Those critics who oppose sham operations state that if an intervention of proven effectiveness already exists, and if there is genuine disagreement among medical experts as to whether the study intervention is equally or more effective, then the study intervention must be compared against the established alternative. If no such established intervention exists, then, and only then, can the study intervention be compared against a benign placebo. The implicit assumption seems to be that we would not want to have our symptoms relieved by a procedure that draws upon our state of mind instead of succeeding through some intrinsic physiologic effect of the intervention itself.

However, it can be argued that we should learn how to enhance the beneficial psychological effects of a sham procedure rather than eliminate them. The real question becomes, “should our focus be to reduce or to stimulate placebo effects?” One may argue that it is unethical not to use sham surgery to thoroughly evaluate a surgical procedure before it is introduced into clinical practice. Unfortunately, there is no governing body that oversees the safety and efficacy of surgical procedures as the U.S. Food and Drug Administration (FDA) does in the evaluation of a novel
pharmaceutical agent. Considering the financial burden various osteoarthritis treatments put on the U.S. medical system, orthopaedic surgeons should exhaust less expensive, less risky, and more effective treatment options for the vast majority of orthopaedic conditions.

**Slide 18: Case conclusion**

- Dr. Janus performed an arthroscopic debridement on Mr. Jimson’s knee after a thorough discussion of the risks and potential benefits of the procedure including the need for further surgery.
- There were no complications to the procedure.
- At the 3-month postoperative visit, Mr. Janus stated that he felt considerably better with less knee pain and swelling. He told Dr. Janus that he was glad he underwent the surgery.
- At 1-year after surgery, Mr. Janus began experiencing recurrent knee pain but no locking or catching symptoms.

**Slide 19: Question and Summary**

*Now, what would you do?*

What should the physician do if a patient in pain who is a good candidate for the intervention comes in and asks for the procedure, saying that he knows that the operation helps only about half the time?

On the one hand, a formerly accepted but challenged article leads Dr. Janus to think that the surgery is not warranted or at best may be successful due to a placebo effect. On the other hand, he has provided arthroscopic surgical care to other patients whose conditions resemble Mr. Jimson’s with apparent success. The patient has requested the treatment and the physician believes that it can be safely done with a beneficial outcome. What is the physician to do?

In the scenario presented, Dr. Janus performed an arthroscopic debridement on Mr. Jimson’s knee after a thorough discussion of the risks and potential benefits of the procedure including the need for further surgery. At the 3-month postoperative visit, Mr. Janus stated that he felt considerably better with less knee pain and swelling. Unfortunately, one year after surgery, Mr. Janus began experiencing recurrent knee pain but no locking or catching symptoms, similar to what the patients in the Mosely trial experienced.

In considering any treatment option, an accurate diagnosis is imperative based on a careful history and physical examination with appropriate
radiographic studies performed. The physician should consider all options of non-invasive and invasive care once a diagnosis is made. Conservative (nonoperative) treatment should be considered initially, followed by more invasive options if they do not bring about improvement. These alternatives should be reviewed and the risks and benefits given careful consideration and explained to patients in terms they can comprehend. The treatment must first do no harm and be of benefit to the patient from an ethical perspective. The concerns and goals of the patient need to be explored relative to the issues presented by the available literature. Informed consent for any treatment is mandatory, yet is associated most commonly with surgical procedures. Whenever a treatment plan is considered, the experience of the physician should also be considered and ample time devoted to the perspective of the patient. This conversation should be documented as part of the informed consent process.

The placebo effect of any treatment should be considered as well. Despite the fact that one can argue that the placebo effect places the patient at risk for questionable gains, one can also argue that the benefits often outweigh the risks. The ethical issues of informed consent, beneficence and non-maleficence need careful consideration in all clinical decisions. Shared decision making, patient-centered health care principles, and cost-effective medicine should be utilized to tailor the care to the individual patient.

As we go forward, decisions like these will continue to be an issue for patients and physicians. Ethical decisions will be pressured by cost considerations and value-driven health care. In the end, physicians may not be allowed to perform certain procedures if treatment choices are dictated by third-party payers despite an ethically sound approach by the treating physician and an informed patient.

References