UNIVERSITAS INDONESIA

EFFICACY OF ORAL PARACETAMOL COMPARED WITH ORAL KETOPROFEN FOR PAIN MANAGEMENT IN OFFICE HYSTEROSCOPY

1ST VERSION JUNE 20TH 2020

RESEARCH PROPOSAL

Andika Widyatama

SUPERVISOR:

dr. Tricia Dewi Anggraeni, SpOG(K)

Dr. dr. Vivian, Sp.FK, Ph.D

RESIDENCY PROGRAM

OBSTETRICS AND GYNECOLOGIST DEPARTMENT

FACULTY OF MEDICINE UNIVERSITAS INDONESIA

JAKARTA

2019

Study Protocol

This study used a double-blind randomized clinical trial to assess the intensity of pain during the OH procedure and cramping within 30 minutes after the OH proce-dure in the group given paracetamol 1000 mg orally compared with ketoprofen 100 mg orally. This study also evaluated the side effects that occurred in both groups. This re-search was conducted at the OH clinic at RSUPN Dr. Cipto Mangunkusumo Kintani over a period of 2 years. All patients who will undergo an OH procedure are checked for eligibility when they arrive and are offered to be research subjects if they meet the inclusion criteria, namely women who underwent an OH procedure and were not using analgesics in the 1 month before joining the study. Individuals are not eligible if they have exclusion criteria, namely women with a history of asthma and women with a history of allergies to paracetamol or NSAID class drugs. Patients were given an ex-planation of the research procedures and asked for informed consent, if they were willing to take part in the research. This research was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia (ND – 0054/UN2.F1.DEPT.25/PDP.01/2022).

Research subjects were divided into two groups. The first group received the an-algesic paracetamol tablet at a dose of 1000 mg orally and the second group received the analgesic ketoprofen tablet at a dose of 100 mg orally, each consisting of 30 subjects according to the sample size calculation formula. The total sample size of 60 patients (30 per group) was determined based on previously published data and feasibility considerations. According to variability reported in comparable trials by Issat et al. (SD ≈ 1.65) and Terán-Alonso et al. (SD ≈ 2.86), a group size of 30 participants per arm provides approximately 80% power ($\alpha = 0.05$, two-sided) to detect a mean difference of about 1.2 visual analogue scale (VAS) points under the lower-variance assumption (Issat et al.) or approximately 2.1 VAS points under a more conservative variance (Terán-Alonso et al.). [1, 2] Therefore, a total of 60 participants was considered a reasonable and practical compromise between statistical power and study feasibility. Subject allocation was carried out by block randomization so that an equal number of subjects were obtained in both groups. The block size was determined at 6 subjects. Randomization was carried out by computer and a randomization code was obtained by a research assistant. Then, the medicines are removed from each factory packaging, then put into sterile medicine plastic with serial numbers 1-60 which are kept by the nurse. The nurse handed over the medicine in the plastic according to the serial num-ber to the research subject patient 1 hour before the OH procedure. Research subjects and researchers did not know the type of drug given (double blind).

All OH procedures were performed using a Karl Storz Bettocchi Office Hyster-oscope (Germany) with an outer diameter of 3.5 mm. Vaginoscopy approach was ap-plied, without the use of a speculum or tenaculum. The uterine cavity was distended with 0.9% normal saline at a pressure of approximately 70 mmHg using a continuous flow system. No cervical preparation (such as misoprostol) was administered prior to the procedure. All procedures were conducted by the same experienced operator.

The primary outcome of this study was the intensity of pain during the office hysteroscopy procedure, measured using a VAS at the time when the hysteroscope entered the external cervical ostium. The secondary outcomes included cramping pain within 30 minutes after the procedure, side effects associated with the administered analgesic, patient comfort, and the occurrence of vagal reflexes.

Assessment of pain intensity during the procedure (when the hysteroscope in-strument enters the external cervical ostium) and cramping within 30 minutes after the OH procedure will use a VAS. Patients are asked to determine the VAS value in the questionnaire according to the intensity of pain and cramping they feel. Side effects of drug administration, comfort, and vagal reflexes will be assessed using the same questionnaire.

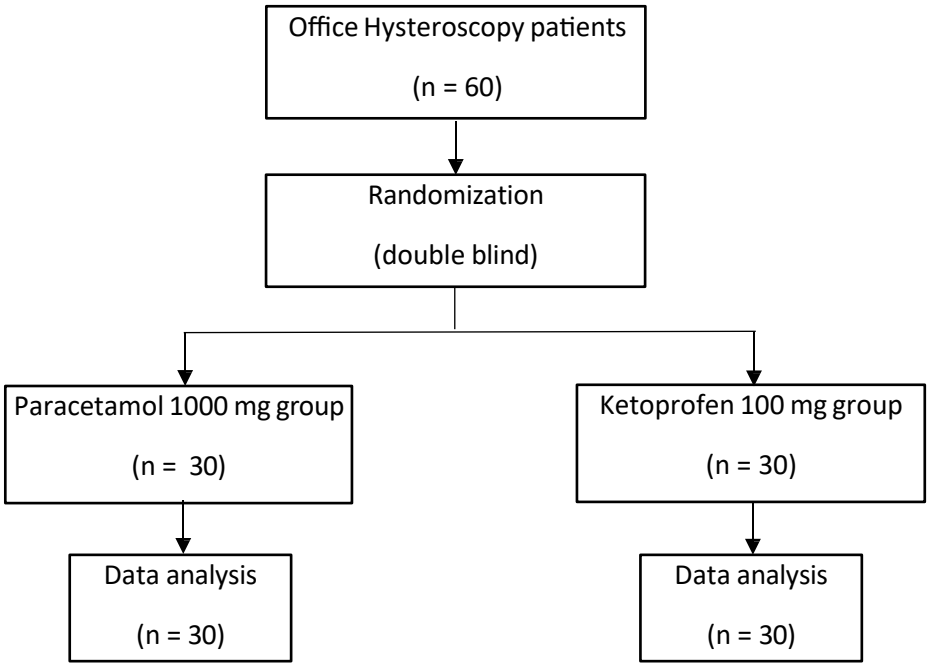

Figure 1. Research Flow Diagram.

References

1. Issat, T.; Beta, J.; Nowicka, M.A.; Maciejewski, T.; Jakimiuk, A.J. A randomized, single-blind, placebo-controlled trial for pain reduction during outpatient hysteroscopy after ketoprofen or intravaginal misoprostol. J Minim Invasive Gynecol. 2014; 21(6):921–927.

2. Terán-Alonso, M.J.; Navarro-Gómez, M.; Rodríguez-Jiménez, B.; Pérez-González, M.; Abadía-Cuchí, N.; Bajo-Arenas, J. Evaluation of pain in office hysteroscopy with prior analgesic medication: A prospective randomized study. Eur J Obstet Gynecol Reprod Biol. 2014; 183:22–26.

Statistical Analysis Plan

Data analysis was carried out using IBM SPSS version 25.0. Data distribution was assessed for normality. The age variable was normally distributed, while the procedure duration, VAS pain, cramping, and comfort scores were non-normally distributed. Between-group comparisons were originally analyzed using unpaired t-tests. Although several variables did not follow a normal distribution and non-parametric methods would have been more appropriate, the reported p-values remain unchanged, and all results were non-significant. Categorical data (such as side effects and vagal reflexes) were compared using Fisher's exact test. Because only two treatment groups and a limited number of predefined outcomes were compared, no formal correction for multiple comparisons was applied.