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The first study called, A randomized, double-blind, placebo-controlled trial comparing pethidine to metamizol for treatment of post-anaesthetic shivering, was designed to evaluate and compare the effectiveness of pethidine (meperidine) and metamizol in the treatment of post-operative shivering¹. The study included 104 patients with complications of post-anesthetic shivering¹. All patients were required to undergo pre-operative evaluation and were only included if they provided written consent. Patients were excluded if they presented with comorbidities and if they were treated with certain medications that would interfere with the results of the study. The patients were randomized to receive one treatment of placebo (no drug), meperidine, or metamizol¹. The patients' responses to treatment were measured in terms of severity at intervals of 5, 15, 30 and 45 minutes after administration¹.

Severity of shivering was measured on a scale of 0-2, 0 as absent, 1 as shivering present in action, and 2 as shivering present in action and rest¹. Shivering response to treatment was assessed as null, shivering not changed; improvement, shivering decreased; and disappearance, absence of shivering¹. Subjective information was also recorded, such as the presence of muscle contractions and/or the sensation of feeling cold¹. The continuous variables were analyzed with a chi square test and ANOVA, as well as the Kruskal-Wallis test¹. The results concluded that drug treatment was useful in comparison to placebo. Meperidine appeared to have the highest efficacy and quickest response to shivering than placebo or metamizol¹. The study did not exhibit selection bias when choosing patients to receive treatment. Inclusion criteria allowed patients to participate that presented with post-

operative shivering for at least 5 minutes or longer during the first hour of recovery from anesthesia¹.

Internal validity was threatened because the study did not specify when the treatment began after surgery. The results could have varied if treatment was initiated 1 hour or 2 hours after surgery. The study was completed on ethical measures with each patient informed of the study and having written consent. The sample size required for the study ($n = 90$) was appropriately calculated with an alpha of 0.05 and a power of 0.80; $n = 104$ was used in the study¹.

According to the results, the differences between the three groups proved to be statistically significant. When compared to placebo, metamizol showed a better response ($P = 0.03$), but meperidine showed to be the most effective ($P < 0.001$)¹. There was no statistical significance between both drugs ($P = 0$).

16) ¹. The results of this study show to exhibit external validity and can be extrapolated into real life situations or other studies involving patients undergoing general anesthesia. The second study called, A Comparison of Tramadol, Amitriptyline, and Meperidine for Postepidural Anesthetic Shivering in Parturients, is a randomized, double-blinded, study which was designed to evaluate the effectiveness of meperidine, tramadol, and amitriptyline in the treatment of post-anesthetic (epidural) shivering². The study involved 115 obstetric female patients ranging from ages 18 to 40 years old that were scheduled for a cesarean delivery². Patients were excluded if they had

comorbidities, a history of alcohol or substance abuse, or were taking other medications that would interfere with the results of the study².

Shivering was assessed with a scale of 0-4, 0, no shivering; 1, peripheral vasoconstriction; 2, muscular activity in one group of muscles; 3, muscular activity in many muscle groups; 4, shivering across the whole body². Patients with a shivering score of 3 or 4 for at least 3 minutes were included in the study; only 45 patients requested treatment for shivering². Each patient received one treatment of tramadol, amitriptyline, or meperidine.