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B R U G M A N N

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At the attention of the EMA

Brussels, 14 July 2021

To whom it may concern,

EudraCT clinical trials results – clinical trial with no patients included

Sponsor	Centre Hospitalier Universitaire Brugmann		
Title	Comparison of two methods of administration of the epidural, by programmed intermittent boluses or continuous perfusion, on the incidence of cesarean sections and instrumented deliveries in primiparous women.		
EUDRACT	2016-000889-35	**Sponsor reference**	CHUB-PIB

I hereby notify you that the study identified above was closed on 06 February 2018 without including any patients.

The reasons for not including patients in this clinical trial were;

- Principal investigator left the institution
- The recommendations regarding the standard of care in obstetric analgesia have evolved, making the protocol unfeasible

The study design is annexed to this letter.

I remain at your disposition for further information on this clinical trial.

Kind regards,

Pr Van der Linden

Title	Comparison of two methods of administration of the epidural, by programmed intermittent boluses or continuous perfusion, on the incidence of cesarean sections and instrumented deliveries in primiparous women.
EudraCT	2016-000889-35
Sponsor	CHU Brugmann
Justification	The epidural has been recognized for many years as the most effective analgesia method for obstetrical labor. Several different administration protocols have been evaluated over the years with the aim of reducing side effects. Epidurals have been incriminated in the increase of instrumented births. It is indeed possible that the motor block induced by the epidural reduces the pelvic tonus and the ability of the mother to push during the second stage of the labor. Furthermore, this motor block might lead to a ill rotation of the foetal head within the pelvis, which could lead to instrumentation (suction cups, forceps). In 2001, the COMET study showed that the use of low anesthetics concentrations decreases the motor bloc and allows to increase the rate of vaginal deliveries and decrease the rate of instrumented births. In the investigator's institution, a study also provided results that showed that the use of a low concentration of local anesthetics (as opposed to a higher concentration) tended to decrease the instrumentation and cesarean sections rate in the institution's population. However, the optimal administration mode of the local anesthetic in the epidural remained unknown. There had been a growing interest for a new method of administration of the solution within the epidural, by programmed intermittent bolus. This method allowed a better distribution of the local anesthetics in the epidural space, compared to a continuous perfusion. Several studies have showed that this mode of administration allowed to decrease the local anesthetics injected doses and give a better maternal satisfaction. A meta-analysis performed in 2013 showed a tendency towards the decrease of instrumented deliveries with this method. Sadly, no studies had the power necessary to prove this point with certainty. This clinical trial therefore focusessed on the relationship between the use of epidural with programmed intermittent boluses and the rate of instrumented deliveries and cesarean

	sections. The exact mode of administration of boluses was also subject to discussion in the literature. One can question whether it is preferable to administer smaller boluses more frequently or larger less frequent boluses. The goal of this study is to compare the incidence of instrumented deliveries (suction cups, forceps) and caesarian sections according to the mode of epidural analgesia received: either a continuous perfusion with small concentrations of local anesthetics, either programmed intermittent boluses of the same solution.
Primary outcome	To determine the rate of instrumented deliveries and caesarean sections according to the administration mode of the local anesthetic in the epidural.
Secondary outcome	- To evaluate the quality of the analgesia according to the administration mode, based on the number of required interventions from the anesthetist - To evaluate maternal satisfaction - To evaluate the presence of a motor block at the beginning of the second stage of labor, defined as the time of complete cervical dilatation
Phase	II
Study design	Controlled, randomized, double blind clinical trial with parallel groups.
Inclusion criteria	•Women over 18 years of age •Primiparous •Pregnancy over 36 weeks of gestational age and <42 weeks of gestational age •Written informed consent •Cervical dilatation between 3 and 6 cm at recruitment •Single pregnancy •Foetus in cephalic position
Exclusion criteria	•Participation refusal or epidural contra-indication •Multiparous •Allergy to the products used •Twin pregnancy •Height <1m55 and/or narrow pelvis, as shown by imagery •Language barrier

	•Patients with a BMI superior or equal to 35 (computed with the weight at the beginning of the pregnancy) •Cervical dilatation at recruitment <3 or >6 cm •ASA 3 or 4 •Foetus in transverse or seat position
Recruitment goals	392 patients per group.
Actual recruitment	0 patients
Study duration	From 26 May 2016 to 06 February 2018
Study location	CHU Brugmann