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Study on Clinical Experimental Methods of the Laborvue Delivery Monitor

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Abstract: Study the clinical effectiveness of Laborvue delivery monitor in Guangzhou Lianyin Medical Technology Co., Ltd., in order to prove that it can reduce unreasonable non-medical indication cesarean section and inappropriate vaginal delivery, realize continuous noninvasive monitoring of multiple parameters of labor process, guide clinical decision and improve natural delivery rate. The design of this research scheme followed the guiding principles of Medical device Test Design. Compared with the main clinical evaluation indexes of LaborPro delivery monitor, the research scheme selected two main clinical evaluation indexes of cervical dilatation and fetal position. The data of control group and experimental group were analyzed by statistical software. There was a linear and highly positive correlation between the data of control group and the data of experimental group. To verify the clinical effectiveness of Laborvue delivery monitor. The clinical research scheme was determined by parallel control trial, the main contents of which were randomization design, incomplete blindness and positive control. The selection criteria and exclusion criteria were established, and the two main clinical evaluation indexes of cervical dilatation and fetal position were selected, and the sample size of each group was set to 95-104. The clinical trial method of Laborvue delivery monitor proposed in this paper has good innovation and applicability, and can be used in future registered clinical trials.

1. Introduction

In the 2018 National Health Commission survey, China's Cesarean section rate has been significantly reduced to 36.7%, but still with the World Health Organization in 1985 recommendations, there is a big gap, this means that there are unreasonable Cesarean section, which does not meet the medical indications. It not only wastes the use and allocation of medical resources, but also increases the long-term and short-term complications and mortality of mother and infant. In addition, in the delivery process, there may be unexpected circumstances, the need to detect the birth process: first, the fetus in utero changing, the most commonly used is the fetal monitor, can detect fetal heart rate, uterine pressure, fetal movement and other parameters. The second is the stagnation of the maternal labor process, the current use of vaginal finger or manual estimation of fetal head position and fetal head direction data, which is currently an urgent clinical problem to solve [1, 2].A

delivery monitor is needed to solve practical clinical problems, to monitor fetal data, but also to monitor the duration of labor, so as to minimize non-medical Cesarean section [3].

Clinical trial is an important process of three kinds of medical devices before they are listed on the market. It is necessary to evaluate their safety and effectiveness objectively [3].The Laborvue Delivery Monitor is an innovative three-class medical device developed by the state key research and development project of digital diagnosis and treatment undertaken by Guangzhou Lianyin Medical Technology Co., Ltd., this article intends to study the clinical experimental method of the new type of Labor Monitor.To validate the clinical efficacy of Laborvue Labor Monitor by comparing the clinical efficacy of Laborpro system from Trig healthcare in Israel with that of Laborvue Labor Monitor from liensign healthcare in Israel [4, 5].

2. The Laborvue Delivery Monitor

The second clinical trial was designed with a domestic Laborvue labor monitor whose main function is to monitor the position of the fetus and the orientation of the head during Labor [6], as depicted in the flowchart (Fig.1).The feature of this method is that AI technology is used to automatically acquire the standard section ultrasound image of the fetus. It can recognize the feature points of the image of the fetus, make the operation more simple and intelligent, and lower the threshold of the equipment The nine-axis sensor is embedded in the wireless b-mode ultrasound system, and the tire monitor is integrated to realize all parameters of the integrated monitoring process. At the same time, the structure of the equipment is more compact, the space occupied by the equipment is effectively reduced, the wireless operation is more convenient, the cost of the whole machine is reduced to one third of the similar products abroad, and the localization of the imported equipment is realized.

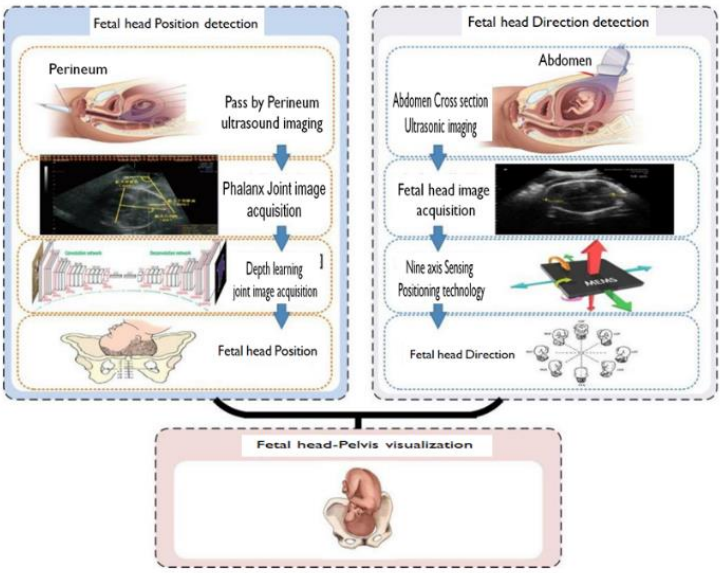

Figure 1: The Laborvue Delivery Monitor

3. Study on Clinical Trial Method

3.1. Parallel Control Test

The parallel control design has the characteristics of random, double-blind and parallel control. The main purpose of this clinical trial design is to provide reliable scientific evidence for avoiding

subjective errors and to reduce errors between the control group and the test group. This approach is generally preferred in clinical trial design. The key to implementing the control principle is to establish a good control group. To objectively set up the control group and the experimental group, to ensure the effectiveness of the control group intervention, we can analyze the clinical effects of each group and draw conclusions. The parallel control experiment can exclude the influence of time factor, that is, the control group and the experimental group get the clinical effect at the same time. The key point of parallel control trial is to ensure the balance between control group and experimental group can be compared. That is, all the factors that might influence the test results were the same between the control group and the test group, except for the main measures to be observed.

3.1.1. Randomization

Randomization of clinical trials, in which subjects are equally likely to enter the trialgroup, is designed so that the protocol is not influenced by either the researcher or the subject's subjectivity. On the other hand, this design can make the two groups of test data have the same factor, and have the comparability in the statistical analysis. Not following the randomized design, except for the factors that may affect the results between the control group and the test group, on the one hand, the covariance analysis may not be able to completely eliminate the error; On the other hand, it is difficult to evaluate the bias caused by the unknown error, so randomized design is generally recommended [7].

This research plan uses the randomized design, according to the experimental group and the control group the sample number accounts for 50% of the total sample number to enter the clinical trial, randomizes the subject to enter two groups, guarantees two groups the result influence factor to be consistent, the errors caused by the same factors can be neglected in data analysis.

3.1.2. Blind Method

If the group information of the experiment is made public, it will influence the researcher, the subject and the evaluator to some extent. The significance of the blind method lies in that it can't make the participants have subjective bias and avoid subjective error. There are three types of blind methods: complete, incomplete and incomplete. The design of blind method is more complex, so it needs a strict implementation scheme. The application must take into account the feasibility of the program, in accordance with ethical principles. There's a protocol in place to keep the subjects safe. In case of emergency, we can timely make relevant cases to understand the grouping information and the trial program, and take appropriate measures. Blind methods are not recommended for severe or complex cases.

This clinical research project uses the incomplete blind method, because the control group and the Test Group's instrument appearance has the obvious difference, the concrete structure and the use method also has the obvious difference, but the function is basically the same, and uses the b-ultrasound technique to determine the fetal position, so at this point, the subjects were blind, and the use of blind data audit.

3.1.3. Cross Reference

The control group included positive control group, Placebo Control Group and Blank Control Group. The Placebo Control Group and the positive control group were the most commonly used. The Positive Control Group had to use commercially available instruments or standard treatment. Its efficacy and safety have been clinically recognized, so the positive control group is given priority in the design of clinical trials. In order to set up the control group reasonably, it is necessary to make a comprehensive evidence-based evaluation according to the experimental instruments in the scheme,

to ensure that the errors of the methods will not cause the violation of the principles of scientific ethics and waste of human and material resources. Therefore here we choose to use the positive control method first.

To sum up, the design of this clinical study used parallel control test, the specific content of the randomized design, not completely blind, positive control. Referring to domestic and foreign studies since 2018, many hospitals in China have introduced Israeli LaborPro birthing monitor to carry out experimental studies, so this study uses Israeli LaborPro birthing monitor as a control group experimental device, so that the test has better security and data comparability.

3.2. Subject Selection

The subject refers to the selection of a group of subjects who meet the requirements from the prospective population of the test apparatus after considering factors such as the requirements of clinical ethics and the safety of the subjects themselves, so the subject should be representative of the sample. Whether the subjects can be selected or not depends on the selection criteria and exclusion criteria stipulated by the researchers. The premise of the successful implementation of the clinical trial program is to establish appropriate selection criteria and exclusion criteria. In the guiding principle, the selection criteria mainly consider the indication, the classification of diseases, the age range of subjects and so on. The purpose of exclusion criteria is to make the test objects have similar properties as far as possible, and to evaluate the test machine effect correctly by excluding the mixed elements that may bring about other possible effects. Some researchers [8] believe that the selection criteria and exclusion criteria for clinical trial protocols should be determined according to the purpose of the trial, and the selection of suitable test subjects should not only be representative of the sample, we also need to exclude subjects who may have influenced the course of the experiment and its results.

In summary, the inclusion criteria for this clinical trial design were: 42 weeks > Gestation > 37 weeks, Singleton, CEPHALIC presentation, absence of pregnancy complications and pregnancy complications, active stage of the first stage of Labor (Cervical Dilatation Measurement & GT; 3cm), the exclusion criteria were multiple births, women of Advanced Age (Age & GT; 35 years), gestational period > 42 weeks or gestational period < 37 weeks, infant weight ≥4 kg, abnormal soft birth canal.

3.3. Determination of Evaluation Index

The clinical trials of medical devices are different from the general scientific research. The physical properties of medical devices may be related to the authenticity of various diseases. The reasonable selection of evaluation index is related to the test result, the test quality and the test cost. The Evaluation Index reflects the influence of the device on the subject, which should be determined according to the purpose of the test and the expected effect of the device. Primary and secondary evaluation indicators and their observation purposes, definitions and measurement methods should be clearly defined in the clinical trial plan. The index types are divided into quantitative index, qualitative index and Grade Index. The main evaluation indexes are related to the purpose of the test, and can accurately reflect the validity or safety of the test instruments. The main evaluation indexes should be those that can be measured repeatedly, expressed by data and not decided by personal consciousness, and generally need professional recognition from relevant experts and guiding principles. In the design of clinical trial scheme, the number of subjects should be estimated according to the main evaluation index and the aim of the trial.

In this clinical trial, qualitative indexes are used, so the main evaluation indexes are cervical dilatation degree and fetal position. The traditional methods mainly judge fetal position and cervical

dilatation degree through vaginal examination and anal examination by midwives several times, at the same time, using the fetal heart monitor, real-time monitoring of labor. While traditional methods may increase the rate of puerperal infection, they may also lead to improper guidance of Labor, which may lead to inappropriate vaginal delivery or unreasonable Cesarean section.

3.3.1. Cervical Dilation

Cervical maturity is the main factor in the occurrence of childbirth. Up to now, cervical maturity is often reflected by cervical test scores in clinical practice. If the score is high, it means that the cervix is more mature, and the more dilated the cervix, the shorter and softer the cervix will appear. This is related to whether vaginal delivery is possible and whether Labor is active, and it is also one of the methods guiding clinical practice. Because each person's clinical experience is different, the measurement result is also different, therefore has the deviation to the cervix maturity judgment, at present does not have a recognized parameter to judge accurately analyzes the cervix maturity. Huang Yanyan et Al. [9] evaluated the cervical maturity by ultrasound, in which the width of the cervix as a related indicator of cervical dilatation, has a certain value in evaluating the cervical maturity and predicting the delivery time. It is suggested that perineal ultrasound should be used to measure the degree of cervical dilatation and fetal head depression to evaluate the progress of labor. Cervical dilatation refers to the distance between the two sides of the cervix. When the cervix dilates enough to allow the full-term head of the fetus to pass through, it means vaginal delivery is possible. Therefore, cervical dilatation is one of the important factors for natural delivery.

3.3.2. Fetal Orientation

In 2018, Haberman S [10] proposed that ultrasound diagnosis could be used during Labor, with a higher accuracy for detecting the head and direction of the fetus, and that it could be measured multiple times. Fetal position refers to the relationship between the indicative point of fetal presentation and the maternal pelvis, and fetal presentation refers to the part of the fetus that enters the pelvis first. Generally speaking, in full-term fetus, the head first exposed to account for 95%-96%, is conducive to natural vaginal delivery, and Breech first exposed and transverse is abnormal fetal position, is not conducive to natural delivery. One of the criteria for inclusion in this clinical trial program is to show the head first, to avoid the withdrawal of too many subjects due to poor fetal position, which may affect the data of the control group and the trial group, indications for similar products also indicate that presentation of the head is suitable for use with a birth monitor.

3.4. Sample Size Assessment

Clinical trials extrapolate their findings to target populations with the same characteristics as the subjects, and collect validity and safety data for statistical analysis. Therefore, we need a certain sample size, that is, the number of subjects, in order to replace the entire target population, sample size estimation is to ensure the reliability of scientific findings, to determine the minimum number of cases. In the process of research project design, researchers need to deeply understand the practical significance of sample size estimation, need to understand why to estimate the sample size, estimate the conditions of the sample size, when the estimation should pay attention to what, how to choose the corresponding statistical formula, how to carry out more complex calculations?

Sample size assessment is an important issue in clinical research design. The number of samples is related to the correctness of research conclusions and budget. The small sample size may result in a loss of credibility and the results may be reversed. The sample size is too large, which will result in heavy task and cost waste. The correct estimation of sample size should be based on the purpose and type of the test, and the corresponding formula should be used to calculate the sample size [11,12].

The following points need to be noted in the estimation of sample size: (1) to fix the value of α, α represents credibility. Normally, Alpha is 0.05 or 0.01, depending on the test. (2) consider the reliability of the test. The accuracy of the test is expressed by 1B, which is usually β = 0.10 or 0.20. (3) fixed population standard deviation (Σ) or population rate (π) is usually determined by searching and reading the same literature at home and abroad, or by preliminary investigation, or by reasonable inference and hypothesis.(4) identification of key evaluation indicators. The main evaluation indexes are used as the basis of sample size estimation. In general, there is only one major indicator, and if there are two or more, the maximum sample size is the best estimate. In addition, the sample size estimation is usually the minimum value in the actual test, in the actual test there are shedding, loss of access and demoulding situation, the incidence rate is about 10-20%. In the course of the test, the number of samples should be increased appropriately.

When the experimental group and the Control Group were randomly assigned to the same number of samples, the main evaluation index was the incidence of events, the variance was uniform, close to 0% or 100%, the sample estimation formula was as follows:

$$n_T = n_C = \frac{(Z_{1-\alpha/2}+Z_{1-\beta})^2[P_C(1-P_C)+P_T(1-P_T)]}{(\Delta-|D|)^2} \quad (1)$$

Among them: P_T is the rate of expected events in the test group, P_C is the rate of expected events in the control group, $|D|$ is the absolute value of the difference between the two groups, $|D| = |P_T - P_C|$, something is the equivalent value (suitable for the case where the bad side value is equal to the good side value), and takes the positive value. n_T and n_C were the sample size of the test group and the Control Group, $Z_{1-\alpha/2}$ and $Z_{1-\beta}$ were the fraction of normal distribution, when α = 0.05, $Z_{1-\alpha/2}$= 1.96, when β = 0.2, $Z_{1-\beta}$ = 0.842; $(Z_{1-\alpha/2} + Z_{1-\beta})^2$ = 7.85.

To sum up, in this clinical trial design, using PASS software to calculate the sample size, based on the estimated sample size in figures 2 and 3, considering the 10%-20% probability of withdrawal, exclusion and so on, the sample size should be set to 95-104 per group.

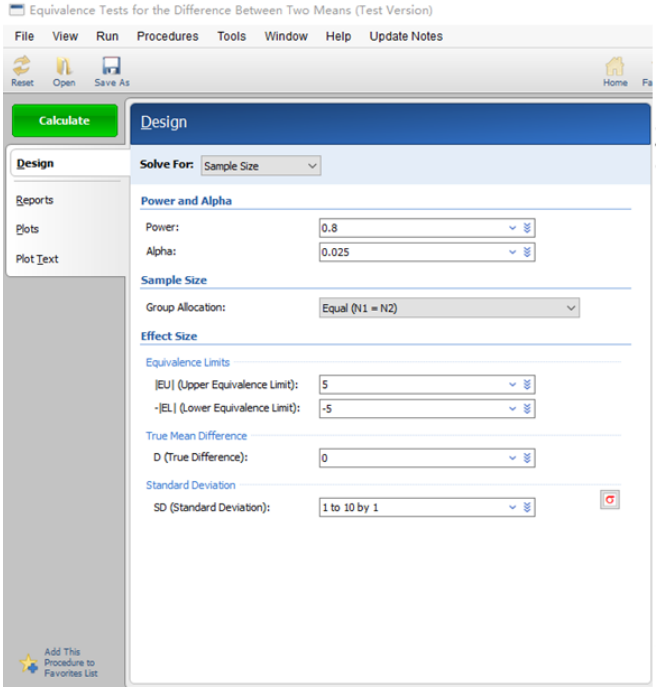

Figure 2: Specific parameters of PASS software

PASS 15.0.5 2021/4/23 16:26:21

Equivalence Tests for the Difference Between Two Means

Testing Equivalence of Two Means Using a Parallel-Group Design

Target Power	Actual Power	N1	N2	N	D	SD	Lower Equiv. Limit	Upper Equiv. Limit	Alpha
0.80	0.98571	3	3	6	0.0	1.0	-5.0	5.0	0.025
0.80	0.86359	5	5	10	0.0	2.0	-5.0	5.0	0.025
0.80	0.82511	9	9	18	0.0	3.0	-5.0	5.0	0.025
0.80	0.82096	15	15	30	0.0	4.0	-5.0	5.0	0.025
0.80	0.82500	23	23	46	0.0	5.0	-5.0	5.0	0.025
0.80	0.81360	32	32	64	0.0	6.0	-5.0	5.0	0.025
0.80	0.81114	43	43	86	0.0	7.0	-5.0	5.0	0.025
0.80	0.80235	55	55	110	0.0	8.0	-5.0	5.0	0.025
0.80	0.80769	70	70	140	0.0	9.0	-5.0	5.0	0.025
0.80	0.80646	86	86	172	0.0	10.0	-5.0	5.0	0.025

Figure 3: Sample size estimation results

4. Conclusion

In this paper, the clinical effectiveness of Laborvue labor monitor is verified by comparing the LABORPRO system of Trig healthcare and Laborvue Labor Monitor. In the design of clinical trials, it includes the types of trials, the selection of subjects, the types of comparison and the hypothesis of testing, the main evaluation indexes and the estimation of sample size. Design of this clinical trial in this study, the validity of Laborvue labor monitor in clinical application is demonstrated if the data from the two groups are linear and highly positive, this suggests that the clinical research protocol needs to be improved, or that the clinical efficacy of Laborvue labor monitor for cervical dilation and fetal orientation needs to be further studied. Only two parameters, cervical dilatation and fetal position, were studied in this study, although it provided a research plan for the application of this system in clinical labor monitoring, however, there is no guarantee to achieve the desired results, and its clinical efficacy remains to be further studied. The follow-up hope is to further optimize the protocol of this study and validate the clinical effectiveness of Laborvue labor monitor through clinical trials.

Acknowledgements

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