Statistical Analysis Plan

Does electromyography improve precision and reliability of neuromuscular monitoring in paediatric patients? (ETCETERA)

A randomized prospective agreement study

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Statistical Analysis

The primary endpoint is the repeatability coefficient "r" defined as 1.96 times the standard deviation of the differences between two consecutive TOF ratio measurements on the same patient under identical conditions:

$$r = 1.96 * \sqrt{2} * \hat{\sigma}_w$$

where $\hat{\sigma}_w$ is estimated by the square root of the residual mean square. The 95% confidence interval for the repeatability coefficient is constructed using its sample variance,

$$\hat{Var}(r) = 1.96^2 * \hat{\sigma}_w^2 * n^{-1}$$

where n is the number of comparisons. The interval (−r, r), known as the 95% repeatability limits, specifies the range within which 2 measurements by the same device will differ in 95% of cases.

The repeatability coefficient and its confidence intervals will be calculated using a linear mixed regression model for EMG and KMG measured TOF ratios independently at baseline (before and after calibration) and at complete neuromuscular recovery, i.e., at TOF ratio > 0.9 and compared between techniques using F-tests with a non-inferiority approach.

Sample size

Non-inferiority of precision is assumed if the repeatability coefficient of the TOF ratios of one device is not greater than that of the TOF ratios of the other. A difference of 0.01 between the repeatability coefficients of EMG and KMG is assumed acceptable. With 0.01 as the critical difference, a repeatability coefficient weighted on the published EMG data of 0.05 [1-4], a significance level p = 0.025 (sharing the two-sided alpha of 5% for the two repeatability coefficients, the one at baseline and the one at complete recovery), and a power of 80%, confirmation of non-inferiority using F-tests needs 290 pairs of measurements. To achieve independent TOF readings they can be repeated every 20 s only. Since the baseline period should not exceed two minutes, i.e. six repeated TOF ratio measurements, 50 children are necessary to end up at 290 pairs, i.e. 13 children in each age group. This is also consistent with the repeated measures approach, in agreement studies the number of pairs per patient must be less than the number of patients [5]. To compensate for expected 3 drop-outs per group, we plan to include 16 children per age group. A hierarchical approach will be used for posthoc analyses in the four age groups, which may only be performed if non-inferiority or superiority of a monitoring method can be demonstrated in the entire study population.

References

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