Meta-analysis of “General Movement Assessments” conducted in neonates included into SafeBoosC III trial in different centres

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BACKGROUND

General movement assessment

General movement assessment (GMA) is a commonly used tool for early detection of neurodevelopmental impairment. The repertoire of spontaneous movement patterns is described in the "Global GMA" according to their age: writhing movements (after birth until 6-9 weeks post term) and fidgety movements (6-9 weeks until 14-20 weeks post term). Normal, abnormal (poor-repertoire, cramped-synchronized or chaotic general movements) or absence of general movements allows valid prediction on later neurological outcome (1)(2)(3)(4). General movements optimality score (GMOS) can be used as an assessment technique (5). It has been shown, that brain dysfunction is associated with changes in normal GM (5)(6). GMA predicted cerebral palsy with 98% sensitivity and 89% specificity (7). The infant is video recorded after feeding, during a period of active wakefulness and lying in a supine position. The recording has to be restarted when the infant has settled after crying, fussing or suckling period (2)(6). The videos can be assessed later.

Cerebral oxygenation and general movements

One recently published study (1) has already demonstrated that the burden of cerebral hypoxia has an influence on GMA in preterm neonates.

SafeBoosC III Trial

In a randomized, prospective, multinational, multicentre, pragmatic phase-III clinically open trial with a two-parallel group design, SafeBoosC III, preterm neonates <28weeks of gestational age, monitored with near-infrared spectroscopy (NIRS) during the first 72h after birth, will be investigated. The aim of the study is to investigate the benefits and harms of clinical interventions, based on NIRS monitoring in order to reduce cerebral hypoxia during the first 72hours after birth. The hypothesis is that treatment based on NIRS monitoring during the first 72 hours after birth will result in a reduction in severe brain injury or death at 36 weeks postmenstrual age.

OBJECTIVE

As an ancillary study to the SafeBoosC III trial, we will analyse GMA conducted on neonates, who were included into the SafeBoosC III trial performed in different centres.

The first aim is to compare the experimental group and control group as regards to the Global-GMA at term age.

The second aim is to investigate GMOS at term age and, if available, GMA at 9-16 weeks corrected age.

PRIMARY OUTCOME

The primary outcome is abnormal Global-GMA at term age.

SECONDARY OUTCOME

The secondary outcomes are GMOS at term age and, if available, abnormal GMA at 9-16 weeks corrected age.

HYPOTHESES

We hypothesise that the surviving preterm neonates in the experimental group of the SafeBoosC III trial show better results in Global-GMA at term age compared to surviving neonates in the control group.

Furthermore, we hypothesise that the surviving preterm neonates in the experimental group of the SafeBoosC III trial show better results in GMOS at term age and, if available, in GMA at 9-16 weeks corrected age.

METHODS

Trial design

A meta-analytic approach will be used, to summarise the simple comparisons of the two groups in each centre.

Eligibility

Neonates will be included, in whom GM assessment was performed routinely at corrected term age or before discharge and optionally at a corrected age between 9 to 16 weeks.

Only infants from centres that perform GMA to established standards can be included: Infants are recorded according to routine after feeding, during periods of active wakefulness and lying in a supine position for 10-20 minutes. To evaluate the GMA, visual Prechtl Gestalt perception is used. Because of the routine use in GMA, handling should reach the quality parameters, necessary for an optimal interpretation of these results.

Blinding

Interpretation of Global-GMA and GMOS must be performed by analysing pseudo-anonymised video-recordings by persons trained in GMA and not involved in the care of the neonates.

GMA Data

Global GMA will be classified as normal and abnormal (poor repertoire, chaotic, cramped synchronised at term age/absent fidgety movements at corrected age of 9-16 weeks). GMOS will be scored from zero to 42.

Data managing plan

Each centre will deliver a list of study-ID's of the infants with GMA to Copenhagen Trial Unit where the statistics on the demographic data will be computed and reported back.

GMA and GMOS data will be pseudo-anonymised at each centre using the study-ID used in the SafeboosC III trial and handled according to local guidelines. Local statistical analyses will be performed in each participating centre and only the results of these statistical analyses will be transferred to Medical University of Graz, Graz, Austria for meta-analysis.

Statistical analyses

Baseline characteristics of neonates will be given as mean and standard deviation or median and interquartile range for continuous data and as numbers and percentages for categorical data. Comparison of baseline characteristics will be done by using t-Test or Mann Whitney U-test for continuous data and Chi-square test or Fisher's exact test for categorical data. To answer the primary hypothesis an OR will be calculated within each center. To analyze the secondary outcome measure GOMS, a modified version of Agresti's (1980) generalized odds ratio (genOR), which accounts for ties, will be calculated within each center.

$$genOR = \frac{Prob(Y_1 < Y_2)}{Prob(Y_1 > Y_2)}$$

Since data are collected in the same study and therefore the study designs are the same, we assume the treatment effect to be the same and differences in the results between centers are due to a random error. As a consequence, data will be combined using fixed effect models. Overall OR for the global GMA and the GMOS will be calculated and Forest plots drawn.

SAFETY

GMA is a non-invasive video-recording of the preterm neonates not effecting the neonate.

PUBLICATION PLAN

Publication plan is according the publication plan of the SafeboosC III protocol in its latest version.

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