



## Comparison of INSURE and Non-Administration of Surfactant for Neonatal Respiratory Distress Syndrome (NRDS)

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### Dear Editor,

We read with much interest the article by Noripour et al. published in your journal online (1), and we would like to make the following comments, clarification to which would benefit the general readers of the journal.

In the present era, on one hand surfactant administration is becoming the standard of care in the management of neonatal respiratory distress syndrome (NRDS) (2) and on the other hand, American Academy of Pediatrics (AAP) recommends "Using CPAP immediately after birth with subsequent selective surfactant administration should be considered as an alternative to routine intubation with prophylactic or early surfactant administration in preterm infants" (3). Thus, such a study showing that surfactant administration does not improve outcome in preterm newborns with NRDS generates much attention.

First: The authors mentioned that the aim of the study was to "evaluate the effectiveness of the INSURE method followed by NCPAP in infants with NRDS hospitalized in NICU", yet they did not provide any precise and measurable objective based on which the sample size was calculated. The methodology only mentioned that "taking into account the quantitative conditions of the sample size with first type error ( $\alpha$ ) at 0.05 level and second type error ( $\beta$ ) at 0.020 level (power 80%), the number of samples for each group was considered to be 54". However, in a comparative study, the sample size would depend on the expected 'effect size'. This is very important as the power of the study is dependent on the sample size and thus the observed non-difference in the study could simply be due to the study actually being under powered to evaluate the objective (4).

Second: The control (surfactant non-administration) group was taken from a historical cohort of preterm newborns with respiratory distress score of 8 or more. They were matched with the case (surfactant administration) group in respect to gestational age, birth weight, and ma-

ternal steroid intake. However, any other inclusion or exclusion criteria for their selection are not mentioned. Therefore, this group was amenable to 'selection bias'. It was also not mentioned whether the 2 groups were similar in respect to other factors, which may influence the outcome in NRDS, such as the degree of respiratory distress (may have been presented here as mean respiratory distress score), degree of hypoxemia, APGAR score, other morbidities (e.g. acute renal failure, meconium aspiration, etc. (5).

Third: The authors do not mention about obtaining ethical clearance for the study.

Fourth: There was also mention of "radiological signs of NRDS" in both inclusion and exclusion criteria yet these radiological signs are not described/defined.

Fifth: The surfactant administration was the main intervention in the study. Though the details of the procedure is well described, the dose and the type of surfactant (human/ synthetic; bovine/ porcine) used in the study, is not mentioned.

Sixth: There was no mention of the definition/criteria and the evaluation method used for outcome measures, such as, chronic lung disease and discharge criteria.

Seventh: The first row of table 3 mentions that out of 52 infants in each group,  $2.5 \pm 7.6$  in the case group and  $2.2 \pm 3.8$  in the control group required Mechanical Ventilation (MV). However, the number of patients requiring MV could never be in decimals.

Finally, the authors' concern about the surfactant administration and its associated complications are well accepted. However, as described in the paper, the complications are mostly associated with endotracheal intubation rather than surfactant. Therefore, lately, there have been efforts of administration of surfactant by other alternate methods, such as use of aerosolized surfactant, laryngeal mask airway-aided delivery of surfactant, instillation of pharyngeal surfactant, and administration of surfactant using thin intra-tracheal catheters, etc. with variable suc-

cess (3).

### Footnotes

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