

Endotracheal Aspirate Microscopy and Culture in Early Prediction of Ventilator-associated Pneumonia in Neonates

We read the article by Gupta, *et al.* [1] with great interest, and would like to point out few issues:

First, the authors have collected endotracheal aspirate (ETA) for microscopy and culture in all the neonates on mechanical ventilation, irrespective of any clinical deterioration at the time of collecting ETA sample. Though the CDC definition of ventilator-associated pneumonia (VAP) [2] lacks specificity in the absence of isolation of the pathogen, the microbiological isolation or identification of pus cells in ETA is attempted only when there is clinical deterioration in terms of worsening gas exchange in patients on mechanical ventilation. The same has been highlighted by CDC while redefining possible VAP in adults [3]. Thus, the mere presence of organism or pus cells in ETA in absence of clinical worsening reflects colonization rather than infection [4]. Moreover, while doing any diagnostic study, the diagnostic test should be performed on those group of subjects in whom it will be applied in the real world clinical setting. Therefore, ventilated neonates having any deterioration in terms of increasing ventilator requirement should have been the ideal subjects for checking the utility of ETA in early diagnosis of VAP rather than enrolling both asymptomatic and symptomatic neonates.

Second, there should be an independent and blind comparison of the diagnostic test with the gold standard while doing any diagnostic study. This is to avoid the bias that might cause the over-or under-interpretation of the gold standard test. The authors have not commented anything about this comparison.

Third, the authors have instilled 0.5 mL of normal saline in endotracheal tube for the sample yield, which is not routinely recommended [5]. This becomes more important in light of no information about the ethics committee approval in the given article.

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AUTHOR'S REPLY

We thank the authors for a critical appraisal of our paper.

Based on the CDC criteria for diagnosis of VAP, a combination of clinical, radiological and laboratory features are essential for diagnosis of VAP. Though such stringent criteria are fine for an epidemiological diagnosis, by the time all criteria are evident, the outlook for the neonate may become grave. Hence the objective of our study was to evaluate the utility of endotracheal aspirate microscopy, culture and endotracheal tube tip culture for early diagnosis of ventilator-associated pneumonia in neonates. We considered the fact that the presence of pathogens in a normally sterile lower respiratory tract or lung parenchyma increases the likelihood of VAP.

We agree with the authors that worsening of gas exchange could have been taken as the criterion for doing the cultures but as this finding could be a harbinger of a worse outcome, we chose the CDC criterion of one of the clinical features used in the diagnosis of VAP "increased respiratory secretions, or increased suctioning requirements". Hence we did the aspirates when the first suction was required for presence of secretions considering this as an early clinical marker for VAP, before frank deterioration possibly occurred. Accordingly we have concluded that ETA culture colony count ($>10^5$ CFU/mL) and ETA microscopy ≥ 5 PMNL/HPF is supportive in the objective diagnosis of VAP with added advantage of early diagnosis.

Unfortunately, there is no single gold standard test for diagnosis of VAP for comparison. Hence we compared the time-to-diagnosis using ET aspirate studies versus time-to-diagnosis based on CDC VAP criteria and found a significantly shorter time-to-diagnosis based on the former

criteria. As far as the ETA microscopy and culture were concerned, these tests were performed by the microbiologists who were blind to the presence or absence of VAP in the study cohort.

Saline instillation was done for few babies where yield of secretions was insufficient and not as a routine as per methodology reported by Hagedorn (Reference 8 of

article). This aspect was part of the protocol put up to the institutional ethics committee, with whose approval the study was conducted.

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Primary Hypothyroidism Presenting as Bilateral Ovarian Torsion

Van Wyk – Grumbach Syndrome, first described in 1960, is characterized by isosexual precocious puberty, delayed bone age and bilateral multicystic ovaries in the background of primary hypothyroidism (secondary to autoimmune thyroiditis) [1,2]. The inherent pathophysiology involves the action of raised Thyroid-stimulating hormone (TSH) on Follicle-stimulating hormone (FSH) receptors, leading to the development of pseudoprecocity. These hormones share a common α -subunit which acts through similar transmembrane receptors [3]. Such cases may present with bilateral ovarian masses and end up with bilateral oophorectomy if the primary physician is unaware of underlying pathophysiology.

An 11-year-old girl presented to us with acute abdominal pain of 7 days duration, associated with vomiting and abdominal distension. The patient had achieved menarche 6 months ago. There were no neurological complaints. The patient had short stature, obesity, and features of peritonism and shock. Contrast-enhanced computed tomography scan showed two multiloculated adnexal masses. Serum α -fetoprotein and β -human chorionic gonadotropin levels were normal.

On surgical exploration, massive hemorrhagic ascites was revealed. Both ovaries were enlarged (15 cm on right and 11 cm on left) with multiloculated cysts. They had undergone torsion and were grossly gangrenous. Bilateral salpingo-oophorectomy was done. Histopathologic evaluation of the specimens revealed bilateral follicular cysts with surrounding edema with large areas of hemorrhage.

Three months post-operatively, the child complained of abnormal weight gain along with muscle weakness. Thyroid profile showed raised TSH level (>100 uIU/mL)

with low free T3 and T4, normal FSH and LH and raised estradiol. On imaging, there was a delayed bone age. Patient was treated with thyroid hormone replacement and within 1 month, she improved symptomatically with a reduction in weight and improved muscle weakness. At present, she is 18-year-old with normal breast and feminine hair development, on oral estrogen and thyroid hormone replacement therapies, and is clinically and biochemically euthyroid.

Any child of isosexual precocious puberty presenting with bilateral ovarian masses should undergo bone age estimation, as delayed bone age in this context clinches the diagnosis of Van Wyk-Grumbach syndrome, which can further be confirmed by hormonal analysis. Initiation of thyroid hormone replacement results in improvement in endocrine abnormalities, final height achieved as well as resolution of ovarian masses, thus preserving ovarian reserve in the child [4]. Only in case of ovarian torsion and ischemia, surgery is warranted. In all other less acute cases, pharmacotherapy may be sufficient and avoids unnecessary surgery [5].

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