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Editorial

Small but Significant, the Clinical Studies on Neonates and Infants

This issue of HKJP focuses on clinical studies involving neonates and infants. These patients are highly delicate and vulnerable, so extra care have to be taken. In addition, since they cannot express themselves, we often have to rely on physical signs and surrogate reports from parents to make a diagnosis. All these factors make clinical study on this cohort of patients relatively difficult and challenging. But clinical study does not need to be complicated always, even relatively simple trials can help to answer some common clinical questions as shown in the original articles selected for this issue.

For a long time, the diagnosis of infantile colic (IC) remains elusive and is hard to document. Some adopted the Wessel's rule of 3 which are "crying episodes lasting for at least 3 hours per day, occurring at least 3 days per week, and persisting for at least 3 weeks" as the basis of diagnosis. The associated clinical signs can be the observation of coiling up of the body, abdominal contraction, or constipation, etc., which further supports such clinical impression. In recent year, the Rome IV criteria (2016) defined IC as recurrent episodes of prolonged crying, fussiness, or irritability that begin and end within the first five months of life. Because of the subjective and non-specific nature of these criteria, it is mainly a diagnosis by exclusion. Kurt F, et al performed a prospective observational study on 210 mother-infant pairs and tried to explore the underlying risk factors. Based on this study, the risk factors are high maternal anxiety during pregnancy, caesarean section and those with fathers who smoked or consumed alcohol. These highlighted the possibility of maternal stress can have a prolonged impact on the foetus even up to the early infancy period. It is known that environmental factors can modify the epigenetic control and affect the genes expression, early psychosocial intervention may be able to alter such trend. Whether such approach is effective during pregnancy must be confirmed by future prospective trials.

Another common problem in neonatal period is infection. Over the years, many biomarkers have been developed and tried to predict the outcome. CRP is one of the commonest used biomarkers with a relatively good and robust positive predictive value. In the study by Kazangi et al, they suggested the neutrophil to lymphocyte ratio (NLR) can be a possible alternative. Since both absolute neutrophil and lymphocyte counts are readily available in routine complete blood count, it may be a very practical and convenient assessment tool. The only drawback is how to define the cut-off value for such ratio. As shown in this study, a significant overlapping can be found in the NLR between the increase length of stay group and the control group (3.5±1.3 vs 2.9±1.2). In addition, the specificity of this ratio is quite low as comparing to CRP (53.45 vs 91.38) even it has a slightly better sensitivity (66.13 vs 48.39). One must be cautious in applying such knowledge in clinical practice. In fact, neutrophil serves as an acute phase reactant can be quite non-specific. While biomarkers are useful and objective tools, good

bedside clinical skills and observations are equally important in day-to-day practice.

In recent years, due to the advancement of medical technology, more and more premature neonates can survive. However, new problems emerge and this is due to various complications occur during the rescuing process of these fragile neonates. One complication in the form of neuro-developmental impairments is a major concern. How to diagnose them early and provide timely intervention is an important task. In the study by Yoon J et al, they compared a simplified version of the Test of Infant Motor Performance (TIMP), known as TIMP screening items (TIMPSI) with the original test. The simplified version reduced the original 42 items to only 29 items so it can significantly reduce the performance time and stress to the young infants. The study showed that the TIMPSI has a very high test-retest reliability and inter-rater reliability. Therefore, it can serve as a good alternative to the original test as a screening tool especially for the young infants. This is important especially in the busy working environment of the public hospitals.

Finally, while we try to ask clinical questions by conducting a clinical trial for children and especially for young infants, we often have hesitancy because we don't know whether the parents will accept the concept. That is even more for randomised trial. In recent years, we started to see some large phase III clinical trials involving paediatric patients from Asia. The recruitment rate appears to be reasonable and some of the trials were even comparable to that of the Western countries. What may be the underlying determinants remains to be explored. The Malaysian group investigated factors influencing parental decision-making in paediatric clinical trials. Obviously, good doctor-patient relationship and trust will be the pre-requisite. And such relationship can be enhanced by effective communication and demonstration of clinical competence. Other supportive factors for participation include serious medical condition, lower economic status of the family especially when it involves the potential use of free and expensive medications. Another important finding is the spirit of altruism, which means the willingness to contribute for the advancement of medical knowledge so it can benefit the other patients in the future. Suggesting that such high moral character is a universally shared value across different cultures and religions.

In short, running clinical trials even for the neonates and infants are feasible and acceptable by Asians. Not all clinical trials need to involve large number of patients and novel diagnostic methods or treatments. Clinical questions can be directed towards simple common problems and manage by relatively non-complex methodology. It can also be inexpensive and non-laborious. Therefore, clinicians in Asia should be more actively involved in clinical trials so we can help to advance our knowledge in clinical medicine, eventually it can benefit all the infants and children in the future.

GCF Chan
Chief Editor