

Comparing the Cost of Standardised and Individualised Parenteral Nutrition in Clinically Stable Infants in a Malaysian Public Hospital

Leao Xin Yi¹, Chan Huan Keat², Hasif A Rusli³, Tan Hooi Kuan³, Lim Li Xin⁴

¹ Hospital Sultanah Bahiyah, Kedah, Ministry of Health Malaysia, ² Clinical Research Centre, Hospital Sultanah Bahiyah, Kedah, Ministry of Health Malaysia, ³ Pharmaceutical Services Division, Kedah State Health Department, Ministry of Health Malaysia, ⁴ Hospital Langkawi, Kedah, Ministry of Health Malaysia

Abstract

Introduction: In Malaysia, some public hospitals are using individualised parenteral nutrition (IPN) in paediatric patients although standardised parenteral nutrition (SPN) is recommended by more recent guidelines.

Objective: This study aimed to compare the costs of SPN and IPN, and to estimate the potential cost saving when SPN is used in place of IPN for clinically stable paediatric patients receiving treatment in a public tertiary hospital in Malaysia.

Methods: A costing study was undertaken in Sultanah Bahiyah Hospital, Alor Setar, between February and April 2017. All IPN preparations compounded at the pharmacy department during the three-month study period were included in the cost analysis. A bottom-up costing approach was used to compute the cost of IPN based on the consumption of resources including ingredients, disposables, personnel and equipment. The cost of SPN was estimated according to the existing literature. The total cost difference between IPN and SPN was estimated based on a hypothetical model, in which SPN will be given to patients who were clinically stable in place of IPN.

Results: The unit costs of IPN and SPN preparations were RM259.52 and RM156.82 respectively, and SPN was cheaper than IPN by 39%. During the three-month study period, 232 IPN preparations were compounded for 35 patients. Based on the hypothetical model, 140 of the IPN preparations were judged to be replaceable by SPN. Therefore, it was estimated that a total RM14,378.00 could be saved (7.5% cost reduction) if SPN instead of IPN was compounded for the clinically stable paediatric patients. The projected annual savings in Sultanah Bahiyah Hospital could be as high as RM60,000.00.

Conclusion: This study suggested that cost saving is achievable if SPN is used in place of IPN in clinically stable paediatric patients. The findings could help healthcare providers to optimise resource utilisation.

Keywords: infant, child, parenteral nutrition, pharmacy, public hospitals

NMRR ID: NMRR-17-207-34280

Corresponding author: Leao Xin Yi

Pharmacy Department, Hospital Sultanah Bahiyah, KM 6, Jalan Langgar, 05460 Alor Setar, Kedah.

Email: xy819_kitty@hotmail.com

Introduction

Parenteral nutrition (PN) refers to the supply of nutrition by the intravenous route instead of through the alimentary canal. A complete PN preparation consists of fluid, carbohydrate, protein, lipids, electrolytes, vitamins and trace elements. PN is given to adult patients whose nutrition needs are not fully met by oral or enteral tube feeding (1-3). In premature neonates, PN is typically initiated early to promote growth and prevent neurological disorders (4-6). PN is generally safe and tolerable, even if it is used in newborns on their first day of life.

As the metabolic pathways are not fully developed in newborns, PN is normally titrated slowly in the first and second weeks of their life. Most of the time, PN is continued until they achieve an ideal body weight and are able to tolerate enteral feeding (7). However, due to the interpersonal variability in nutrition needs and physical conditions of infants, PNs are extemporaneously prepared in most hospitals (6,8). PN that is adjusted daily according to the laboratory readings of patients is termed as individualised parenteral nutrition (IPN) and it has long been used worldwide (9). Nevertheless, following the recommendations made by more recent international guidelines, standardised parenteral nutrition (SPN) is becoming more common. Different from IPN,

SPN is prepared based on a fixed formula tailored to an age- or weight-based category, mainly used in clinically stable infants despite minor changes in the laboratory findings. The existing literature suggests that IPN and SPN do not differ in safety, efficacy and product stability (13-17).

SPN is believed to have a cost-saving potential, mainly through lowering the preparation time and cost (9-13). Waste minimisation is also possible, as the preparations made for a cancelled order could be used for another patient with similar age and weight. Additionally, resource utilisation is likely to be optimised as PN preparations can be produced in batches. The cost incurred by the management of medication errors could also be reduced due to the use of a standardised PN formula (10).

In accordance with the recommendations of local and international guidelines for nutrition care (19-21), some hospitals in Malaysia have started using SPN in infants. However, the cost implication in Malaysia is yet to be determined. This study was carried out to compare the costs of SPN and IPN, and to estimate the potential cost saving when SPN is used in place of IPN in clinically stable patients receiving treatment in a Malaysian public tertiary hospital.

Methods

Study Setting

We performed a three-month study on PN orders received between February and April 2017 from the three paediatric wards at the Sultanah Bahiyah Hospital, Alor Setar. All the PN preparations were made in a cleanroom located at the Pharmacy Department, which was equipped with a Grade A laminar flow cabinet. PN orders will be screened and authorised by the pharmacists before the PN preparations are being compounded by the pharmacy technicians. Each preparation was contained in a TPN compounding bag, consisting of carbohydrate, protein, electrolytes and trace elements. To ensure product stability, lipid emulsion and fat-soluble vitamins were packed separately in a capped syringe.

All PN preparations made for premature infants with body weight less than 1.5kg during the three-month study period were included for the cost analysis. Preparations that failed the quality control process or that were made for infants undergoing surgery were excluded.

Cost Calculation

A bottom-up costing approach was used to compute the cost of IPN based on the observed consumption of resources. The costs of ingredients, disposables, equipment and personnel were included in the cost calculation (22). The summary of these cost elements were presented in Table 1.

Table 1: Summary of cost elements

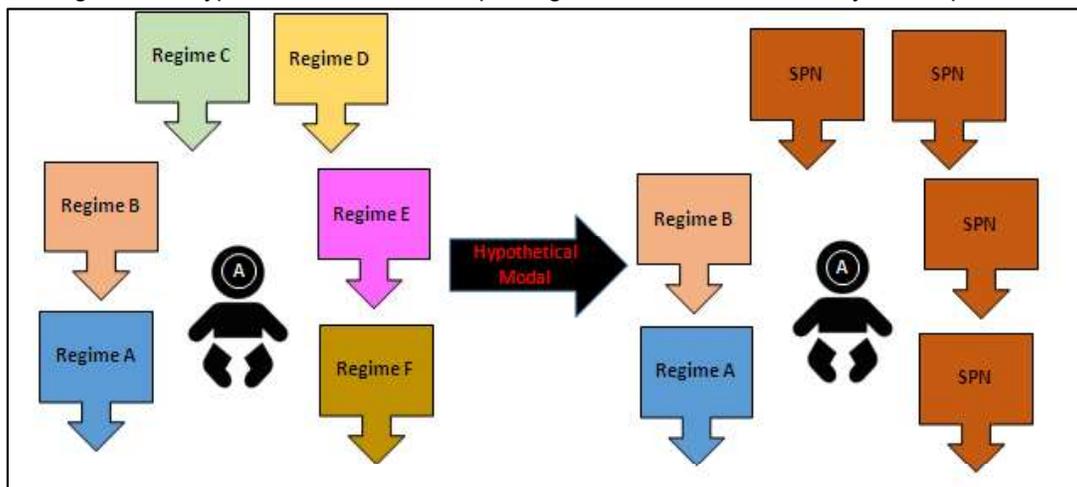
Ingredients	The total costs of ingredients were estimated based on the quantity consumed and their acquisition costs (current market prices).
Disposables	The total costs of disposables were estimated based on the quantity consumed and their acquisition costs (current market prices).
Equipment	Current market prices were used for equipment costs. Depreciation was calculated linearly over a 5-year period for installation and devices (laminar flow hood / bench, compounder, infusion pump, isolator). Information about the price and yearly maintenance costs for the equipment was derived from the recruited sites, which took the information from hospital records.
Personnel	The PN activities of physicians, pharmacist and nurse were systematically timed by the investigators. Time spent by each category of personnel to produce the parenteral nutrition regime (prescription, preparation for compounding, installation / connection of equipment, compounding, supplementation, monitoring, compounder disconnection, stock management / requisition, quality control and training time) were recorded. These timings were combined with the average wage per category of the personnel involved in the activities. The corresponding salary information was obtained from hospital administration data.

Cost Saving Estimation

Renal and liver functions in the premature neonates continue to develop after birth. The fluid and electrolyte balance is affected by extra-renal systems, illness, medications and interventions. Hence, the fixed electrolyte contents of SPN may not be tolerated well by the sick premature neonates. However, Devlieger et al. proposed that the premature neonates are capable, within certain limits, of appropriate homeostasis as early as the first week of life and hence may be managed with few combinations of standard PN formulations and they found that SPN formulations were sufficient to manage most of the very low birth weight (VLBW) neonates without significant electrolyte disturbances (9,23).

Hence, a hypothetical model was applied to estimate the total cost if SPN was used in place of IPN for clinically stable patients (Figure 1). Clinically stable patient refers to those neonates who had no kidney or liver dysfunctions or significant electrolytes disturbances that need daily blood monitoring and adjustments.

Figure 1: A hypothetical model for replacing IPN with SPN in clinically stable patients



Ethic Approval and NMRR

This study was registered with the National Medical Research Register (NMRR) and approved by the Ministry of Health Medical Research and Ethics Committee (MREC). It was conducted in compliance with ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice Guideline.

Results

The unit costs of ingredients and disposables used in the compounding of IPN were presented in Table 2 while the workflow of prescribing and preparing PN preparations and the hourly wage of personnel involved were presented in Figure 2 and Table 3.

A total of 232 bags of IPN and 476 syringes of lipid emulsion were compounded for 35 patients during the three-month study period. The overall cost for preparing these PN preparations during the study period was RM190,530.87. The average costs per bag of IPN and SPN preparations were RM259.52 and RM156.82 respectively.

Based on the hypothetical model, 140 of the 232 IPN preparations were judged to be replaceable by SPN when patients were clinically stable, and 92 bags should be remained as IPN for the clinically unstable period. There were no changes in the use of lipid emulsions in the hypothetical model. When the hypothetical model was applied, the total cost of PN preparations over the three-month period became RM176,152.87. Therefore, it was estimated that a total RM14,378.00 could be saved, which was equivalent to 7.5% cost saving, if SPN instead of IPN was compounded for the clinically stable paediatric patients (Figure 3 and Table 4). When this amount was extrapolated, the projected annual savings in Sultanah Bahiyah Hospital could reach around RM60,000.00.

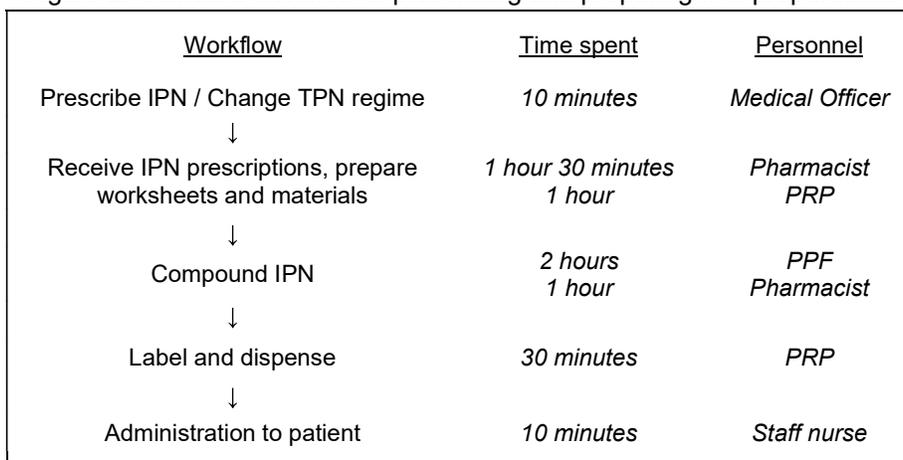
Table 2: Unit costs of ingredients and disposables used in the compounding of IPN

Ingredient	Unit Cost (RM)	Disposable	Unit Cost (RM)
Water for Injection 500ml	2.27	Nutrimix Bag 200ml	21.00
Glucose 50% 500ml	8.00	Nutrimix Bag 500ml	31.00
Aminoven INFANT 10% 250ml	118.75	Sterifix Injection Filter 0.2µm (UFO)	6.20
Peditrace 10ml	35.73	Sterifix IV Filter 0.2µm	15.50
Sodium Acetate 2mmol/ml 20ml	23.99	Mini Spike Blue	4.00
Sodium Chloride 20% 10ml Inj	1.70	Needle 19G	0.07
Potassium Acetate 2mmol/ml 20ml	29.30	Syringe 1ml (luer slip)	0.28
Potassium Chloride 10% 10ml Inj	0.63	Syringe 3ml (luer slip)	0.25
Calcium Gluconate 10% 10ml Inj	4.50	Syringe 5ml (luer slip)	0.30
Magnesium Sulphate 2mmol/ml 5ml Inj	14.17	Syringe 10ml (luer slip)	0.40
Glycophos 20ml	14.00	Syringe 20ml (luer slip)	0.77
Smoflipid 20% 100ml ^a	48.70	Syringe 50ml (luer slip)	2.24
Vitalipid N-Infant 10ml ^a	34.70	Alcohol Swab Sterile	0.04
Soluvit N 10ml ^a	34.70	Nursing Csp	7.20
		Face Mask 3ply	0.38
		Nitrile Gloves (pair)	0.40
		Sterile Gloves (pair)	3.00
		Antiseptics Klercide 1000ml	103.80
		Tyvox Jumpsuit	36.50
		Shoe Cover	17.51
		Sterifix Filter Straw 5µm ^b	4.30
		Intrapur IV Filter Adult 1.2µm ^b	15.50
		Sterifix Filter 5µm ^b	2.60
		Combi Red Stopper ^b	0.50
		Syringe 20ml (luer lock) ^b	1.82
		Syringe 30ml (luer lock) ^b	3.01
		Syringe 50ml (luer lock) ^b	5.30
		Sterilised paper bag (lipid) ^b	0.35

Source: Pharmacy Department, Sultanah Bahiyah Hospital

^a Ingredients for lipids; ^b Disposables for the compounding of lipids

Figure 2: Standard workflow of prescribing and preparing IPN preparations



Abbreviations: IPN – individualised parenteral nutrition; PRP – provisionally registered pharmacist; PPF – pharmacist assistant

Table 3: Cost of personnel

Personnel	Hourly wage (RM)
Medical Officer	25.00
Pharmacist	25.00
Provisionally registered pharmacist (PRP)	19.00
Pharmacist assistant (PPF)	14.00
Staff nurse	17.00

Source: hospital administration data (Sultanah Bahiyah Hospital)

Figure 3: Illustration of cost saving using the hypothetical model

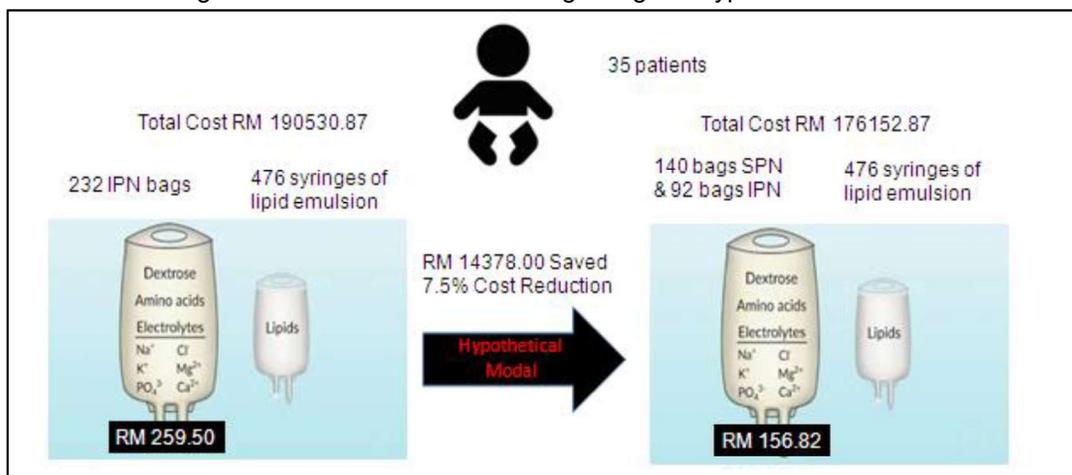


Table 4: Estimated cost saving of the hypothetical model

	Study Data	Hypothetical Model
Quantity of bags compounded	232 IPN	140 SPN + 92 IPN
Quantity of lipids compounded	476	476
Ingredients and disposables cost (bags)	RM60,208.45	RM45,830.64
Ingredients and disposables cost (lipids)	RM27,946.23	RM27,946.23
Equipment Cost	RM75,000.00	RM75,000.00
Personnel cost	RM27,376.00	RM27,376.00
Total	RM190,530.87	RM176,152.87

Discussion

Cost analysis studies are increasingly important in order to support and justify medical procedures and operation expenses. The aim of this study was to compare the cost if standardised instead of individualised parenteral nutrition is compounded for clinically stable paediatric patients by constructing a hypothetical model. To the best of our knowledge, it is the first hypothetical model study done in Malaysia and one of the very few studies that estimate the costs for non-drugs. This study may give policy makers a brief overview about the costs of PN compounding in Malaysian public hospitals and hence may help to develop better policy for supplying PN at lower cost with equivalent effectiveness. Hence, the overall healthcare cost may be saved.

The use of SPN solutions has been reported to be feasible in several observational studies and appears to benefit in some but not all clinical settings. Some reported the use of SPN increased energy and amino acid intake, calcium and phosphate intake, prevent early weight loss, and reduced costs (18-21). The ANZNN consensus Group agreed that SPN offers advantages over routine IPN in terms of providing adequate nutrition without significant alteration in biochemical responses, and with the potential for reduced cost and prescription error. The consensus group agreed on three types of SPN solutions which were starter PN, standard normal sodium PN and high sodium PN for preterm infants (19).

In this study, we demonstrated that the cost of SPN was lower than the cost of IPN. In our calculation, the cost difference between an IPN and SPN was due to the cost of ingredients and disposables. As SPN can be compounded in bulk at one time and it is stable to be stored at 2°C - 8°C up to 7 days, there were savings in the quantity of ingredients and disposables. On the other hand, for compounding of IPN, the amount of ingredients and disposables used were more because new ingredients and disposables items were used on daily basis or according to prescription. In addition, cost of personnel could have been saved for SPN because the workloads may be less especially in terms of weekend on-calls. Nevertheless, we did not attempt to calculate the savings in the personnel cost and just assumed that the personnel costs were the same for the preparation of both IPN and SPN. On the other hand, it is undeniable that wastage may occur if the compounded SPNs

expired before consumption as it may be difficult to estimate the exact usage all time. For neonatal PN compounding, lipid emulsion is prepared separately and it is not mixed into the PN bag because it will affect the stability. In this study, we did not extrapolate the hypothetical model for the lipid emulsion and all patients were given 1 syringe of lipid emulsion per day together with to the PN bags regardless of SPN or IPN.

In some studies, SPN regime was also found to be cost saving due to the proposed prolonged infusion time over 48 hours compared to IPN which is infused over 24 hours. However, there were concerns over the higher potential of bacterial or fungal colonisation if the PN infusion time were longer. In a randomised trial, there was no significant difference in bacterial or fungal colonisation of parenteral or neonatal sepsis in infants receiving 24 or 48 hour infusions of PN solution. The study reported extending PN solution hang time from 24 to 48 hours did not increase the risk for central line associated blood stream infection and in fact it reduced PN related cost and nursing workload (18-21).

The findings on cost comparison between IPN and SPN were consistent with data from the literatures that the cost for SPN was lower than the cost for IPN (19-20). However, this study has a major limitation that it was based on a hypothetical model and we did not do head to head comparison between SPN and IPN. There could be bias if the observations were incomplete or incorrect. The study might have underestimated or overestimated the overall cost saving. Therefore, we recommend conducting a head to head comparison study on SPN versus IPN, so that we could get deeper picture on the pharmacoeconomics of local PN compounding. The other limitation of this study was that it was a single centre study. The study was only reflecting the cost incurred in HSB and cannot represent the other government hospitals settings as the other hospitals might have different practices on IPN and SPN and different brands of products could be used. For example, up to the date of this manuscript preparation, the Kuala Lumpur Hospital has adopted the SPN formulations published by the Ministry of Health Malaysia while Sungai Buloh Hospital has its own SPN formulations. This study also did not consider about the different brands of PN ingredients that may be different in IPN and SPN formulations. As there are a few local and international manufacturers that manufacture PN ingredients of different prices, the cost incurred may differ among hospitals.

Conclusion

This study compared the total costs of IPN versus SPN based on a hypothetical model by considering all cost elements involved in the process. This study suggested that the total cost of SPN was lower than that of IPN in clinically stable paediatric patients receiving treatment in a public tertiary hospital. While financial constraints remain a challenge for the public healthcare system, the findings could help pharmacists to optimise resource utilisation. While more detailed studies should be carried out to gather more information, this information will be helpful in determining the cost of PN therapy and help the healthcare providers and policy makers to formulate healthcare policies.

Acknowledgement

We would like to thank the Director General of Health Malaysia for his permission to publish this article. We thank our colleagues from Sultanah Bahiyah Hospital who provided insights and expertise that greatly assisted the research.

Conflict of Interest Statement

No external funding was received and the authors declared no conflict of interest.

References

1. Boullata JI. Overview of the parenteral nutrition use process. JPEN J Parenter Enteral Nutr. 2012; 36:10S-13S.
2. ISMP's List of High-Alert Medications. Horsham, PA: Institute for Safe Medication Practices; 2012.
3. Andris DA, Mirtallo JM, Guenter P, eds. ASPEN parenteral nutrition safety summit. JPEN J Parenter Enteral Nutr. 2012;36(2 Suppl 2):1S-62S.
4. Moyses HE, Johnson MJ, Leaf AA, Cornelius VR. Early parenteral nutrition and growth outcomes in preterm infants: a systematic review and meta-analysis. Am J ClinNutr; 2013; 97(4):816-26.

5. Usmani SS, Cavaliere T, Casatelli J, Harper RG. Plasma ammonia levels in very low birth weight preterm infants. *The Journal of pediatrics*; 1993; 123:797-800.
6. Guidelines on pediatric parenteral nutrition of the European society of pediatric gastroenterology, hepatology and nutrition (ESPGHAN). *J PediatrGastroenterolNutr*; 2005; 41(2):81-84.
7. Hussain Imam, *Paediatric Protocols for Malaysian Hospitals*, 3rd Edition, Ministry of Health Malaysia. 2012 Chapter 12: Total Parenteral Nutrition for Neonates, page 71.
8. Vaidya UV, Hegde VM, Bhave SA, Pandit AN. Reduction in parenteral nutrition related complications in the newborn. *Indian Pediatr*. 1991;28(5):477-84.
9. Karen Simmer, Abhijeet Rakshasbhuvankar, Girish Deshpande. Standardized Parenteral Nutrition. *Nutrients*; 2013 Apr; 5(4): 1058-1070.
10. Srinivas Bolisetty, David Osborn, John Sinn, Kei Lui and the Australasian Neonatal Parenteral Nutrition Consensus Group. Standardized neonatal parenteral nutrition formulations—an Australasian group consensus 2012. Bolisetty et al. *BMC Pediatrics* 2014, 14:48.
11. Lucie Bouchoud, How are standardized pediatric parenteral nutrition formulations in Europe? *EJHP Science* 2010 Volume 16• Issue 1 • P. 1-4.
12. Evelyn Walter, Cost analysis of neonatal and pediatric parenteral nutrition in Europe – a multi-country study. *European Journal of Clinical Nutrition* volume 66, 2012, pages 639–644.
13. Yeong MY, Evaluation of Standardized versus Individualized total parenteral regime for neonates less than 33 weeks of gestation. *J Pediatr Child Health*. 2003 Nov; 39(8):613-7.
14. Beecroft C, Martin H, Puntis JW: How often do parenteral nutrition prescriptions for the newborn need to be individualized? *Clin Nutr* 1999, 18:83–85.
15. Iacobelli S, Bonsante F, Vintejoux A, Gouyon JB: Standardized parenteral nutrition in preterm infants: early impact on fluid and electrolyte balance. *Neonatology* 2010, 98:84–90.
16. Lenclen R, Crauste-Manciet S, Narcy P, Boukhouna S, Geffray A, Guerrault MN, Bordet F, Brossard D: Assessment of implementation of a standardized parenteral formulation for early nutritional support of very preterm infants. *Eur J Pediatr* 2006, 165:512–518.
17. Smolkin T, Diab G, Shohat I, Jubran H, Blazer S, Rozen GS, Makhoul IR: Standardized versus individualized parenteral nutrition in very low birth weight infants: a comparative study. *Neonatology* 2010, 98:170–178.
18. PN Standard Solution (Malaysia Neonatal Parenteral Nutrition Consensus Group Formulations) KKM-55/BPF/104/012/01/Jld17(20)
19. Balegar VK, Azeem MI, Spence K, Badawi N: Extending total parenteral nutrition hang time in the neonatal intensive care unit: is it safe and cost effective? *J Paediatr Child Health* 2013, 49: E57–E61.
20. Matlow AG, Kitai I, Kirpalani H, Chapman NH, Corey M, Perlman M, Pencharz P, Jewell S, Phillips-Gordon C, Summerbell R, Ford-Jones EL: A randomized trial of 72- versus 24-hour intravenous tubing set changes in newborns receiving lipid therapy. *Infect Control Hosp Epidemiol* 1999, 20:487–493.
21. Gamsjager T, Brenner L, Schaden E, Sitzwohl C, Weinstabl C. Cost analysis of two approaches to parenteral nutrition in critically ill children. *Pediatr Crit Care Med* 2009; 10: 163-165.
22. Petrelli MD, Nicolai E, Tucci A, Giambenedetti M, Taus M, Busni D *et al*. Total parenteral nutrition: economic investigations comparing hospital prepared nutritional bags versus similar bags prepared by the pharmaceutical industry. *Riv Ital Nut Par Ent* 2004; 22, 186–192.
23. Devlieger, H.; de Pourco, L.; Casneuf, A.; Vanhole, C.; de Zegher, F.; Jaeken, J.; Eggermont, E. Standard two-compartment formulation for total parenteral nutrition in the neonatal intensive care unit: A fluid tolerance based system. *Clin. Nutr*. 1993, 12, 282–286.