Iranian Journal of Pharmaceutical Sciences
2013:9 (3):37- 44
www.ijps.ir

Original Article

A Survey on Total Parenteral Nutrition (TPN) in the Intensive Care Unit (ICU) of a Teaching Hospital in Iran

Hajebi G.[a], Tavakoli Ardakani M*[a], Salamzadeh J[a], Barzin A[b]

[a]*School of Pharmacy, Pharmaceutical Research Center Shahid Beheshti University of Medical sciences, Tehran, Iran.*
[b]*Students Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Abstract

Total parenteral nutrition (TPN) has a vital role in controlling nutritional deficiencies especially in patients with critical conditions who are confined to bed in Intensive Care Unit (ICU). Complete evaluation of the nutritional status of these patients is necessary to achieve their nutritional goal. The aim of this investigation was to study the Complete Blood Count (CBC), coagulation parameters, renal function and electrolyte status of patients hospitalized in ICU of a teaching hospital in Iran. A retrospective study was designed in which adult patients hospitalized in the ICU of Ayatollah Taleghani general hospital in Tehran, Iran, during March 2006 to September 2008, were enrolled in the study. The medical records of 203 patients admitted in the ICU were reviewed. 22 (10.8%) patients had received TPN. Hospitalization days were 12±8 (mean±SD) and the days of TPN were 8±6 (mean±SD). CBC results, coagulation parameters, renal function tests, electrolyte status, mortality rate and duration of hospitalization of patients were extracted from their hospital records. Data relevant to baseline (before starting TPN), 1st, 2nd and the last day of TPN was analyzed/compared by Statistical Package for Social Sciences software (SPSS, version 19.0). CBC and coagulation status did not significantly change during TPN. Serum sodium did not also change significantly during TPN, however serum potassium in the last day (4.71±1.44 mg/dl) was higher than the 1st day (3.77±1.04 mg/dl), (P=0.02), and 2nd day (3.84±0.81 mg/dl), (P=0.04), of TPN. Not surprisingly, Blood Urea Nitrogen (BUN) in the last day (58.00±35.90 mg/dl) was more than the baseline (32.27±22.59 mg/dl), the 1st day (34.50±21.40 mg/dl) ($p<0.01$) and the 2nd day after starting TPN (36.55±19.80 mg/dl), (P=0.04).Our results showed that TPN in ICU patients can be associated with changes in potassium and BUN levels. However, further studies with higher sample size are required leading to more comprehensive Conclusion.

Keywords: *CBC, Electrolytes, ICU, Iran, TPN, Renal function.*

1. Introduction

From the early 17th century, attempts to perform non-oral feeding via peripheral veins were approached. Unfortunately, peripheral 5 liters veins were unable to accept large and concentrated volumes of parenteral fluids (up to per day). In addition, this method of feeding often leads to inflammation of the veins (thrombophlebitis) (1).

In1960, Dudrick and colleagues placed an intravenous (IV) catheter in subclavian artery. Central vein with rapid blood flow, allowed them to administer higher volumes of solutions with higher concentrations to the blood circulation (1).

Currently, significant advances in techniques for intravascular catheterization and IV nutrition

*Corresponding Author: Maria Tavakoli Ardakani, School of Pharmacy, Pharmaceutical Research Center Shahid Beheshti University of Medical sciences, Tehran, Iran.
Tel: (+98)21-88873704
Email: mariatavakoli@sbmu.ac.ir
Cite this article as: Hajebi G, Tavakoli Ardakani M, Salamzadeh J, Barzin A. A Survey on Total Parenteral Nutrition (TPN) in the Intensive Care Unit (ICU) of a Teaching Hospital in Iran. *Iranian Journal of Pharmaceutical Sciences* , 2013, 9 (3):37- 44.

Table1. Complete blood count (CBC) and related findings in the patients (n=22).

	Baseline	24 hours after TPN	48 hours after TPN	Last dayof TPN	P-Value
WBC(*1000)	14.44± 8.56	12.93± 7.22	11.95± 6.43	10.95± 5.41	0.421
RBC(*10^6)	3.56±0.67	3.51± 0.57	3.31± 0.93	3.65± 0.63	0.485
Hb g/dl	10.06± 1.78	9.81± 1.53	9.66±1.38	10.45± 1.86	0.448
Hct %	31.31± 5.02	30.79± 4.36	30.56± 3.63	32.96± 5.98	0.384
MCV fl	88.61± 6.79	88.15± 6.67	88.96± 7.67	90.2±5.91	0.79
MCH pg	26.33± 5.81	27.79± 2.06	26.55± 6.02	28.51± 2.03	0.467
MCHC g/dl	31.73±1.62	31.5± 1.32	31.29±1.59	31.67±2.09	0.834
PLT(*1000)	170.57±144.21	155.8±152.71	135.25± 136.2	135.57± 112.77	0.808

solution formulations have been obtained. Care for patients in critical condition in the intensive care unit requires special measures. Nutrition is one of the most important issues in these patients which has an essential role in the recovery of patients. In many cases, acute internal complications or surgery make the oral nutrition or even intestinal nutrition of patients difficult.

Nutritional support can significantly reduce mortality in the ICU patients. Studies showed that most of the ICU patients die due to complications related to malnutrition. (2-7)It should be contemplated that TPN itself can cause complications such as electrolyte abnormalities, metabolic adverse effects, and beta lactamase resistant catheter related infections. (7) Resistant catheter related infections are important adverse events because serious infection caused by bacteria which are resistant to commonly used antibiotics has become a major health care problem in the 21st century. (8)

After decades of defining the role of nutritional support in reducing mortality, malnutrition remains a serious problem in hospitalized patients. Incidence rates of 30-60% have been reported for malnutrition in hospitalized patients between (9). Almost all patients in critical condition and mechanical ventilation show some degree of malnutrition. Malnutrition has been seen in 94% of patients even 14 days after nutritional support (10).

Table2. Comparison of PT and PTT, and INR values on different days receiving TPN (n=22)**.**

	Baseline	24 hours after TPN	48 hours after TPN	Last day of TPN	P-Value
$PT_{(sec)}$	16.83± 3.16	20.49± 7.82	18.98±5.73	17.34± 3.96	0.12
$PTT_{(sec)}$	50.69±22.4	44.39±10.1	47.45±15.8	43.16±1.5	0.39
INR	2.07± 0.78	2.35± 1.52	2.44± 1.41	2.09± 0.99	0.68

Baudouin et al. compared enteral nutrition with TPN in patients undergoing major surgery. They concluded that there is little evidence to support the use of special feeds and the role of immunonutrients remains unproven. Nutritional support cannot completely prevent the adverse effects of catabolic illness and overfeeding should be avoided (11).

Chan *et al* (1999) have attempted to show that TPN could increase intestinal infection

Table3. Changes in blood sodium during TPN from baseline (n=22).

	Baseline	24 hours after TPN	48 hours after TPN	Last day of TPN	P-Value
Mean serum sodium	141.45±6.82	136.59±29.5	142.95±7.63	142.19±8.48	0.56

comparing with intestinal nutrition. Although with using the same calories in both methods, rising rates of infection could not be verified

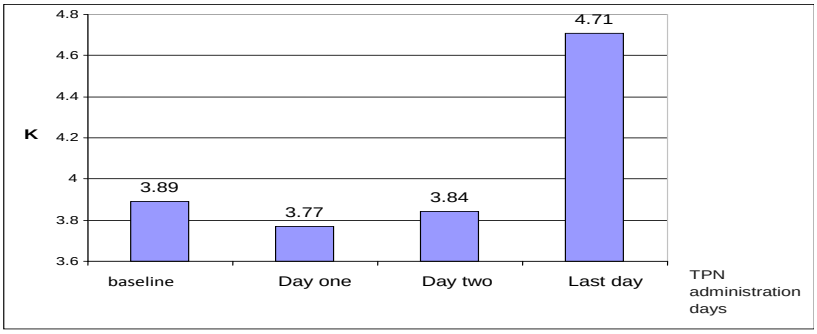

Figure 1. Changes in blood potassium during TPN from baseline (N=22).

(12).

Ovayolu *et al*. evaluated the data of 44 patients admitted to the ICU of a university hospital. Their results showed that TPN has no association with the mortality rate of surgical ICU patients. However, the rate of complications; especially in patients with malnutrition was decreased (13). They also found that organizing a nutritional support team to improve the quality of nursing, providing care and treatment as well as careful follow-up of patients with TPN would be useful (13).

Deegan *et al*. (14) in a retrospective study to determine the effect of TPN supplementation on duration of stay in ICU and hospital as well as the mortality rate in patients with critical condition did not show any significant clinical benefit.

Despite administration of TPN for millions of patients worldwide, it is not taken seriously in the health policy and therapeutic protocols of many countries including our country. In Iran, there are few studies performed appropriately on the adverse events due to TPN and its effectiveness in critically ill patients. Therefore, evaluation of TPN programs and TPN related problems is recommended to be performed in hospitals of Iran. . (15, 16)

2. Materials and Methods

This was a retrospective study in which all patients admitted into the ICU ward of the Ayatollah Taleghani hospital (a teaching hospital affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran) during March 2006 to September 2008 were undergone preliminary evaluation and those patients who had taken TPN were included in the study.

The data collection form consisting of the data illustrated in tables 1-3 was designed.

2.1. Statistical Calculations

SPSS software was used for data analysis. To compare the quantitative variables at various measurement times, the Analysis of Variance (ANOVA) test was applied. The Pearson`s correlation analysis was used to evaluate any

association between quantitative variables where appropriate. The significance level of P-Value <0.05 was considered in data analysis.For ethical reasons, patients' data were coded and entered the analysis software anonymously.

3. Results and Discussion

Medical records of 203 patients admitted to the ICU were reviewed. Among them, 29 patients had taken TPN; 7 cases were excluded due to missing data in their files. Information of 22 patients (including 54.5% male and 45.5% female) were used in this study. Mean±SD age of these patients was 58.8±17.5 years. Their mortality rate was 86.4% (n=19).Although, laboratory tests are usually conducted on a daily basis, we used the laboratory results of 30-60 minutes before TPN (baseline), 24 and 48 hours after initiation of parenteral nutrition, and those related to the last day of TPN.

The blood count (CBC) and related findings of the study patients are summarized in table 1. Coagulation blood tests of INR, PTT and PT of patients during TPN therapy were not significantly different (table 2).

Difference between baseline and follow-up measurements of the serum sodium levels was not statistically significant (table 3).

Potassium levels measured on different follow-up days were significantly different (P=0.01) so that significant differences were in serum potassium levels on the 1st day (3.77±1.04 mg/dl), with that of observed on the last day (4.71±1.44 mg/dl) (CI=95%, P=0.02). Also, difference between potassium levels in the 2nd day of TPN (3.84±0.81 mg/dl???) and the last day of administration of TPN (4.71±1.44 mg/dl???) were statistically significant (P=0.04) (figure1).

Although, mean±SD Cr level in the last day was higher than that of the 1st day, nevertheless this difference was not statistically significant (P=0.73). BUN level at the last day of TPN was statistically different from those BUN levels observed as baseline, and those related to the 1st and 2nd days after TPN. In the last day, BUN (58±35.9 mg/dl) was significantly higher than baseline (32.27±22.5 mg/dl), (P<0.01). Similarly, the difference between BUN in the 1st day after starting TPN (34.5±21.4 mg/dl) and the last day was significant (CI=95%, P= 0.02). BUN levels in the last day were also significantly higher than its level in the 2nd day after initiation of the TPN (36.55±19.8mg/dl), (CI=95%, P=0.042), (figure 2, 3).

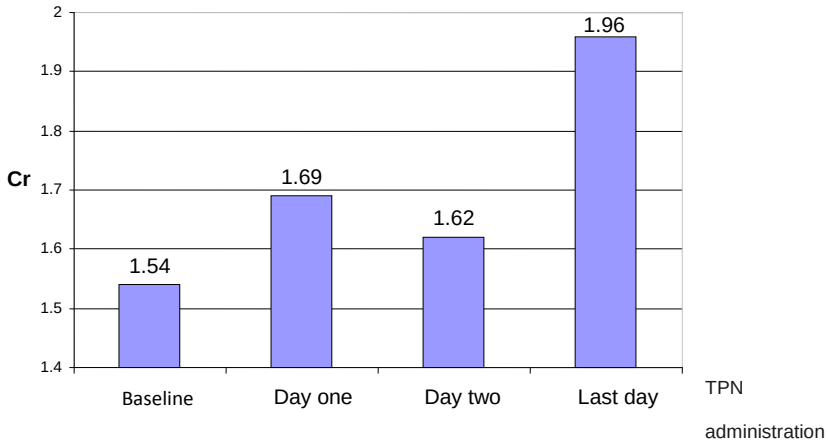

Figure 2. Changes in blood level Cr during the TPN from baseline (N=22).

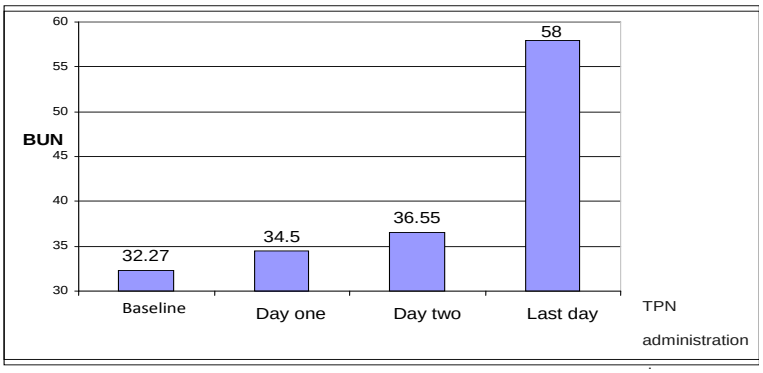

Figure 3. Changes in blood level of BUN during TPN from baseline (N=22).

Mean±SD urinary output volume of the patients during TPN was 2445.7±844.68 ml, (minimum 690 and maximum 3642.5 ml, with a median of 2550 ml) (figure 4).

The average number of days of receiving TPN was 7.82±5.93 days (minimum 2 and maximum 21 days) (table 4).

We did not find any correlation between correlation between the length of receiving TPN and the length of hospitalization (as bed day) was not observed (P =0.22).

There are still controversies about the benefits and complications of parenteral nutrition in critically ill patients. Applying standard nutrition strategies are certainly more efficient than non-documented homemade or

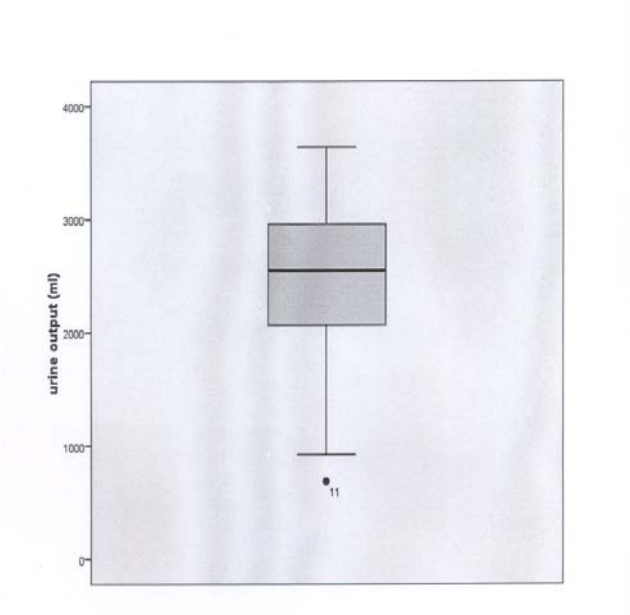

Figure 4. Mean urine output volume of the patients uring TPN days (n=22).

levels of Cr, BUN, K and Na with the amount of urine output. Furthermore, Cr, BUN, and urine output were not significantly associated with duration of hospital stay or TPN administration days (figure 5). Although, there was a direct relationship between the length of stay in the ICU (as bed day) and the bed days of receiving TPN ($p< 0.001$); nevertheless, a significant other kind of feedings used for ICU patients (18). Although, there is a consensus about improvement of nutritional outcomes, such as body weight and muscle mass of the arm after parenteral nutrition, there is no agreement on the beneficial impact of TPN on important clinical outcomes such as duration of mechanical

Table 4. The mean duration of hospitalization and total intravenous nutrition (n=22).

	Mean	Standard deviation	Middle	Minimum (Min)	Maximum (Max)
Total days of hospitalization	20.32	9.99	19	8	**40**
Admission in the ICU (days)	11.86	7.88	10.5	3	**34**
Days receiving TPN	7.82	5.93	5.5	2	**21**

ventilation, length of hospital stay, infection and mortality rates (19, 20).

Roberts *et al*. concluded that although TPN is beneficial in ICU patients with critical conditions, it may increase the incidence of complications. In those patients who are severely malnourished, TPN reduces complications but still has no effect on mortality (21).The clinical impact of this inconsistency probably depends on the start time of nutritional support (19).

In our study, leukocyte count indicated a non-significant decreasing trend from the first day of TPN to the last day of parenteral nutrition. Red Blood Cell (RBC), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin **(**MCH), mean corpuscular volume (MCV), hematocrit (HCT), and hemoglobin (Hb) also did not change significantly during treatment with intravenous nutrition. Platelet count was from about171000 at the baseline to 156000 on the1^{st,} 135,000 on the 2nd and 136,000 on the last days. This reduction trend was not statistically and clinically significant.

Similarly, coagulation status of patients on parenteral nutrition including INR, PTT and PT was relatively stable during TPN therapy and did not show significant differences.

Due to the lack of inclusive information on all of the electrolytes recorded in the patient's medical records, evaluation of the whole electrolyte profile of the patients was not possible. The missing data included calcium, phosphorus, magnesium, zinc, and chloride levels.

During parenteral nutrition, sodium intake levels were within normal range and mean sodium had not significant changes. In contrast, potassium levels on the last day (4.71 ± 1.44) of TPN was significantly higher than those at the baseline (3.89 ± 0.72), 1st (3.77 ± 1.04) and 2nd days (3.84 ± 0.81). This is surprisingly different from the fact that hypokalemia is usually expected during parenteral nutrition (23). This finding may be due to administration of excess potassium during parenteral nutrition days to avoid possible hypokalemia.

Waitzberg DL *et.al* concluded that an adequate follow-up must include clinical and biochemical parameters. Several trials evaluated the impact of TPN in postoperative patients, but further well designed, controlled clinical trials are still necessary to address a great number of unanswered questions. (22)

Donna Chrisanderson and colleagues showed that statistically significant changes between 1979 and 1992 included a decline in the incidence of hyperglycemia from 47% to 22% and in hypokalemia from 12% to 3% of surgical patients and an increase in hypomagnesemia from 0% to 23% of surgical patients and from 2% to 14% of medical patients. The incidence of hypophosphatemia remained > 20% in both medical and surgical patients. So, hypokalemia has remained as one of the metabolic complications of TPN (23).This difference may be due to administrating of excess potassium during parenteral nutrition days because of fearing of TPN induced hypokalemia.

Another possible reason for observed hypokalemia could be renal involvement i.e. reduction in excretion of potassium, intake of certain drugs such as heparin and angiotensin-converting enzyme inhibitors, and an increase in cell damage (e.g. hemolysis) which could increase the levels of serum potassium.

Creatinine increased in the last day compared to the early days and before receiving TPN, but these differences were not statistically significant.

The reason of elevated levels of this product, suggests renal dysfunction, due to the fact that these patients were often at the last days of life and usually suffer from multi-system organ involvement. So, we need to compare these patients to others who did not receive TPN. Elizabeth S. Dodds *et al*(4) showed that one third of patients who received TPN had at least one abnormal laboratory test during TPN therapy and only in 0.5% of these patients the clinical signs were not compatible with laboratory tests.

In our study, there were not significant differences between the mean age of deceased patients and survived patients in the ICU. Lorenzo M. Donini et al. (24) concluded that the mortality rate was significantly higher in patients older than 80 year. No significant association between age and mortality rate of patients in our study, could be due to the small number of very older people (over 80 years) in our patients, and age is not the only factor that can be affect on patient's mortality.

In Marik and colleagues's study (25) were shown that TPN, is the indirect predictive factor of mortality, the likely causes are due to: lack of enteral feeding, adverse effects of TPN (metabolic, immune, endocrine and infectious), by pass the liver (TPN are associated with progression of liver disorders).

Many articles which had a nutritional support in ICU patients showed that reduction in complications, particularly sepsis and catheter related complications were induced by TPN (2, 3, 4, 5, 6, 7); but the numbers indicated that nutritional support in these patients did not have any effect on the incidence of infectious and catheter related complications (26, 27), but only was effective on reducing metabolic effects (26) or mechanical complications (27).

In the interpretation of the results of this study, one should note the limitations including retrospective and observational nature of the study and the missing data of the patients in the medical records as well as the small sample size. We could not have access to data of possible hyperglycemia,hypophosphatemia, hypomagnesemia, and hyperlipidemia. In addition, there were potential confounding factors that may have affected the study outcomes.

4. Conclusion

Based on our study, TPN can be a safe nutritional support in ICU patients who are candidate for this method of nutrition. Our results show that TPN in ICU patients can be associated with increase in potassium and BUN levels. Further studies with higher sample size are required leading to more comprehensive conclusion.

Acknowledgements

The authors of this paper, which is a production of a Pharm,D. thesis, would like to thank all personnel and nursing staff of the ICU of the Ayatollah Taleghani hospital, Tehran, Iran.

References

[1] Gervasio JM and Ash JL. Nutrition Issues. In: Koda-Kimble M.A, Young Y.L, Alldredge BK, Corelli RL, Guglielmo BJ, Kradjan WA. (eds) Adult parenteral nutrition. *Applied Therapeutics*. 9th ed. Lippincott Williams and Wilkins (2009) 37: 1-22.

[2] Wesley JR. Invited Review: Nutrition Support Teams: Past, Present, and Future. *Nutr. Clin. Prac.* (1995) 10 (6): 219-228.

[3] Schneider *PJ*. Nutrition Support Teams: An Evidence-Based Practice. *Clin. Prac. (*2006) 21 (1): 62-67.

[4] Dodds ES, Murray JD, Trexler KM, Grant JP. Metabolic Occurrences in Total Parenteral Nutrition Patients Managed by a Nutrition Support Team. *Nutr. Clin. Prac.* (2001) 16 (2): 78-84.

[5] Goldstein M, Braitman LE, Levine GM. Medical and financial costs associated with termination of a nutrition support nurse. *JPEN (*2000) 24(6): 323-327.

[6] Traeger SM, Williams GB, Milliren G, Young DS, Fisher M, Haug MT. Total Parenteral Nutrition by a Nutrition Support Team: Improved Quality of Care. *JPEN* (1986) 10(4): 408-412.

[7] Faubion WC, Wesley JR, Khalidi N, Silva J. Total Parenteral Nutrition Catheter Sepsis: Impact of the Team Approach. *JPEN* (1986) 10(6): 642-645.

[8] Sistanizad M, Kouchek M, Miri M, Goharani R, Solouki M, Ayazkhoo L, Foroumand M, Mokhtari M.. Carbapenem Restriction and its Effect on Bacterial Resistance in an Intensive Care unit of a Teaching Hospital. *Iranian J. Pharm. Res.* (2013) 12 (3): 503-509.

[9] Allison SP. Malnutrition, disease, and outcome. *Nutrition* (2000) 16 (7-8): 590-3.
[10] Huang YC. Malnutrition in the critically ill patients. *Nutrition* (2001) 17 (9): 745-46.
[11] Baudouin SV, Evans TW. Nutritional support in critical care. *Clin chest med* (2003)24: 633-644.
[12]Chan S, Mc Crowen KC, Black burn GL. Nutrition Management in the ICU. *Chest* (1999) 115 (5): 145s-148s.
[13] Ovayola N, Torun S, Ucan O, Ozdemir P, Buyukhatipoglu H, Pehlivan Y, Geyik R. Review Of Data of the patients receiving total parenteral nutrition at the intensive care unit of a university hospital. *J Natl Med Assoc* (2006) 12: 1958-62.
[14] Deegan H, Dent S, Heyland DK, Keefe L, Drover JW. Supplemental parenteral nutrition in the critically ill patient: A retrospective study. *Crit care med* (1999) 27 (1) suppl: A76.
[15] Khalili H, Mojtahedzadeh M, Oveise MR, Tavakoli M. Evaluation of serum trace elements levels in critically ill patients. *Journal of Oloom pirapezeshki* (1384) 1 (2): 313-9.
[16] Khalili H, Mojtahedzadeh M, Oveise MR, Tavakoli M. Is critically ill patients recieved enough metabolic support? *Pajuhandeh* (1383) 1 (1): 45-51.
[17] Kamgarpoor A, Kazemzadeh E.SH, Ravanshad SH. Parenteral-enteral versus enteral nutrition on calorie, protein intake and nitrogen metabolism of head injured patients. *The Journal of Qazvin Univ. of Med. Sc.* (2001) 19 Autumn.
[18] Sarafzadeh F. Sohrevardi S. M. Gharehghozli M. Ahmadinejad M. Detection of the Most Common Microorganisms and Their Resistance against Anti-microbials in Intubated Patients in an ICU in Kerman, Iranian *J. Pharm. Res.* (2010) 9 (4):437-443.
[19] Bellini LM. Nutritional support in the critically ill. (2009) Available from: http://www.uptodate.com/online/content/topic.do?topicKey=cc_medi/18117&view=print/ Accessed September 8, 2009.
[20] Winker MA. Total Parenteral Nutrition for Critically Ill Patients. To the Editor. *JAMA* (1999) 282(15): 1423-1425.
[21] Roberts SR, Kennerly DA, Keane D, George C. Nutrition support in the intensive care unit. Adequacy, timeliness, and outcomes. *Crit care nur* (2003) 23:49.
[22] Waitzberg DL, Plopper C. Postoperative Total Parenteral Nutrition. *World J. Surg* (1999) 23: 560–564.
[23] Chrisanderson D, Heimburger DC, Morgan SL, Geels WJ, Henry KL, Conner W, Hensrud DD, Thompson G, Weinsier RL. Metabolic Complications of Total Parenteral Nutrition: Effects of a Nutrition Support Service. *JPEN (*1996) 20(3): 206-210.
[24] Donini LM, Savina C, Ricciardi LM, Coletti C, Paolini M, Scavone L, De Felice MR, Laviano A, Rossi Fanelli F, Cannella C. Applied nutritional investigation; Predicting the outcome of artificial nutrition by clinical and functional indices. *Nutr* (2009) 25: 11–19.
[25] Marik PE. Death by total parenteral nutrition: the saga continues. *Crit Care Med* (2011) 39 (6): 1536-7
[26] Dalton MJ, Schepers G, Gee JP, Alberts CC, Eckhauser FE, Kirking DM. Consultative Total Parenteral Nutrition Teams: The Effect on the Incidence of Total Parenteral Nutrition-Related Complications. *JPEN* (1984) 8(2): 146-152.
[27] Naylor CJ, GriffithsRD, Fernandez RS. Does a Multidisciplinary Total Parenteral Nutrition Team Improve Patient Outcomes? A systematic review. *JPEN* (2004) 28(4): 251.