Economic assessment of different administration modes for total parenteral nutrition

Karine ACHACH (1), Eliane PEROUX (2), Xavier HÉBUTERNE (3)


RÉSUMÉ

Buts — Les différents nutriments nécessaires à la nutrition parentérale peuvent être administrés sous forme de flacons séparés ou de mélanges nutritifs complets. Ces derniers peuvent être commercialisés par l’industrie pharmaceutique, réalisés par les pharmacies hospitalières ou fabriqués par des laboratoires façonniers. Le but de ce travail a été d’estimer le coût d’une journée de nutrition parentérale cyclique en fonction des différentes modalités d’administration.

Méthodes — Le coût de production des mélanges nutritifs hospitaliers a été calculé en considérant 5 postes de dépenses (matières premières et contenant, consommables, amortissement, contrôle et personnel). Celui des autres alternatives thérapeutiques a été évalué pour une formule identique. Le temps infirmier et le matériel nécessaires aux branchements et débranchements ont également été estimés afin de déterminer le coût total de la journée de nutrition parentérale.

Résultats — Les coûts observés étaient respectivement de 46,04 €/journée par la méthode des flacons séparés, de 50,61 €/journée pour les poches hospitalières, de 65,41 et 72,87 €/journée pour les poches industrielles supplémentées et de 82,02 €/journée pour les poches réalisées par les façonniers.

Conclusion — Les poches hospitalières permettent, pour un surcoût minimum, d’offrir des conditions de facilité et de sécurité d’emploi optimales par rapport à la méthode des flacons séparés.

RéSUMÉ

Aim — Total parenteral nutrition can be administered with separate bottles or complete admixtures prepared by commercial firms, the hospital pharmacy, or hospital subcontractors. The aim of this study was to compare overall cost of total parenteral nutrition using different administration modes.

Methods — Overall production costs of hospital parenteral admixtures were calculated from five expenditures (raw materials, consumable items, annual depreciation, control costs, staff costs). Cost for the other administration modes were evaluated for an identical formula. Time spent by nurses and the cost of connecting material was estimated to determine the overall cost for one day of parenteral nutrition.

Results — Total cost was 46.04 euros/day with separate bottles, 50.61 euros/day for hospital preparations, 65.41 and 72.87 euros/day for industrial preparations and 82.02 euros/day for formulations prepared by subcontractors.

Conclusion — Hospital preparations offer, for minimal outlay, an alternative for parenteral nutrition of much higher quality than the separate bottles method.

Total parenteral nutrition can be proposed for gastroenterology patients if oral or enteral nutrition is insufficient, ineffective, or impossible, or contraindicated (when rest of the digestive tract is required). Its widespread use has lead to several therapeutic modalities. The different nutrients required for parenteral nutrition can be administered either with separate bottles or with specially prepared admixtures. Several type of admixtures are marketed by the pharmaceutical industry or prepared by hospital pharmacies or subcontracting laboratories [1].

Hospital formulations are prepared as sterile solutions for injection under the responsibility of the hospital pharmacist. The final presentation cannot be re-sterilized. In France, the production process must comply with strict quality standards defined by Good Practices for Manufacturing Solutions for Injection promulgated by the French Ministry of Health [2]. These quality and safety standards require production in a protected unit, in accordance with well-defined and detailed techniques, by motivated and specially trained personnel [3, 4].

The production laboratory at the Nice University Hospital General Pharmacy has prepared nutritive formulations since 1989, mainly for adult and pediatric gastroenterology and intensive care units. In June 1991, this unit was granted approval to produce admixtures for adult home parenteral nutrition in compliance with the decree of December 18, 1984 [5]. Since this time, the activity of the unit has grown steadily with 2,509 formulations produced in 1989 and 4,252 in 2000.

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The nutritive admixtures produced by the Nice University Hospital General Pharmacy are standard formulations identified as P1 to P5 depending on the energy and protein levels (1,530 to 2,880 non-protein calories and 10-20 g nitrogen content). These ternary formulations are supplemented with electrolytes, trace elements, and vitamins.

The purpose of this study was to assess the total cost of one day of parenteral nutrition for gastroenterology patients using formulations manufactured by the hospital pharmacy in comparison with administration using separate bottles, supplemented admixtures manufactured by commercial firms, or admixtures prepared by subcontractors.

### Material and methods

#### Organization of the hospital production unit and the production process

The personnel working in the production unit were a part-time hospital consultant, a pharmacy resident, an associate pharmacist, three full-time pharmacy assistants, and a half-time hospital agent. The nutrient formulations were prepared aseptically under a class A horizontal laminar flow hood situated in a class B controlled atmosphere. Formulations were prepared twice a week for inpatients and once a week for outpatients.

Ethylvinylacetate bags were filled with the different solutions using a sterile nitrogen pressure pump. The bags were labeled, weighed, and packaged individually in a thermosealed sack and held 24 hours at 4°C in the dark [6].

A total of 3,239 bags were prepared for adult patients in 2000: 1,958 for inpatients and 1,281 for outpatients. During this same period, 4,525 bags were produced during these five days, giving a total of 435 bags produced during 25 processing sessions. The cost of producing a hospital formulation was calculated for the number of bags produced during the study period.

#### Cost analysis

In order to compare therapeutic alternatives of equivalent nutritional value, the study was performed for the most frequently employed formulation and similar commercial preparations. The most widely prescribed formulation for gastroenterology patients was the P3 formulation (57% of the prescriptions). Commercial admixtures with a ternary formulation and included the cost of the raw material and the container.

### Cost of producing a hospital formulation

Different parameters were taken into account to determine the cost of producing a hospital formulation. Variable costs depended on the type of formulation and included the cost of the raw material and the container. Fixed costs included consumable items, bacteriology controls, depreciation of equipment and facilities, and personnel costs [7-10].

All raw materials and all equipment used during a five-week period were included in the cost analysis. Time spent by each category of personnel to produce the nutritive preparations (reception of the prescriptions, preparation and control of the production charts, production process, bacteriology controls, preparation of the refrigerated boxes) as well as time spent to operate the unit (storage and handling stocks, operation of the sterile unit, maintenance and decontamination of the sterile unit, upkeep, organization) were recorded daily during this five-day period. A total of 384 adult formulations and 51 pediatric formulations were produced during these five days, giving a total of 435 bags produced during 25 processing sessions. The cost of production was calculated for each type of adult or pediatric bag while operating costs of the sterile unit were determined per bag produced.

Raw material used to produce the formulations were:

- Hyperamine®: 20%, 250 and 500 ml; 30% dextrose, 250 and 100 ml; Lipoven®: 20%, 500 ml; acid potassium phosphate 13.6%, 10 ml; Lantin®: 40 ml; Nonan®: 40 ml, and Cemevir® lysophilate. The ethylvinylacetate bags (Stedim, Aubagne, France) contained 3 liters.

Consumables were:

- Disposable material (kit for filling the adult bags, needles, syringes, swabs), garments (sterile gloves, disposable headwear, masks, overshoes), antiseptics and decontaminants, material for laboratory maintenance, thermosealed sacks, HEPA filters, and nitrogen nozzles.

The cost of the filters and nozzles was divided by the number of bags prepared annually while the cost of the other consumable items was calculated for the number of bags produced during the study period.

Depreciation was calculated linearly over 5 years for equipment (filling station, refrigerated boxes), and determined for the number of bags prepared in one year. Depreciation of the unit itself was not calculated since it was constructed more than ten years ago.

### Tableau I

<table>
<thead>
<tr>
<th>Bag content</th>
<th>P3 formulation</th>
<th>Clinomel® N7-1000</th>
<th>Kabimix® 2400</th>
<th>Separate bottles</th>
<th>Subcontractor bags</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrogen (g)</td>
<td>15.5</td>
<td>13.2</td>
<td>14</td>
<td>15.5</td>
<td>15.5</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>37.5</td>
<td>320</td>
<td>330</td>
<td>375</td>
<td>375</td>
</tr>
<tr>
<td>Lipids (g)</td>
<td>74.2</td>
<td>89</td>
<td>120</td>
<td>74.2</td>
<td>74.2</td>
</tr>
<tr>
<td>Non-protein energy (kcal)</td>
<td>2168</td>
<td>2080</td>
<td>2400</td>
<td>2168</td>
<td>2168</td>
</tr>
<tr>
<td>Volume (mL)</td>
<td>2460</td>
<td>2000</td>
<td>2400</td>
<td>2460</td>
<td>2460</td>
</tr>
</tbody>
</table>
The cost of quality control for the bags and the sterile unit was calculated from the billing prices provided by the bacteriology laboratory. It was determined for the number of adult bags and for the total number of bags produced during the study period for the sterile unit.

Personnel costs took into consideration that the laboratory had other activities besides production of the parenteral nutrition bags. The time spent for each category of personnel retained for analysis included only time spent for the unit’s nutritional activity. Time required to produce the bags was calculated per adult bag while the time spent for sterile unit operation was calculated for all bags produced during the study period.

### Cost of other administration modes, excluding line connection

As the commercial admixtures available for parenteral nutrition do not contain vitamins, trace elements, or electrolytes (for Kabimix®), their cost was calculated after supplementation. The supplementation process requires strict aseptic conditions, preferably under laminar flow, under the control of a pharmacist [11]. The commercial bags were supplemented in accordance with the manufacturer’s recommendations: one bottle of Nonan® and one bottle of Cernevit® for Clinomel® N7-1000 and one bottle of Lonitan®, one bottle of Nonan and one bottle of Cernevit® for Kabimix® 2400. The criteria taken into account for the cost analysis were: cost of the raw material and equipment used, and the time necessary to prepare the commercial bags for use as well as the extra time needed for vitamin, electrolyte, and trace element supplementation. Consumable items were needles, syringes, swabs, sterile gloves, sterile drapes, and thermosealed sacks. The time required for supplementation under the laminar flow hood, labeling and packaging were recorded for two successive manipulations.

Parenteral nutrition with separate bottles was performed in a sequential manner using bottles containing carbohydrates, proteins, lipids, vitamins, electrolytes, and trace elements. The costs of the raw material required for separate-bottle parenteral nutrition were calculated for a regimen with the same calorie content as the P3 formula.

For the bags produced by subcontractors, the cost of the raw material was calculated per milliliter from the market price paid by the University Hospital for each component. Cost of production, quality control, packaging and delivery was added. This cost varied with monthly demand and was 47.26 euros for a monthly order of more than 120 bags.

### Evaluation of the overall cost of one day of parenteral nutrition

Discontinuous parenteral nutrition is generally the rule for gastroenterology patients, so the cost of setting up and disconnecting the infusion line was included in the calculation of each mode of administration.

The infusion line was generally connected in the evening, under sterile conditions after rinsing the catheter with 20 ml 0.9% NaCl. The time required to set up the line and the material used during the infusion were the same for the hospital bags, the supplemented commercial bags, and the subcontractor bags.

All consumables required for infusion (dispensable headwear, masks, sterile drapes, sterile gowns, pump line, needles, syringes, swabs, sterile gloves, 10/10 dressings, and 0.9% NaCl vials) were included as cost items.

The different manipulations performed by the nursing staff were timed several times at the patient’s bedside in order to establish a mean time for each manipulation.

For administration of separate bottles, reconstitution of the products and supplementation procedures were carried out at the bedside. Consumables included material needed to administer all of the different mixtures, a 4-way line, a 1-way line, and an infuser.

The time required to set up the line was comparable for the different modes of administration. Parenteral nutrition was discontinued in the morning and the catheter was closed under sterile conditions. Consumables were disposable headwear, masks, sterile drapes, sterile gowns, needles, syringes, swabs, sterile gloves, 20/10 dressings, 500 IU heparin vials and 0.9% NaCl vials.

### Results

#### Cost of the hospital bag, formulation P3

The cost of the P3 bag was itemized as follows: 29.44 euros for variable costs (raw products and containers), 1.30 euros for consumables, 0.15 euros for depreciation, 3.07 euros for quality control, and 4.15 euros for personnel (table II). The total cost of a P3 bag was thus 38.11 euros, 77% of the cost being raw material and container. The time to complete an adult bag including all activities and personnel categories was 18 minutes.

#### Cost of other modes of parenteral nutrition

The purchasing price of the commercial bags was 42.69 euros for Clinomel® and 47.26 euros for Kabimix®, to which the cost of supplementation must be added. The supplementation cost included raw materials, consumables, and personnel. The cost for supplementation was 10.22 and 13.11 euros for Clinomel® and Kabimix®, respectively; the supplementation process required 10 minutes for a laboratory assistant. The total cost of the commercial bags after supplementation was thus 52.91 euros for Clinomel® (full tax purchasing price + 10.22 euros) and 60.37 euros for Kabimix® (full tax purchasing price + 13.11 euros).
The cost of the raw materials required for administration of separate bottles was 24.39 euros for a content equivalent to the P3 formulation.

The cost of bags prepared by a subcontractor for P3-equivalent bags was 69.52 euros, with 22.26 euros for raw materials. These results are summarized in Table III.

### Cost of connecting and disconnecting the infusion line

Time required by specialized nurses to set up the parenteral nutrition infusion line using the complete admixtures, as measured at the bedside for several patients, was 10 minutes (2.67 euros). It took 35 minutes for separate bottles (9.35 euros). Cost of consumable items was 4.80 euros for complete admixtures and 7.27 euros for separate bottles. The total cost of connecting the line was thus 7.47 euros for complete admixtures and 16.62 euros for separate bottles.

Ten minutes (2.67 euros) were needed to disconnect the lines for all the different administration modes. Consumable items cost 2.36 euros, giving a total cost of 5.03 euros.

### Total cost of a day of parenteral nutrition

The total cost of a day of parenteral nutrition was then calculated which included cost of infusion (line set up and disconnection) for the different modes of administration (table IV). The total cost was 46.04 euros for the separate bottle method, 50.61 euros for the hospital P3 bags, 65.41 euros for the supplemented Clinomel® N7-1000 bags, 72.87 euros for the supplemented Kabimix® 2400 bags, and 82.02 euros for bags prepared by subcontractors.

### Discussion

Cost analysis is one of many approaches useful for determining an optimal strategy for nutritional support, which must be chosen on the basis of medical and economic effectiveness [12]. The overall cost of parenteral nutrition depends on the type of products administered, the administration modalities, monitoring protocols, and treatment of potential complications [13]. The different methods developed to estimate cost have produced quite different results. The different figures reported must be interpreted in terms of the type of nutritional support provided, the quality of which may vary greatly.

In our study, separate bottles was found to be the most economical means for administering parenteral nutrition. This method offers the advantage of greater latitude for the prescriber who can use different combinations to rapidly adapt nutritional needs.

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**Tableau III.** – Cost of different administration modes before connection of the infusion line.

<table>
<thead>
<tr>
<th>Total cost (euros)</th>
<th>Separate bottles</th>
<th>P3 hospital formulation</th>
<th>Supplemented Clinomel® N7-1000</th>
<th>Supplemented Kabimix® 2400</th>
<th>Subcontractor pouches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw materials for nutritive support</td>
<td>24.39</td>
<td>38.11</td>
<td>42.69</td>
<td>47.26</td>
<td>22.26</td>
</tr>
<tr>
<td>Raw materials for supplementation</td>
<td>—</td>
<td>—</td>
<td>6.71</td>
<td>9.30</td>
<td>—</td>
</tr>
<tr>
<td>Consumables for supplementation</td>
<td>—</td>
<td>—</td>
<td>1.22</td>
<td>1.52</td>
<td>—</td>
</tr>
<tr>
<td>Personnel for supplementation*</td>
<td>—</td>
<td>—</td>
<td>2.29</td>
<td>2.29</td>
<td>—</td>
</tr>
<tr>
<td>Processing</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>47.26</td>
</tr>
<tr>
<td>Total cost</td>
<td>24.39</td>
<td>38.11</td>
<td>52.91</td>
<td>60.37</td>
<td>69.52</td>
</tr>
</tbody>
</table>

* Time required for supplementation in the hospital pharmacy: 10 minutes.

**Tableau IV.** – Total cost for one day of parenteral nutrition.

<table>
<thead>
<tr>
<th>Total cost (euros)</th>
<th>Separate bottles</th>
<th>P3 hospital formulation</th>
<th>Supplemented Clinomel® N7-1000</th>
<th>Supplemented Kabimix® 2400</th>
<th>Subcontractor pouches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritive support</td>
<td>24.39</td>
<td>38.11</td>
<td>52.91</td>
<td>60.37</td>
<td>69.52</td>
</tr>
<tr>
<td>Connecting*</td>
<td>16.62</td>
<td>7.47</td>
<td>7.47</td>
<td>7.47</td>
<td>7.47</td>
</tr>
<tr>
<td>Disconnecting*</td>
<td>5.03</td>
<td>5.03</td>
<td>5.03</td>
<td>5.03</td>
<td>5.03</td>
</tr>
<tr>
<td>Total cost</td>
<td>46.04</td>
<td>50.61</td>
<td>65.41</td>
<td>72.87</td>
<td>82.02</td>
</tr>
<tr>
<td>Total cost compared with hospital bag</td>
<td>– 9 %</td>
<td>—</td>
<td>+ 29 %</td>
<td>+ 44 %</td>
<td>+ 62 %</td>
</tr>
</tbody>
</table>

* Nurse time for connection: 35 minutes for separate bottles, 10 minutes complete admixtures. ° Nurse time for disconnection: 10 minutes.
support to the patient’s individual needs. The sequential nature of the infusions can however have unfavorable metabolic consequences. In addition, daily administration requires more time for preparation and surveillance and a greater number of manipulations which increases the risk of bacterial contamination despite a correctly applied aseptic protocol [14-16].

Administration of a complete nutritive admixture in a ready-to-use bag reduces the risk of infection since a single infusion line is used. The time required for nurse surveillance is also shorter.

Admixtures prepared in the hospital pharmacy allow prescribers to establish a precise formulation specifically designed for the nutritional needs of the individual patient, both in terms of quantity and quality. This type of organization requires a certain number of prerequisites, namely appropriate pharmaceutical logistics and good collaboration between the different units.

Nutritional products manufactured by pharmaceutical firms offer the advantage of meeting well-established standard requirements and, because of their longer shelf-life, of more convenient stock management and distribution to the different units [17]. The need for supplementation does however limit this advantage because after supplementation the stability of these products can be guaranteed for only 2 or 3 days at 4°C. Supplementation also has to be organized and requires several manipulations. The cost of these admixtures is largely dependent on the purchase price, which can vary greatly depending upon local supply.

It should be noted that the nutritional support systems considered in this study were very similar but not exactly equivalent in terms of nutritional content, especially lipid content. The comparisons were also made with formulations ordered by primary care units. Such formulations generally correspond to a high level of nutritional support to meet the specific needs of the different health care units or staffs.

Our cost assessments are nevertheless quite similar to those reported by others using similar methodologies. Hospital bags can be prepared either in a sterile unit under laminar flow or in an isolator. For hospital bags prepared under laminar flow, reported costs have been 38,72, 44.06 and 44.82 euros [7, 8, 11]. These costs are higher than those observed for units operating with an isolator [9, 18]. The personnel cost depends on whether bag preparation is an exclusive activity or whether the personnel also participate in other activities. The time required to prepare the bags reported in other studies have ranged from 15 to 25 minutes depending on the level of activity of the unit [8, 11, 19]. Most of the comparative studies have demonstrated a higher cost for the use of commercial bags supplemented by the hospital pharmacy in comparison with hospital prepared bags [10, 11, 19, 20]. In one recent study reported by Pichard et al. [21] who compared separate bottles, hospital bags, and supplemented commercial bags, there was a net savings with the use of supplemented commercial bags. In that work, the high cost of the raw materials required to produce the nutritive admixtures explained the higher cost of the hospital preparations. Inversely, in our study, the cost of the hospital preparations would have been higher if the processing unit had not already been depreciated.

### Conclusion

Our experience with hospital bags for parenteral nutrition, prepared with optimal safety and providing maximal convenience, demonstrates that the extra cost was minimum when compared with separated bottles, was small. Total cost for supplemented commercial preparations and admixtures prepared by subcontractors was higher than hospital preparations with equivalent nutritional value, safety, and convenience of use. This extra cost would be justified if the existing hospital facilities are poorly adapted or would require important transformations. For hospitals with currently operating units, preparation of hospital formulations might be focused on preparing a specific type of bag (particularly pediatric bags) for more patients.

### REFERENCES

5. Circulaire ministérielle B176 du 18 décembre 1984 relative à la thérapeutique de la nutrition parentérale à domicile.


