Original Paper

A Simple Method of Calculation in Excel for the Protein Requirements in Preterm New Borns

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ABSTRACT: Introduction: The nutritional balance between the nutritional requirements of the organism and the intake is a very delicate thing to adjust especially when it comes to the premature new-born in whom often the oral feeding is very challenging and the need for parenteral feeding is very pressing. Purpose: The goal of this article is to present a simple method of calculation for the amino acid parenteral intake in preterm infants using the Excel spreadsheet platform as a platform. Material and Method: Using Excel commands, we translate the algorithms for the protein requirements calculation into an electronic format. This will allow the creation of a template that quickly identifies the need for proteins according to the clinical and evolutional features of the premature new-born, significantly reducing the duration of the calculation. Results: This method is easy to perform, simple and efficient. The calculation template has significantly reduced the errors and the actual working time with the algorithms. These effects are very obvious in intensive care units that take care of a large number of premature babies. Conclusions: Computerized calculation allows a decrease in calculation errors and also reduces the time actually allocated for the calculation, especially for the very complicated algorithms. Following this template in Excel, we can create separate modules for the algorithms necessary to calculate the needs for the intake of liquids, calories, lipids, and minerals.

KEYWORD: *Software; protein equilibrium; preterm infants; excel platform*

Introduction

The early intake of amino acids and proteins in premature infants brings significant changes in the composition of the body with long-term benefits. The role of proteins and amino acids in the prevention of malnutrition and neurocognitive development is known [1].

Proteins also play a protective role in the intestine, lungs and eyes. The reduced capacity of the digestive system in preterm, makes the enteral intake to be optimal for a long time. Compensation for this deficiency is possible through parenteral administration of amino acids [2,3].

The ability of medical staff to manipulate parenteral nutrition can prevent a number of complications induced by prematurity [4].

Because proteins play a key role in the recovery and development of prematurity, but also in the prevention of premature sequelae, we intend to develop a simple application for accurately calculating the need and contribution both parenterally and enterally, using a relatively universal platform found in personal computers-Microsoft Excel.

Material and Method

Use the section protocol recommendations or recommendations in the utilized guides for parenteral and enteral nutrition.

Remember, there is still no consensus, and the recommendations may be different from the ones used. We have used the recommendations of the Canadian Pediatric Society (1995) for parenteral nutrition as reference for parenteral nutrition: at the prematurity with a birth weight below 1000g: 3.5-4g/kg/day and at the prematurity with a birth weight above 1000g: 3-3.5/kg/day.

For enteral nutrition, the recommendations used were 3-3.6g/kg/day in premature babies with birth weight above 1500g, 2.5-4.2g/kg/day in premature babies with birth weight 1000-1500g and 4-4.5g/kg/day in premature babies with birth weight below 1000g.

The first 24 hours of life were scored on Day 1. If you use other nutritional items, it will be necessary to change the progression and target values from the equations presented-not their syntax [5-8].

In the first step, one should determine which are the reference cells in which will enter the data, these cells will appear in the working formulas.

On a column (or line), type the following labels: day (postnatal day) (d), birth weight (Bw), current weight (Cw), the volume of mother milk/day (MM), the volume of powder milk/day (PM), the fortifiants/day (F), protein supplement per day (PS).

Inside these labels leave a free box, where the data should be entered.

We want to avoid the use of cell coordinates in the equations so select each cell and at the top left, near the function bar instead of the displayed coordinates, type a short label (ex. Instead of A1, type Ga).

In the parenthesis we have marked the short label that we recommend to be used in the equations.

It is necessary to choose a new column or line for the biological values inputs, such as: pH, Na^+, K^+, Cl^-, $HCO3^-$ (Bicarbonate), Urea (BUN), Creatinine, GPT, GOT, FAL.

Somewhere on the page, assign a space with the following labels: anionic gap (Gap), enteral protein intake (EPI), parenteral amino acid intake (PAI); total protein intake (TPI); minimum requirement (NPmin) and maximum in parenteral nutrition (NPmax), respectively minimum (NEmin) and maximum in enteral nutrition (NEmax); conditions of limitation; and the minimum and maximum differences (Dmin and Dmax).

These fields will be required to facilitate expression in the final equations.

Central allocate three cells with the following labels: Minimum Aminoven volume required; Maximum Aminoven volume required; Volume Aminoven administered.

Another central field must be allocated to the final report. Add the following tags: Daily needs of amino acids and proteins; Total Input; Enteral Intake and Parenteral Intake. These cells will automatically display the results of the calculations. It is imperative to select all the cells that will serve as inputs, then uncheck "Lock cell" from the "Home-Format-Protection" menu.

In the second step, using the excel functions, we introduce algorithms for calculating minimum and maximum needs in parenteral and enteral nutrition and the minimal and maximum computation equation required for amino acid perfusion. Last but not least, the references that load the data into the report area. The most requested excel function will be the conditional if. It is also necessary to use the operators "and" "or" due to the complexity of the conditions. The if function has the syntax "=if (condition; true; false)". All functions will be preceded by the "=" sign, so the platform understands that there is a function instead of a text.

We will begin by calculating the anion gap, only in case of acidosis. In the box corresponding to the tag, type:*=if (pH<7,35; Na-Cl-Bicarbonat; 0)*. Easily type equal, then select the input cell for Na, select minus, then select the chlorine input cell, and repeat the HCO3 operation. Next, calculate the AGAPK (the anion gap with the K concentration included in the equation) and modify the cell name containing the equation with AGapK. Type:*=if (pH<7,35;K+Na-Cl-Bicarbonat;0)* [9].

In the box labeled "conditions of limitation" (Cond_restr), we type:*=IF (OR (Gap>16; AGapK>20; BUN>80; Creatinine>1; AND (GPT>80; GOT>80; FAL>200)); "yes"; "no").*

The equation returns "yes" if one of the conditions up to the operator "and" is fulfilled or if all the conditions after the operator "and" are met. Returns "no" if the conditions are not validated. The equation decides whether or not there are conditions restricting parenteral amino acid intake (Acidosis with gap> 16, respectively GapK> 20, renal failure, hepatocitolysis).

We will introduce the minimum computational algorithm for parenteral nutrition. The algorithm has the following statement: if the postnatal day is less than 7 days and the restrictive conditions are validated, the minimum amino acid dose will be 0.5/kg/day [5]. If there is no reason to restrict and the birth weight is less than 1000g, start with 1g/kg/day on Day 1 and increase daily to 3.5g/kg/day on Day 3-th. If birth weight is over 1000g, it will start on day 1 with 1g/kg/day and increase to day 3 to 3g/kg/day. For more than 7 days of age and current restrictions, the amount will be 0.5g/kg/day based on the current weight of the prematurity. If there are no restrictions, we have a minimum requirement of 3.5g/kg/day for preterm birth weight below 1000g and 3g/kg/day for preterm with Bw>1000g (using current weight) [5,7]. The progression equation has the form: Bw+1,25(d-1) Bw for preterm less than 1000g, and Bw+(d-1) Bw for prematurity with Bw>1000g. [5] Because the expressions use Kg measurement units, avoid weighting in grams.

The algorithm must return the result in the space allocated for the minimum requirement in parenteral nutrition (NPmin). The excel function that goes through the algorithm and chooses the right equation for the conjuncture, is the conditional if repeatedly.

=IF (d<=7; IF (Cond_restr="yes"; 0,5*Bw;
IF (Bw<1; IF (d<=3; Bw+1,25*(d-1)*Bw;
3,5*Bw); IF (d<=3; Bw+(d-1)*Bw; 3*Bw)));
IF (Cond_restr="yes"; 0,5*Cw; IF (Bw<1;
3,5*Cw; 3*Cw))).

With this syntax, excel initially checks the child's age. If it is less than or equal to 7 days, continue to go through the chain of the algorithm (blue text) in the order: Limiting conditions, Bw below 1Kg or over 1kg, and stops to calculate the formula for the minimum where the condition is validated. If the age is greater than 7 days, it will go through the green algorithm, using the equation corresponding to the condition to be confirmed.

For the maximum parenteral requirement-we use the same rules, but the difference: 2g/kg/day if there are reasons for restriction, 4g/kg/day in preterm with Bw below 1000g, 3.5g/kg/day in premature babies more than 1000g [5].

Of course, the progression equations for the 3 days are changed as follows: for preterm less than 1kg: 1,5Gn+1,25(d-1) Bw and for Bw>1kg: 1,5Bw+(d-1) Bw. [5]

The syntax of the equation will be:

IF (d<=7; IF (Cond_restr="yes"; 2*Bw;
IF (Bw<1; IF (d<=3; 1,5*Bw+1,25*(d-1)*Bw;
4*Bw); IF (d<=3;1,5*Bw+(d-1)*Bw;
3,5*Bw))); IF (Cond_restr="yes";2*Cw;
IF (Bw<1;4*Cw;3,5*Cw)))

Proceed to the introduction of the algorithm for calculating the recommended minimum in enteral nutrition: under 7 days postnatal-3g/kg/day for preterm with Bw>1500g; 3.5g/kg/day for premature babies with Bw 1000-1500g and 4g/kg/day for prematurity with Bw below 1000g [5,10]. Over 7 days of life, the landmarks are the same, only we will refer to Cw (current weight). The syntax will be:

=IF (d<=7; IF (Bw<1; 4*Bw; IF (Bw>1,5;
3*Bw; 3,5*Bw)); IF (Bw<1; 4*Bw;
IF (Bw>1,5; 3*Cw; 3,5*Cw)))

For the calculation of the maximum requirement in enteral nutrition, the markers are: 3.6g/kg/day in the preterm with Bw>1500g, 4.2g/kg/day in the preterm with Bw 1000-1500g and 4.5g/kg/day in the preterm with Bw<1000g, with reference to Bw for ages less than 7 days and Cw for ages greater than 7 [5,10]. The syntax of the equation will take the form of:

=IF (d<=7; IF (Bw<1; 4,5*Bw; IF (Bw>1,5;
3,6*Bw; 4,2*Bw)); IF (Bw<1; 4,5*Cw;
IF (Bw>1,5; 3,6*Cw; 4,2*Cw)))

Next, we will establish the equations for the calculation of enteral protein intake. We have as sources: maternal milk (MM), formulas (PM), fortifiants (F) and protein supplement (PS).

Enteral intake can be defined at a time by all these sources, so first we have to calculate how many grams of protein each participates [11,12].

Next to the box where you enter the total volume of breast milk consumed within 24 hours, enter the following: =IF (d<=5;0,02*MM; IF (d>28; 0,0105*MM; 0,014*MM)) to calculate the amount of protein in the mother's milk, customized to the duration of birth. With a good approximation, in the first 5 days, colostrum has an average of 2g protein/100ml (equivalent to 0.02g/ml), then premature milk, averaging 1.4g protein/100ml (0.014g/ml) after the first 3-4 weeks postnatally, contains about 1.05g/100ml [11]. The protein concentration per ml, multiplied by the amount of milk consumed/24 hours, will return the amount of protein/24 hours, as a source of breast milk. Do not forget to add the extra label for the box in which you will enter the total daily milk volume (TMV).

To calculate the amount of protein from the formula, we'll have to do some pre-fireworks. Somewhere on the Excel page without being visible, make a list on the column, with the names of the most commonly used formulas in your department. We have introduced: pre-NAN; pre-NAN stage 1 and 2, Prematil, Lactana-pre, Humana 0. Return to the left of the box where you enter the total formula volume, select the box and from the Date menu, choose Date validation. In the options window, choose the validation list, and in the source box enter the coordinates from the first to the last line in the milk formula column. This will allow one to produce a vertical list from which to select the formula. To the right of the box where one should enter the volume of the formula used, type the function:

=IF (Formula="pre-NANstg1"; 0,0288*PM;
IF (Formula="pre-NANstg2"; 0,0205*PM;
IF (Formula="pre-NAN"; 0,0232*PM;
IF (Formula="Prematil"; 0,026*PM;
IF (Formula="Lactana-pre"; 0,017*PM;
IF (Formula="Humana 0"; 0,021*PM; 0))))))

Of course, we should not forget to rename the cell in which you enter the formula volume, with the label you will use in the equation syntax. The tag in the example is: "PM". The formula list box has been renamed "Formula". In fact, in the equation, we must keep in mind the composition declared by the manufacturer (the amount of protein/100ml after preparation). The list allows us to switch the calculation quickly by simply choosing the milk formula. So, we can make repetitive simulations to choose optimally if you have more milk formulas available.

Another source of protein is the fortifiers. We introduced the program, FM85 and FMS, being the most used. For switching, make a list of options, as we have shown in milk formulas. The box in which we enter the daily amount of fortifier, rename it as "F". List box, rename it

"Fortifiant". The syntax of the excel function will take the form:

=IF (Fortifiant="FM85"; 0,2*F;
IF (Fortifiant="FMS"; 0,25*F; 0))

For the protein supplement, it is no longer necessary to create a list, with just one product available on the market-Aptamil PS. The box where we entered the daily supplement amount, re-enter it PS. The amount of effective protein coming from the supplement will be calculated in the near by:=PS * 0.821.

Type a space for the automatic calculation of total enteral protein intake, (short label: "EPI"), defined by the sum of the effective amounts of protein from the four sources (breast milk, formula, fortifying, protein supplement). We put it in the final report area. The syntax for the calculation formula will be:=SUM (E5: E8), where E5 is the box with the calculation coordinates for the amount of protein from the mother's milk, and the column continues with the proteins in the formula up to E8-protein from the protein supplement. The parenteral amino acid input is desirable to display in the report area. It is calculated by dividing by 10 the volume of Aminoven that we will administer. Basically, the syntax is=the coordinates of the cell in which you will enter the volume of Aminoven/10. The box was renamed with the abbreviation "PAI". Total protein intake will also be placed in the report area. Make the sum of the enteral and parenteral contributions (syntax is:=EPI+PAI). The box where the result will be displayed, we have renamed it "PTI". We still need to fix the need for amino acid infusion. The recommendation is to use Aminoven infant 10% because of the essential amino acid content. We have several situations where we can fit in, and which compels different calculations: enteral intake is subliminal, the main source being parenteral intake. Enteral intake is significant, but it does not provide the required amount for enteral nutrition alone. Completion with Aminoven approaches or integrates total protein intake into the nutrition guidelines. Enteral intake is almost complete, and its gradual increase requires a relatively proportional decrease in Aminoven infusion to avoid overcoming the upper limit of enteral nutrition. In order to integrate these situations into the program, we need the intersection of the recommendations (required) for parenteral and enteral nutrition with enteral and parenteral intake. We will first calculate the differences between the minimum recommendation for enteral nutrition and the amount of enteral protein, then the maximum recommendation for enteral nutrition and enteral intake. These differences will be recorded in a box in the intermediate area (where you calculated the anion gap and the conditions for restriction in the NP). Change the name of the excel box in Dmin and Dmax (corresponding to minimum and maximum differences) to use these labels instead of the coordinates. In the box designed for the minimum difference, type the function: =NEmin-EPI. For the maximum difference, in the cell, type the function:=NEmax-EPI. These differences may be subunit (enteral intake is higher than the NE recommendation), zero when they are equal. Positive differences mean that enteral intake is lower than the recommendation in enteral nutrition. In the latter situation, the parenteral amino acid requirement is either lesser than recommended in parenteral nutrition recommendations. Avoid the situation where the amino acid needs of parenteral nutrition exceed the parenteral nutrition recommendations. This situation must be provided and there must be an "operational limiter" in the equation. The minimum and maximum difference, help the computer decide which of the situations we are in, and calculate the corresponding volume of Aminoven.In the cell you've decided to target for the minimum recommended Aminoven volume, enter the following:

=IF (Dmin>=0; IF (OR(AND(d<=3; EPI=0);
AND (EPI>0; Dmin>NPmax); OR
(Dmin>NPmin)); NPmin*10; IF (AND (EPI>0;
OR (Dmin<=NPmin; AND (Dmin>NPmin;
Dmin<=NPmax))); Dmin*10;0)); 0)

In the cell that is intended to calculate the recommendation for the maximum recommended Aminoven volume, enter:

=IF (Dmax>=0; IF (OR(AND(d<=3; EPI=0);
AND (Dmax>=NPmax; EPI>=0;
PTI<=NEmax)); NPmax*10; IF (AND
(EPI>=0; Dmax<=NPmax); Dmax*10; 0)); 0)

In both formulas, the first condition is that the difference is positive, to avoid displaying a negative Aminoven need. The following conditions try to identify the situations in which the minimum and maximum recommendations are used in the parenteral mutation. If they do, then the amount of protein calculated for parenteral nutrition will be multiplied by 10 to display the volume of Aminoven and corresponds to the situation where we have total or predominantly parenteral parenteral nutrition. If these conditions are not met, the program checks another set of conditions to use the calculated amount based on the difference. The difference multiplied by 10 will be returned as a minimum and maximum volume recommendation for Aminoven. This corresponds to the situation where the main protein source is enteral, and parenteral nutrition brings a minimum complement below the threshold for recommendations for parenteral nutrition.

We are at the end of the application. For a quick feed, we recommend oset the cell in which we should enter the volume of Aminoven that we intend to administer and the cell with APT (Aminoven Parenteral Total Intake), change the background color to red if: Aminoven volume on which you intend to administer, exceeds the recommended maximum volume, and if APT exceeds the maximum recommendation in Parenteral Nutrition. This setting will attract more attention and do not risk using inadequately large volumes. For Aminoven, select the box to enter the volume, then choose Conditional Formatting from the Home menu. From the Edit formatting rule box, choose Use the formula to determine which cells to format. At the bottom of the window, we have the Format values field where this formula is true. In this field, type the equal sign, then select in the Aminoven volume entry page, type the ">" sign, then select in the work page the box where the program returns the maximum volume recommended for Aminoven. Click the "Format" button. The cell format window opens. From the Fill tab, select the alarm color (red example), press the Ok button to validate the operations. The result is that if one types a larger volume of Aminoven than the recommended maximum, the cell will have a red background. Do the same for TPI, as a landmark NEmax. We can repeat the TPI operation to enter other warning colors (eg. green when PTI is within NE, or yellow PTI falls below the lower NP recommendation, brick when PTI is within NP recommendation and red when PTI exceeds the maximum recommendations in enteral nutrition).

To navigate easily, with jumps directly to the cells that represent data inputs, we recommend unblocking for editing the input cells and the cells with the milk and fortifying formula lists as well as the cells in the biological balance. Block the worksheet by following the steps: Home-> Format-> Protect Sheet. Uncheck the select locked cell option and type a simple password (in our example-*user*), re-enter the password and validate by clicking the Ok button. Now we can move quickly using the arrows or the Tab key, only between the cells where we need to enter the calculation data. Of course, protect it against accidental overwriting the cells where the computations have been entered.

Results

Five neonatal physicians were asked to read the instructions (article), without receiving additional instructions, and edit the application. None had additional training for working with Excel spreadsheets.

The actual training time was of 4 hours. Only two were able to finish without mistakes (40% vs. 60% in binomial test p=0,63).

The most common mistakes were the punctuation in the syntax of functions: opening the function by the equal sign; type of quotation marks, semicolon (;) as separating element, spaces were blown in function, number of brackets not respected.

Frequently, it was wrong to rename the key cells, or they used a label other than the one in the instructions without altering the equation accordingly.

For these reasons, we found it appropriate to provide physicians with the exemplary excel sheet with the application in the article (http://enutrilab.ro/doc1.xlsx).

Working with the application on the case cases, the calculation time decreased by 90%. But most importantly, it has diminished also the errors of "appreciation".

Most often the importance of the biological balance was missed, with the loss of the moments when the restriction had to be applied. Secondly, there was underdosing of the intake due to the lack of intersection between the parenteral and the enteral nutrition.

The same reason caused an inadequate decrease in perfusion volume as an increase in enteral intake.

Discussion

In the absence of a consensus on recommendations for optimal intake (divergence of opinions on this topic, are exemplified in Table 1), we also imagined a universal module that can be easily adapted to different recommendations by setting the following variables: target for parenteral intake, target for enteral intake, how you measure postnatal day, the duration you want to make progression (http://enutrilab.ro/doc3.xlsx).

Table 1. Unbalances between the recommendations of variate international groups and authors, regarding the protein intake in premature new-born [13]

	Weight <1200g (g/kg/zi)	Weight >1200g (g/kg/zi)
Ziegler EE	**4,0**	**3,6**
Kashyap and Heird	**-**	**3,0**
Rigo	**3,8-4,2**	**3,4-3,6**
LSRO (Life Sciences Research Office)	**3,4-4,3**	**3,4-4,3**
ESPGHAN 2010 (European Society for Pediatric Gastroenterology, Hepatology and Nutrition)	**4,0-4,5**	**3,5-4,0**

Several aspects are universally accepted: initiation of parenteral protein intake should be done immediately after birth, progression to the target of the recommendations to be achieved gradually over a period of three days (one to five day); the calculation for the first week is related to the birth weight, the need for premature babies weighing less than 1000g is different from premenstrual requirements with a birth weight above 1000g [13].

One of the advantages of a computerized systems is its adaptability-one can program to calculate the way he wants, according to the rules he wants [14**]**.

The disadvantages are that in the absence of a consensus, the applications cannot be exhaustive and remain dependent on the operator.

In any case, no matter what the protocol or guide you are working on, whether or not it resembles the nutrition model presented, you will be able to make an application following the general pattern that we have presented to you, either by customizing some of the calculation equations or by creating your own functions [15**]**.

Finally, the computer and application are just a faster calculation tool and remain a dependent operator.

Healthcare professionals need to know the program and its purpose well in order to avoid entering incorrect data that would produce erroneous calculations.

In other words, these programs remain dependent operators.

Conclusions

The application is very useful as a computing tool designed to refine the recommendations of the guides accurately and quickly.

Fast, efficient, attractive, enables dynamic personalization of the need and detailing protein intake, providing clear benchmarks. We recommend that one should daily save his work data file in separate files (Save As, and postnatal day to the file name) to get the nutrition dynamics and save time by specifying the necessary reintroduction of all data.

However, our recommendation is not to try to "force" parenteral or enteral nutrition to keep up with the program suggestions.

Care should be taken about the signs of intolerance of the newborn whenever a change is made.

Finally, we should not forget that nutrition is the most important drug for premature, and there are side effects.

Also, remember that it is not enough just to get a correct protein intake. It is important to provide adequate caloric support from non-protein sources, and a good balance between metabolisms to avoid protein catabolism.

Abbreviations list:

AGapK: idem AGAPK, 5
AGAPK: the anion gap with the K concentration included in the equation, 5
PAI: Parenteral Total Intake, 4, 13, 14, 15
Bicarbonat: Bicarbonate, 5
BUN: Ureea Nitrogen, 4, 5
Bw: birth weight, 3, 6, 7, 8, 9
Cond_restr: Restrictions condtion (in equations), 5, 6, 7
Cw: current weight, 3, 7, 8, 9
d: in ecuation-postnatal day, 3, 6, 7, 8, 9, 13
Dmax: the maximum difference in protein intake needed, 4, 12, 13
Dmin: minimum diference in protein (gr) aport-requirement, 4, 12, 13
EPI: enteral protein intake, 4, 11
F: gr fortifiants /day, 3, 17, 18
FAL: alkaline phosphatase, 4, 5
Gap: anionic gap, 4, 5
HCO3: Bicarbonate, 4, 5
MM: volume of mother milk/day, 3, 9
NEmax: Maximum protein (gr) requirement in enteral nutrition, 4, 12, 13, 15

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NEmin: Minimum protein (gr) requirement in enteral nutrition, 4, 12
NPmax: maximum gr protein requirement in parenteral nutrition, 4, 13
NPmin: gr protein minimum requirement, 4, 6, 13
PM: volume of powder milk/ day, 3, 9, 10
PS: gr protein supplement per day, 3, 9, 11
TMV: the total daily milk volume, 9
TPI: total protein intake, 4, 11, 13, 15

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