Platelet Kinetics

M Dal, Martini ziekenhuis, Groningen

1. Introduction

Thrombocytes, also called platelets, are small irregularly shaped cells without a nucleus. They are derived from megakaryocytes, which are produced in the bone marrow. Several diseases cause thrombocytopaenia. To assess the cause, autologous thrombocytes are labelled with ^{111}In. After intravenous administration, blood samples as well as gamma images of the liver and spleen are acquired on several days. The average lifespan, or mean platelet life (MPL), can be assessed from the resulting blood disappearance curve. The gamma camera is then used to identify the location of platelet destruction. The spleen should be assessed with care as this is often the site of destruction. Donor platelets are not recommended unless absolutely necessary.

2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

3. Indication

To determine the pathophysiological mechanism of thrombocytopaenia of unknown cause (deposition, decreased platelet production, increased platelet destruction or consumption).

4. Relation to other diagnostic procedures

None

5. Medical information necessary for planning

a. Blood results: thrombocytes and haematocrit (Ht)
b. Weight and height of the patient
c. List of medication

6. Radiopharmaceutical

Tracer:	^{111}In autologous thrombocytes
Nuclide:	Indium-111
Activity:	10 MBq labelled autologous thrombocytes
Administration:	intravenous

7. Radiation safety

Foetal radiation exposure is 0,95 mGy.
According to ICRP 106 there is no need to interrupt breastfeeding.

8. Patient preparation/essentials for procedure

- Stop prednisolone use at least one week prior to the investigation.

- Use a 3-way stopcock to enable the radiopharmaceutical-containing syringe to be rinsed three times.
- Using a 19G needle obtain 43 ml of blood in a syringe which contains 7 ml ACD (acid-citrate-dextrose). The amount of blood you need is dependent on the patient's platelet count. As a rule of thumb you need at least 10^{10} platelets. When the platelet count is normal, 30 to 40 ml of blood will be enough. For a platelet count of 20-30 x 10^9, 200 ml blood will be required. The assessment of platelet kinetics consists of processing of the platelet disappearance curve and organ quantification. These are outlined below.

Platelet disappearance curve

Obtain exactly 2 ml blood in a tube containing EDTA, according to the following timetable: after 1, 2, 3 and 4 h, then twice daily for a maximum of 7 days. When the activity drops to 40 % of the initial measurement, no further blood samples are required. When expecting short platelet survival, more frequent blood samples can be drawn during the first couple of days. Blood samples should be analysed with a gamma counter (^{111}In range).
If required, counts in full blood can be corrected for the unbound activity in plasma. The fraction of re-injected platelets in the blood sample is plotted as a function of time on a semi-logarithmic scale. In order to determine the fraction of labelled platelets in blood, a standard is also measured. The patient's total blood volume (BV) is estimated using Bowring's formula:

BV(men) = $0{,}417H^3 + 0{,}0450W - 0{,}03$ [L]
BV(women) = $0{,}414H^3 + 0{,}0328W - 0{,}03$ [L]
BV =blood volume (in L) ; H = height (in m); W =weight (in kg)

In the majority of cases the curve is not mono-exponential. The MPL can be estimated more accurately by using the 'multiple hit' method based on iterative algorithms for non-linear estimations. The initial recovery is determined by extrapolating the plotted curve to time point T=0.
The daily thrombocyte production (TP) is calculated using the following formula:
TP = BV x NPL x (0,9/MPL) x IPR [10^9/day]
TP = platelet production (10^9/day); BV = blood volume (L); NPL = number of platelets per litre (10^9/l); MPL = mean platelet life (day); IPR = initial platelet recovery.

Organ quantification

To assess in-vivo quality, dynamic anterior images of the liver and heart are acquired during the first hour following administration of autologous platelets.
To correct for decay and variations in scintillation camera efficiency, static posterior views of the spleen and liver, along with an ^{111}In standard, are required. These are obtained at one hour and three hours post administration, as well as once on each subsequent day that blood samples are taken for the platelet survival measurement.
The absolute uptake in the liver and spleen should be determined using the geometric mean. To accomplish this the camera should be recalibrated, at least one anterior image of the liver and spleen must be acquired and the size of the patient must be known. 100% minus the percentage of uptake in the liver and spleen must correspond with the platelet recovery derived from the disappearance curve.

9. Acquisition and processing

Energy: ^{111}In, peaks at 173 and 247 keV

Window: 20% of the peaks

Collimator: MEAP

Counting : to assess the size of the liver and spleen, posterior images of the liver and spleen are acquired for 300 sec on the day of administration of the platelets.

Camera: the liver and heart are visualized anteriorly by gamma camera with 60 frames of 1 min following administration of autologous platelets, followed by a 5 min static posterior view of the liver and spleen along with an ^{111}In standard after 1 h and 3 h. Posterior views are repeated daily as long as blood samples are taken for the platelet survival measurement. Anterior acquisition should be made at least once for quantification of the liver and spleen.

10. Interpretation

a. Normal
   - Mean platelet lifespan: 9,0 ±1,5 day
   - Platelet production: (200 ± 65) x 10^9 per day
   - Spleen uptake (after 1 h): 32-40% of the administered dose; remains stable over the course of time
   - Liver uptake (after 1 h): 8-12% of the administered dose; remains stable over the course of time
   - Initial recovery of labelled platelets: 50-70%

b. Damaged platelets or labelling error
   Under normal circumstances the plots for liver and heart activity will rise in parallel for the first few hours; the liver will not be much more active than the heart. The platelet recovery obtained from the disappearance curve should correlate with 100% minus the uptake percentage of spleen and liver. A significant difference is likely to be the result of platelet damage or a labelling error.

c. Very short MPL (2< days) suggests idiopathic thrombocytopaenia purpura (ITP) and is accompanied by normal or increased platelet production. The uptake in the liver and spleen remain normal at 1 hour post administration. During the course of the investigation, 70% of patients with ITP will show increasing splenic uptake.

d. MPL is slightly decreased in patients with hypersplenism. The platelet production rate is normal. Uptake in the spleen is increased at one hour post administration and remains stable during the following days.

e. Patients with thrombocytopaenia due to reduced platelet production rate will exhibit decreased MPL. The degree of MPL decrease correlates with disease severity. This is caused by the daily need for a fixed number of platelets for physiological haemostasis and coverage of the vascular system. These patients usually have normal splenic and liver uptake. Though, increase over time does occur.

f. Platelet production rate and MPL can be reduced or normal when thrombocytopaenia is due to drug use. The uptake in liver and spleen will likewise be reduced or normal.

g. Thrombocytopaenia may also be caused by platelet deposition outside physiological pooling of spleen and liver (e.g. an aneurysm).

11. Report

The following findings should be reported:

- MPL (mean platelet life (day))
- IPR (initial platelet recovery)
- Absolute uptake (geometric mean counts) of liver and spleen, calculated as a percentage of the amount of radioactivity injected
- Progression of uptake in liver and spleen over time
- TP (platelet production (10^9/day))
- Total body findings

Discrepancies or deviations from standard protocol with regard to acquisition and results (e.g. length of investigation, errors in blood sampling, mismatch between IPR and geometric mean counts of liver and spleen calculated as a percentage) should also be mentioned.

12. Literatuur

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