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RESEARCH ARTICLE

MANAGEMENT OF PLASMA-DERIVED MEDICINAL PRODUCTS: SUPPLY AND TRACEABILITY ISSUES

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Abstract

Background: Plasma-derived medicinal products (PDMPs) represent a particular field of pharmaceutical industry. Produced mostly from human blood, PDMPs production follows strict procedures for biological safety and traceability. It comes to albumin, immunoglobulins, coagulating fractions, antiprotease fractions as well as biological glues.

Resources and procedures: Our study aimed to define PDMPs management in Morocco, as well as their biological safety procedures, while specifying constraints related to their supply and traceability.

Results and discussion: Moroccan market supply by PDMPs is ensured by the National Blood Transfusion Center (NBTC) that shipments Moroccan collected plasma to the French Laboratory of Fractionation and Biotechnology (LFB). The latter produces PDMPs for the Moroccan market under an agreement signed in 1999 and PDMPs prices are fixed by a decree of the Ministry of Health. PDMPs production follows strict procedures for biological safety and traceability from blood donations collection to administration in patients, allowing their routes to be retraced in case of hemovigilance or pharmacovigilance alerts. In Morocco, only two traceability labels are provided on the primary packaging of PDMPs, unlike in some other countries where PDMPs are provided with three sticky labels, all essential for mastering product's traceability. PDMPs shortages are due to insufficient amount of plasma sent to LFB, which is aggravated in case of batch recall.

Conclusion:PDMPs are indicated to support critical patients, which imply mastering biological safety and traceability from production to delivery, and optimizing their supply in order to ensure their availability by emergency times.

Introduction:-

Plasma-derived medicinal products (PDMPs) represent a particular sector of the pharmaceutical field. They are produced by physicochemical fractionation of human plasma. Also called "plasma therapeutic proteins", their administration to patients, often in critical condition, aims at compensating some quantitative or qualitative

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deficiencies. They include albumin, immunoglobulins, coagulant fractions, antiprotease fractions and biological glues.

Material And Methods:-

Our study was based on a review of the literature and on field observations, through which we were able to highlight the different aspects of PDMPs management, as well as their biosafety and traceability processes from blood donations collection to the administration of PDMPs to patients, while specifying the constraints related to their supply and traceability methods.

Results And Discussion:-

Supply

The Moroccan market is supplied with PDMPs by the National Blood Transfusion Center (NBTC), which collects Moroccan plasma and sends it for fractionation to the French Laboratory of Fractionation and Biotechnology (LFB) as shown on Fig 1 (MSM, 1995, 2003). The LFB produces PDMPs for the Moroccan market according to an agreement. Indeed, NBTC signed a custom contract in 1999 with LFB for the fractionation of surplus fresh frozen plasma (FFP) from whole blood for the preparation of certain PDMPs, namely albumin, VIII Factor and IX Factor. Fractionation within the framework of this agreement began in the year 2000 and enabled the availability of PDMPs on the Moroccan market at a lower price, as sampling, bag and reagents used for plasma testing (provided by NBTC) are not invoiced by LFB (Table 1). Thereby, the price of PDMPs corresponds solely to the fractionation cost paid to LFB and it is set by a decree of the Ministry of Health. It also strengthened and consolidated the quality approach for better transfusion safety (Boulahdid, 2014; MSM, 1995, 2003; MS-MFPM, 2003).

According to the NBTC, for an average annual shipment of 4000 liters of fresh frozen plasma, the savings for patients would be about 7.109.444,00 MAD (Moroccan dirham) (MSM, 1995, 2003; MS-MFPM, 2003).

This supply mode presents certain constraints:

- The quantity of plasma sent to LFB remains insufficient. This may be aggravated in case of unsatisfactory FFP quality control. In this sense, a study conducted over 3 years reported more than 4% of rejected FFP units among a total of 206.522 units that were sent to LFB for fractionation. These rejections were due to biological non-conformities in 2.57% of cases and to physical anomalies in 1.47% of cases (Boulahdid, 2014);
- Sometimes, quantities of imported PDMPs are not proportional to the national demand (e.g. albumin);
- PDMPs shortages are aggravated in case of batch recall.

Biological safety:

The production of PDMPs is subject to strict biological safety and traceability procedures, from the collection of blood donations to the administration of PDMPs to patients, making it possible to trace their circuit in case of hemovigilance or pharmacovigilance alerts. This production complies with both transfusion good practices and drug manufacturing good practices, thus allowing a high level of quality and safety control for this category of products (ANSM, 2020, 2021).

Traceability:

As shown on Fig 2, upward and downward traceability allows at any time to establish the link between:

- Donors and batches of medicines (and vice versa);
- Batch of drugs and patients who received it (and vice versa);
- Complete donor/patient traceability (and vice versa).

The main benefit from this traceability is being able to anticipate and avoid potential problems in patients, and if necessary, being able to take corrective actions.

PDMPs must be carefully tracked. This is done through the use of special prescriptions, tracking records, and traceability tags as shown on Fig 3.

The main constraints for this management system is that in Morocco, only two traceability labels are provided on the primary packaging of PDMPs, unlike in some other countries where PDMPs are provided with three labels, all of which are essential for the control of these products traceability.

Batch recall

The National Drug Control Laboratory can recall some PDMPs batches in case of suspension of use, or in case of recall by the manufacturer of products in stock (pharmacies, care units, patients). In this sense we distinguish 2 types of recalls:

- « Precautionary recall » following new information on the donor, as a precaution, insofar as in the state of knowledge and techniques at the time, the product safety is not called into question.
- Recall related to a proven health risk to patients when a risk using the product is detected. In this case, it's proceeded to an immediate recall and media announcements.

Conclusion:-

PDMPs are indicated for the management of patients in critical condition within emergency timeframes, which implies biological security and control of their traceability from manufacture to administration, as well as control of their supply in order to guarantee their availability within emergency timeframes.

PDMPs made from "French" Plasma have recently been commercialized in Morocco. They would be a good alternative in case of shortage of PDMPs supplied by the NBTC, but their high price remains a constraint that limits their access to health care structures.

Table 1:- PDMPs prices reduction thanks to the agreement signed in 1999.

PDMPs	Price fixed by the agreement	Price out of agreement
Albumin 20 %	20.00 MAD per gram	60.00 MAD per gram
Factor VIII	3.50 MAD per (UI)	8.10 MAD per (UI)
Factor IX	3.50 MAD per (UI)	8.10 MAD per (UI)

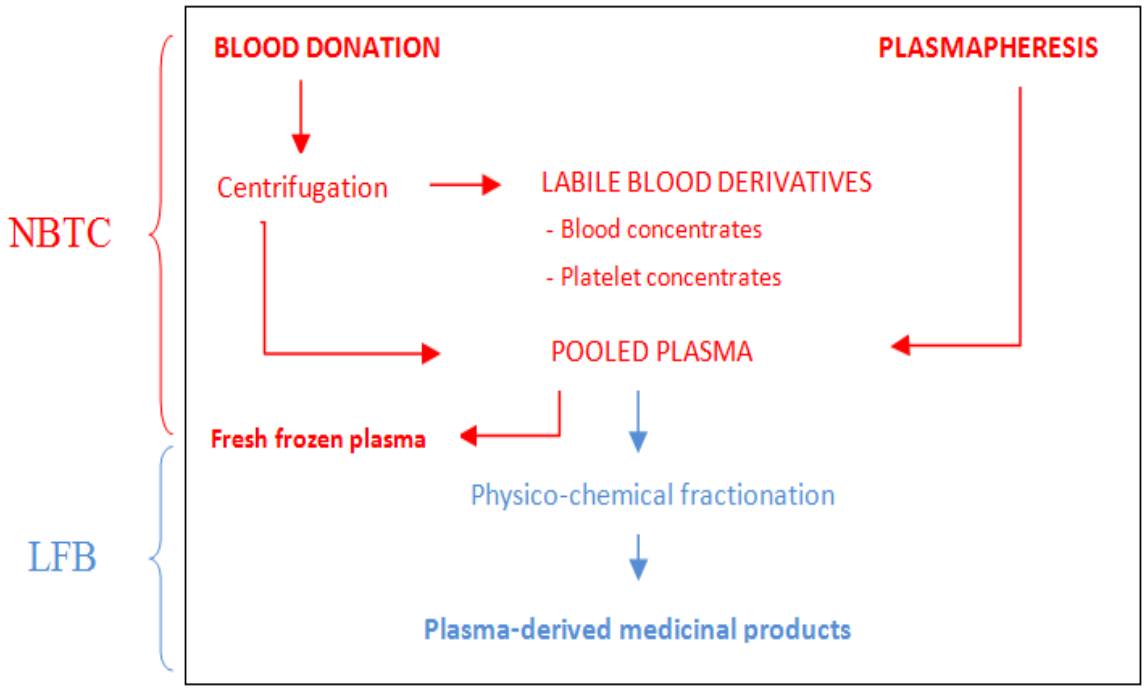

Fig 1:- General production scheme for Plasma-derived medicinal products.

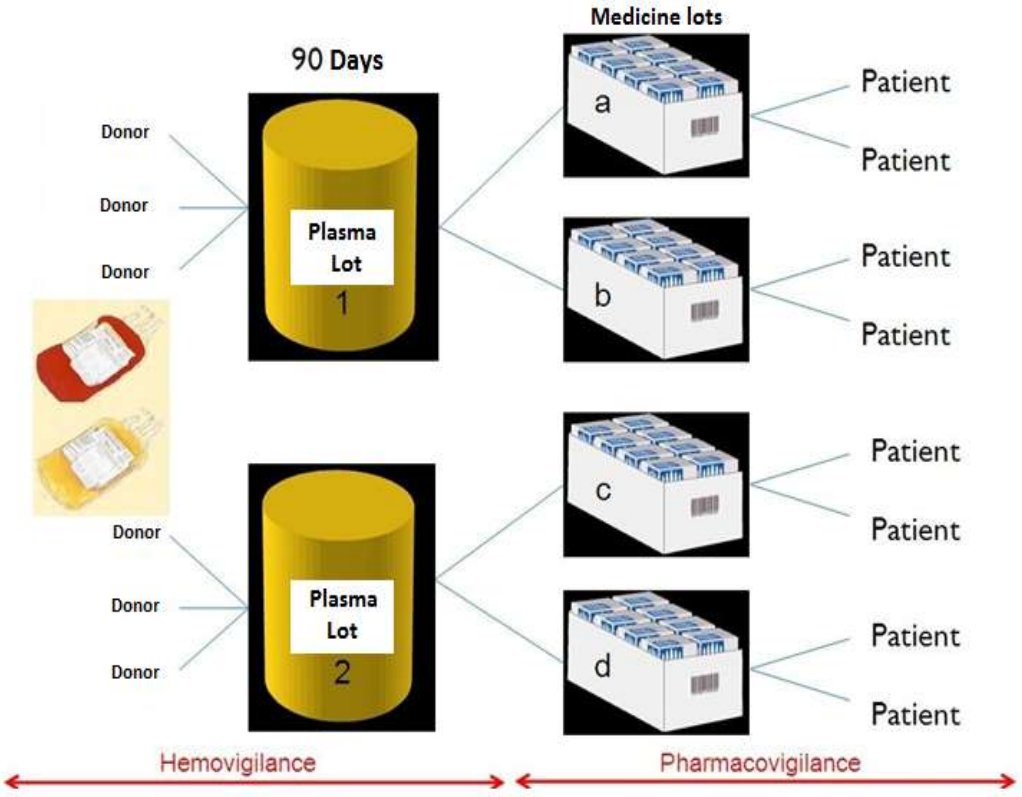

Fig 2:- Traceability principles for plasma-derived medicinal products.

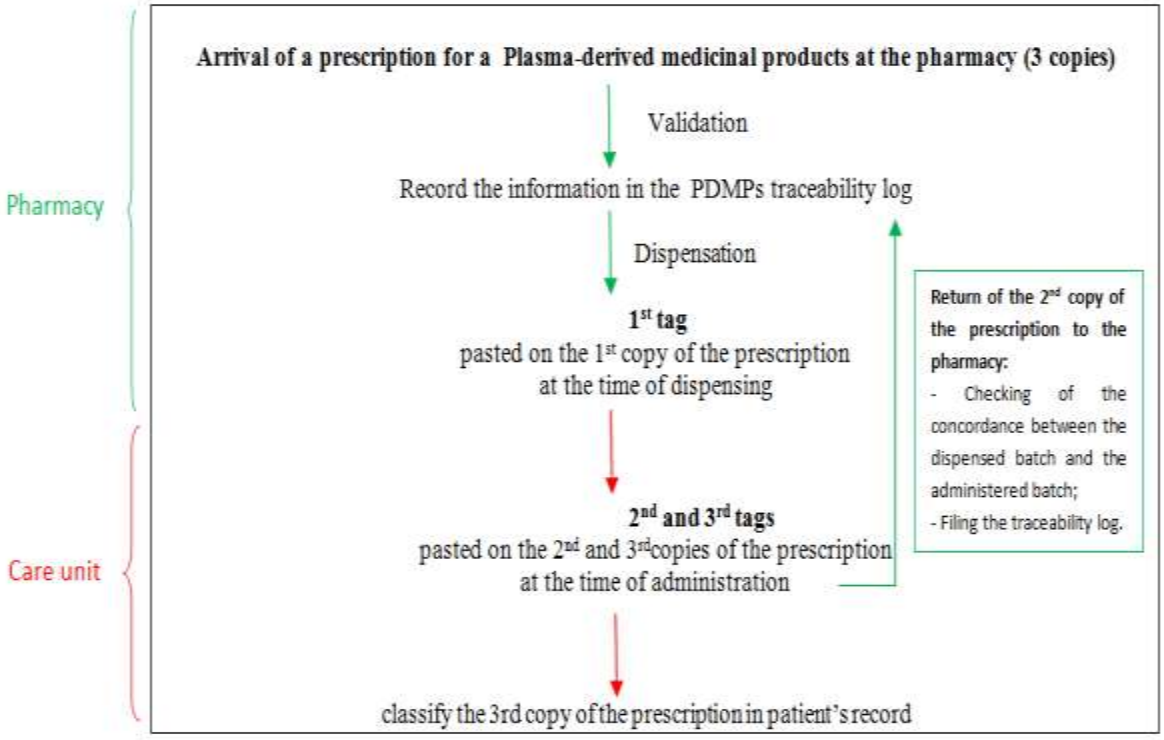

Fig 3:- Advisable plasma-derived medicinal products management at hospital.

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