Appropriate use of Albumin in Japan

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- 30 year trend of Albumin use in Japan
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The blood supply system in Japan

- Whole blood collection
- Apheresis collection
- Component transfusion

Blood donation Patients

Blood products

Source Plasma

Plasma products
The blood supply system in Japan

Whole blood collection

Apheresis collection

Blood donation

100% VNRBD (1974~)

Source Plasma

Blood products

RBC

FFP

PC

FFP

Ministry of Health, Labour and Welfare

Regulate

Domestic Fractionators

Overseas Fractionators

Plasma products
Self-sufficiency rate of PDMPs in Japan (2015)

- Fibrinogen
- Antithrombin III
- Coagulation Factor IX
- Thrombin
- Activated Protein C
- Haptoglobin
- Immune Globulin
- Albumin
- Tissue Sealant
- Coagulation Factor VIII
- Anti-HBs Immune Globulin
- Coagulation Factor XIII
- Anti-D(Rho)Immune Globulin
- Anti-tetanus immune Globulin
- C1-Activater

*Self-sufficiency rate of pdFVIII (including recombinant FVIII)

Reference: Ministry of Health, Labour and Welfare
On 1985, the use of albumin in Japan was extremely high, approximately 1/3 of the total produced worldwide being consumed in Japan, which depended on up to 95% importation.
30 year trend of Albumin use in Japan

384 = 1/3 of the world consumption

modified from Ministry of Health, Labour and Welfare materials
30 year trend of Albumin use in Japan

- **1999**: Criteria for the Use of Blood Products (1999)
- **2006**: Transfusion management Fee (2006)

384 = 1/3 of the world consumption

1985

1990

1995

2000

2005

2010

2015

125

modified from Ministry of Health, Labour and Welfare materials
Blood Law* - Principles

● To improve the safety of blood products

● To secure the stable blood supply of blood products through the domestic non-remunerated blood donations

● To promote appropriate use of blood products

● To ensuring fairness and improving transparency in managing the blood program

* The Law on Securing a Stable Supply of Safe Blood Products
Blood Law* - Basic Policy

The Basic policy of the Blood Law is revised every five years. （2003, 2008, 2013）

- To use of blood products appropriately
- To achieve domestic self-sufficiency of Albumin
- To obtain informed consent from the patients on the origin of the blood products

* The Law on Securing a Stable Supply of Safe Blood Products
Transfusion Management Fee

Transfusion management fee is paid for the institutions

- with the blood transfusion management system
  - Physician responsible for blood transfusion
  - Medical technologist responsible for blood transfusion
  - 24-hours-a-day provision of blood transfusion tests
  - Hospital transfusion committee

- Unified management of ALB by the division of transfusion*

- perform safe and appropriate transfusion practices (Appropriate use addition)
  - ALB / RBC < 2.0
  - FFP / RBC < 0.54* or 0.27**

* Transfusion Management fee (I)
* *Transfusion Management fee (II)
Self-Sufficiency of Albumin in Japan

Criteria for the Use of Blood Products (1999)


Transfusion management Fee (2006)

modified from Ministry of Health, Labour and Welfare materials
Clinical Guidelines for the use of Albumin

- Guidelines by the government
  Guidelines for the use of blood products (1986)
    RBC, FFP, Albumin

  Criteria for the use of blood products (1999 → 2017 → 2018)
    RBC, FFP, PC, Albumin

- Evidence-Based Guidelines for the Use of Albumin Products by the Japan Society of Transfusion Medicine and Cell Therapy (2015～)
Clinical questions (CQs) were formulated regarding a total of 17 pathological conditions.

Searches were conducted based on domestic and overseas papers on albumin.

<table>
<thead>
<tr>
<th>Edition</th>
<th>Years of Search</th>
<th>Hit Counts of Papers on Search</th>
<th>Number of Papers Included in Primary Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st (June. 2015)</td>
<td>1972-2014</td>
<td>3059</td>
<td>310</td>
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<tr>
<td>2nd</td>
<td>2014-2016</td>
<td>892</td>
<td>126</td>
</tr>
</tbody>
</table>
Clinical Questions on Albumin

- Hemorrhagic shock
- Severe sepsis
- Ascites secondary to liver cirrhosis
- Nephritic syndrome with refractory edema or pulmonary edema
- Extracorporeal circulation with unstable hemodynamics
- Therapeutic plasma exchange not requiring the replacement of coagulation factors
- Severe burns
- Pulmonary edema or marked edema due to hypoproteinemia
- Markedly decreased circulating plasma volume
- Cerebral ischemia (head injury)
- Heart surgery with cardiopulmonary bypass
- Hypoalbuminemia with stable hemodynamics during the perioperative period
- Pregnancy-induced hypertension
- Inflammatory bowel disease
- Nutritional support as a source of protein
- Terminally ill patients
- Pathological conditions that are not eligible for other plasma expanders
Evidence levels and grades of recommendation were determined according to the *Minds Handbook for Clinical Practice Guideline Development 2014*.

- The strength of recommendations was presented in 2 ways: “1”: strongly recommended “2”: weakly recommended (suggested)

- Overall strength of evidence across outcomes (A,B,C,D) was put down with the above strength of recommendations.

<table>
<thead>
<tr>
<th>A (strong)</th>
<th>strongly confident of the estimate of effect</th>
</tr>
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<tbody>
<tr>
<td>B (moderate)</td>
<td>moderately confident of the estimate of effect</td>
</tr>
<tr>
<td>C (weak)</td>
<td>limited confidence of the estimate of effect</td>
</tr>
<tr>
<td>D (very weak)</td>
<td>very little confident of the estimate of effect</td>
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</table>
Strongly recommended administration of hypertonic albumin product (25%, 20%)

Liver Cirrhosis patients

- Type 1 hepatorenal syndrome (1A)
- Spontaneous bacterial peritonitis (1A)
- Large volume paracentesis (1A)
- Management of refractory ascites (1B)
Strongly recommended administration of isotonic albumin product (5%)

- Therapeutic plasma exchange for neurological disorders, such as CIDP, GBS (1A)
- Therapeutic plasma exchange for removing anti-A or anti-B antibodies in ABO-incompatible transplantation when used in combination with immunosuppressant agents (1B)
No strong evidence to support the use of albumin product

- Hypoalbuminemia
- Cardiac surgery
- Volume resuscitation for hypovolemia
- Cerebral ischemia / hypovolemic brain injury
- Hypotension during dialysis therapy
Promotion of Appropriate Usage of Albumin at Osaka Medical College Hospital

- Changing the entity in charge of the management of albumin from the Department of Pharmacy to the Division of Transfusion Medicine in 2007.

- Setting the similar management of RBC, PC, and FFP on Albumin.
  - Individual identification numbering
  - Prohibition of keeping albumins in wards
  - Management by standard medical record form
The format consists of

i) Purpose of transfusion

ii) Pre-transfusion laboratory data

iii) Side Effects

iv) Post-transfusion laboratory data

v) Assessment

The documents should be completed by the doctors on each administration and are evaluated by the Transfusion Division on the basis of the clinical guidelines.
Concluding Remarks

- To promote an appropriate usage of albumin, legal approach, economical approach, and setting the evidence-based guidelines were all effective in Japan.

- The most important and difficult thing is how to change the experience-based administrations of each doctor.
Thank you very much for your attention.