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Letter to the Editor

Correcting an unintentional injustice: a comment on the doctorate thesis 'Transfusion' by José Carvalho Tolentino presented in 1878



Dear Editor,

In 2005, my esteemed professors, Pedro Clóvis Junqueira and Jacob Rosenblit, and I published, in this journal, a very thorough article on the history of hemotherapy in Brazil.¹ But unfortunately, we made a historic mistake in the article, which I aim about to correct here.

We first learned of this mistake eight years later, when Dr. Rodrigo Falconi, a scholar of the History of Medicine, called me. In our article, we cited a study by José Vieira de Marcondes, presented to the Medical School of Rio de Janeiro on September 27, 1879, as the first ever thesis on hemotherapy in Brazil. Falconi read our article and, through his research, discovered a thesis about transfusion by Dr. José de Carvalho Tolentino, presented in the same Medical School on August 28, 1878, one year earlier.²

The thesis by Marcondes, son of the Baron and Baroness of Taubaté, had been rejected by the Medical School for being too controversial. The author had then defended his thesis at the Medical School of Bahia, on December 30, 1879.³ Marcondes' thesis described some empirical experiments in blood transfusion that had been conducted up to that time, and discussed whether the best type of transfusion would be from animals to humans or from humans to humans. The interesting aspect of the study was its detailed description of an acute hemolytic reaction with renal abnormalities and the presence of hemoglobin in the urine. Tolentino's thesis, presented one year earlier, also discussed similar aspects, which probably served as the basis for Marcondes' thesis.

Tolentino,² in the first part of his thesis, gives a historical summary of blood transfusion organized in three eras: the first gives the occasional descriptions from the times of the ancient Egyptians, through the fifteenth century and then up to 1667. These are descriptions of the ingestion of blood and the collection and intravenous administration of blood from humans and animals. These early descriptions also mentioned the occurrence of air embolism. The second era, from 1668 to 1818, was one of total discrediting of transfusion practices,

and transfusions were practically abandoned. The third, truly scientific era, began in 1818 with James Blundell. Called to examine a woman with uterine bleeding, he saw the patient die within a few hours. Moved by this experience, he began to conduct numerous experiments between 1818 and 1827 and reached the conclusion that transfusion could sometimes be of use. Tolentino cites other scientists who had studied transfusions in animals and humans, such as Prévost, Dumas, Milne-Edwards, Dieffenback and Bischoff. From these reports comes the recommendation for pre-transfusion defibrination, and cooling of the syringe or pot used in the procedure. Tolentino cites other great physicians who were starting to recommend transfusions, highlighting a publication in the Rio de Janeiro Medical Journal from July 31, 1877: this was the first Brazilian reference on the subject. The author was Dr. Felício dos Santos, who attributed the failure of one transfusion to the fact that the patient was already close to death.

In the second part of his thesis, in Chapter I, Tolentino² describes the physiology of blood and its composition of plasma, red and white cells, but his description shows that little was known at that time about coagulation. The author discusses defibrination of the blood, and its advantages and disadvantages. In this part of the thesis, he gives an interesting statistical report: of 174 observations of transfusions made with whole blood, 95 resulted in cures and 79 in deaths, i.e. a mortality rate of 45%. On the other hand, with defibrinated blood transfusions, 76 transfusions resulted in 53 fatalities and 23 cures, i.e. a mortality rate of 69%. The author concluded that there were highly-regarded professionals advocating both for and against defibrinated blood, and that he preferred not to take part in the discussion.

In Chapter II, Tolentino described successful cases of blood transfusion: successes and failures of experimental transfusions between different classes of animals, between different animal species of the same animal group, and between different animals of the same species; transfusions of human blood into the blood vessels of animals, and from animals to humans, and finally human-to-human transfusion

experiments, with higher chances of success. Tolentino defended the use of arterial blood, but at the same time, he describes the difficulties of its use in humans. The author preferred to use blood taken from men, as they have a higher amount of red blood cells than women, and the blood used should preferably be from strong, healthy individuals aged between 20 and 40 years old. He advocated that 30–700 mL of blood should be collected and chilled prior to transfusion in order to reduce clotting time, and he suggested the addition of anticoagulants, but concludes that the substances that were available at the time had not been recommended for human use. Transfusion devices should be made of glass or silver, so as not to interfere with clotting. As for the blood components, in this part of the thesis, Tolentino² describes the importance of red blood cells, which would give vitality and benefits to dying individuals.

In the third part of his thesis, Tolentino² gave a very interesting report on the indications and contraindications of blood transfusions as summarized below.

Indications:

- Bleeding of traumatic nature
- Passive or spontaneous bleeding
- Constitutional bleeding (hemorrhagic diathesis)
- Before major surgery
- Anemia
- Fainting
- Malarial cachexia
- Inaction
- Apparent deaths (syncope by hemorrhage, shock)
- Poisoning
- Asphyxia
- Agony
- Nerve diseases
- Organic diseases

The circumstances among which transfusions should not be used, according to Tolentino,² were:

- Hypervolemia: in heart and lung disease, particularly hemoptysis
- Chronic inflammation of the brain, in which the softened capillaries may rupture with the input of transfused blood
- Changes in the nervous centers (because one patient developed what they called a “shaking palsy”, with tonic contractions of the limbs, convulsive vomiting, coma, increased temperature and death in 4 h)
- Kidney disease

Tolentino² dedicated the fourth part of his thesis to practical considerations about blood transfusions:

- The dilemma of “when” to transfuse: during hemorrhage? Or should the physician wait till the hemorrhage has slowed down, avoiding the acute phase, and expecting the patient to recover with other measures? The author concludes that we must resort to transfusion whenever the futility of all other therapeutic resources employed is evident; where there is a presumption that the patient can withstand the transfusion; and when the transfusion was not indicated too late.

- The author suggests that large, surface vessels should be used for phlebotomy, and that an assistant should hold the limb in which the transfusion is running, observing the pulse. If the pulse is close to normal, the transfusion should be interrupted or reduced in speed. Tolentino advised that the physician should be cautious during the post-transfusion period too, indicating rest, stimulating drinks, tonics and easily digestible foods. The physician should also take steps to prevent complications such as blood clotting, air embolism and phlebitis.
- Finally, the text describes the principles to be considered and apparatuses to be used in transfusions. The author postulates that the apparatuses must be kept in a perfect state of cleanliness; they must have the capacity to contain the required amount of blood to be transfused; that they be easy to handle and accurate; allow the desired temperature to be maintained, and ensure that air bubbles cannot be introduced into the veins. The author recommends the following devices: the Moncoq-Mathieu apparatus, the M. Belina, the Collin, and the defibrination chamber.

Tolentino’s descriptions of the transfusion practices of his day reveal some important observations. Firstly, at that time, it was already possible to conclude that transfusion between humans was the most appropriate form, and that the initial concerns with air embolism, fluid overload, anticoagulation and storage of blood were emerging. A manual was published giving the indications and contraindications of blood transfusions. An important aspect of that era was the practice of clinical hematology and transfusion medicine: the hemotherapist was recognized as being directly involved in the care of the patient.

Nowadays, we can control most of the adverse effects of transfusions, we have knowledge of hundreds of blood groups, and are able to properly identify the blood and its components. We have quality programs, accreditations and audit committees, we have machines that separate blood into components, and we can perform cell therapy. It is amazing how far we have come in 136 years!

I hope that our descendants, 136 years from now, when they read our theses on hemotherapy, will be able to compare them with the new era of recombinant blood substitutes that do not pose a risk to the recipient’s health, and will appreciate the efforts made by their ancestors in the search for better practices in medicine.

Conflicts of interest

The author declares no conflicts of interest.

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