Use of Umbilical Cord Blood for Stem Cell Research

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Abstract

Umbilical cord blood (UCB), long treated as waste material, is today considered a valuable source of hematopoietic stem cells. UCB is used, mostly in children, for the treatment of blood malignancies and inherited blood and metabolic disorders. In addition to blood precursor cells, UCB also contains stem cells that can differentiate into other types, such as cartilage, fat, hepatic, cardiac, and neural cells, fuelling speculation about the use of cord blood stem cells for regenerative medicine. Further research is therefore needed to investigate the expanded potential of UCB and its therapeutic use in cell and tissue therapies. According to a recent survey, practices for the procurement of UCB for research vary widely across Canada, so this area may not yet be ready for uniform regulation. However, some harmonization of practices to increase the availability of UCB for research would be useful for Canadian investigators. In this article, we address several important ethical and legal issues relating to the use of UCB in research and recommend guidelines to serve as a source of useful information for researchers. While their legal acceptability may vary across Canada, it is hoped that these recommendations foster more harmonized UCB research practices.

Résumé

Le sang de cordon ombilical (SCO), longtemps considéré comme un déchet, constitue aujourd'hui une source précieuse de cellules souches hématopoïétiques. Le SCO est utilisé, principalement chez les enfants, pour la prise en charge des affections malignes sanguines et des troubles métaboliques et sanguins héréditaires. En plus des cellules précurseurs du sang, le SCO contient également des cellules souches qui peuvent se différencier en d'autres types (cellules du cartilage, du tissu adipeux, du foie, du cœur, du système nerveux, etc.), ce qui alimente les spéculations quant à leur utilisation aux fins de la médecine régénérative. De plus amples recherches s'avèrent donc requises pour explorer le potentiel élargi du SCO et son utilisation thérapeutique dans les thérapies cellulaires et tissulaires. Selon un récent sondage, les pratiques utilisées pour l'obtention du SCO à des fins de recherche varient grandement au Canada; ainsi, ce domaine pourrait ne pas être prêt à se voir imposer une réglementation uniforme. Cependant, une certaine harmonisation des pratiques visant à accroître la disponibilité du SCO à des fins de recherche s'avérerait utile pour les chercheurs canadiens. Dans cet article, nous traitons de plusieurs des importantes questions éthiques et juridiques liées à l'utilisation du SCO à des fins de recherche, et nous recommandons des lignes directrices qui constitueraient une source de renseignements utiles pour les chercheurs. Bien que leur acceptabilité sur le plan juridique puisse varier d'une province et d'un territoire à l'autre, nous espérons que ces recommandations pourront favoriser l'harmonisation des pratiques de recherche en ce qui concerne le SCO.

Key Words: Umbilical cord blood, research, ethical issues, legal issues

Competing Interests: None declared.

Received on July 14, 2009

Accepted on July 22, 2009

J Obstet Gynaecol Can 2010;32(1):58–61

INTRODUCTION

Umbilical cord blood, long treated as waste material, is today considered a valuable source of hematopoietic stem cells. UCB is used, mostly in children, for the treatment of blood malignancies and inherited blood and metabolic disorders. In addition to blood precursor cells, UCB also contains stem cells that can differentiate into other types, such as cartilage, fat, hepatic, cardiac, and neural cells,[1] fuelling speculation about the use of cord blood stem cells for regenerative medicine.[2] For example, recent studies have led to speculation that UCB may be useful to treat autoimmune type 1 diabetes in children.[3] In addition, it seems that particular HLA mismatches are more successful with UCB than with bone marrow transplants,[4] although HLA mismatches do seem to have an impact on efficacy.[5] UCB can be collected at birth, without pain to the mother or child, and can be quickly typed, tested, and frozen after collection, making it rapidly available to any recipient.

These advantages are offset by certain disadvantages, such as a longer time to engraftment, during which the recipient is vulnerable to infections, and the risk of transmission of yet-undiagnosed hereditary diseases. The most important disadvantage, however, is the comparatively low stem cell count in UCB, which has made it difficult to use in treating adults weighing more than 110 pounds.[6]

Although initially seen as research, UCB transplantation is now viewed as an accepted therapy for the treatment of various diseases; in the United States it is near to attaining the

status of standard therapy.[7] Because of the potential of UCB, clinical research has focused on techniques that can expand the utility of cord blood transplantation, such as cell expansion and transplantation of cells from multiple cords. Various clinical trials of such techniques are under way.[6] Further research is therefore needed to investigate the expanded potential of UCB and its therapeutic use in cell and tissue therapies.

A recent survey (Survey Report) was conducted to assess the current needs and state of UCB research practices in Canada.[8] It concluded that future demands for human UCB research will likely remain stable or continue to increase. The Survey Report also revealed that practices for the procurement of UCB for research vary widely across Canada, so this area may not yet be ready for uniform regulation. Yet, some harmonization of practices to increase the availability of UCB for research would be useful for Canadian investigators.

In this article, we address several important ethical and legal issues relating to the use of UCB in research and recommend guidelines to serve as a source of useful information for researchers. While their legal acceptability may vary across Canada,[9,10] it is hoped that these recommendations foster more harmonized UCB research practices.

INFORMATION FOR PARENTS AND PHYSICIANS

Parents' lack of knowledge concerning the utility of UCB has been documented.[11] Ideally, parents should have access to a neutral source of information on the utility of UCB for both treatment and research to further develop its potential. This neutral source should also provide information about their various options: discarding UCB, banking it in a private bank, or donating it to a public bank.[12] Many obstetricians and physicians involved in the care of pregnant women do not provide much or any information on UCB collection and use, and future parents are sometimes left with documentation from private banks and what information they can find independently as their only sources of information on these topics.

The Survey Report revealed a lack of information concerning the fate of cord blood in Canada, with the only practical sources of such information being the public and private banks themselves. The concern is that information provided by private banks may not be objective. The Survey Report therefore suggests providing information about the possible uses of UCB through prenatal health care programs and identifying a national hub responsible for the production and dissemination of such information for physicians, future parents, and the general public.[8]

Recommendation 1

Due to the lack of awareness of the potential utility of UCB for both treatment and research, mechanisms should be made widely available for disseminating information about UCB to physicians, the public, and prospective parents. National professional associations and researchers should be encouraged to develop more educational materials on the clinical and research uses of UCB and to promote their use.

UCB FOR RESEARCH: SOURCES AND CONSENT

The Survey Report revealed that most responders obtained UCB for research from hospital labour and delivery departments (over one third), from obstetrician-gynaecologists (one fifth), or by direct solicitation of samples from parents (almost a quarter of investigators). Only one investigator obtained UCB samples from a local private cord blood bank, and the remainder obtained their samples from public banks.[8]

Like all tissue, UCB can reveal important information about not only the child, but also the mother and the father. The practice of collecting UCB without the parents' consent undermines respect for tissue donors' autonomy and should therefore be discouraged. For that reason, research ethics boards should inquire into the collection process of any tissue if they authorize its use without consent of the patient.

The Survey Report mentioned that many investigators would support a move towards national guidelines for the systematic collection and storage of cord blood across the country to ensure quality control for epidemiological research.[8] In the current ethical and legal environment, such an approach would require that parents be notified of the default collection of UCB and its anonymized use in such research and be allowed to opt out. Parents should also be adequately informed of other possible uses of cord blood, such as public and private banking, and asked explicitly for their consent to other types of research.[13]

Recommendation 2

Hospital admission consents could provide for the routine collection of anonymized UCB for quality control or for research of an epidemiological or public health nature. Hospitals could also notify parents of the general nature of such research and provide for the possibility to opt out. For

ABBREVIATIONS

HLA	human leukocyte antigen
REB	research ethics board
UCB	umbilical cord blood

other types of research involving UCB obtained from hospitals, REBs should require parental consent.

PUBLIC BANKS

Collected UCB may not be suitable for transplantation. About half of the cord blood units collected and intended for banking are not frozen for potential transplant use.[9] A strong case exists for using these samples in non-clinical research. Public banks, whose purpose usually involves collecting large numbers of samples, are therefore in a privileged position to make UCB samples available for research.

Recommendation 3

If cord blood does not meet the criteria for clinical use, it should be made available for research, subject to donor consent. Public banks can and should play a role in making such UCB samples available for research within an ethically appropriate framework that protects research participants and ensures equitable access of scientists to the UCB samples. In addition, public banks could cooperate with researchers to facilitate UCB collection for research projects in those hospitals where they operate.

In addition to, or in lieu of, a default system, public banks could offer different options for the collection of UCB for research, with different written consents.

Recommendation 4

Public banks should consider using broad written consents to collect UCB for future research projects. Such consents should (1) include a description of the areas of research to be carried out with the samples, (2) clearly indicate that the donor will not be consulted on specific uses of the UCB, and (3) provide general information as to how the sample will be used and who will have access to it, including assurances that the sample will be used for health research only, and that a REB will approve all studies that make use of the sample. Such information should include the fact that international collaborations are a possibility. If UCB samples are coded, the consent should also include information about how to withdraw from research, how information about ongoing studies will be made available, and what mechanisms (if any) will be used for the communication of research results.

Alternatively, public banks could require specific consent for each research project and provide a detailed description of the type of research for which the consent is sought.

UCB OBTAINED FROM PRIVATE BANKS

Private banks differ in their approaches to UCB that is unsuitable for transplantation. Relevant contractual provisions of 10 Canadian private cord blood banks (Canadian Cord Blood Registry, Cells for Life, Cord Blood Bank of Canada, CReATE Umbilical Cord Blood Bank, Healthcord, HemaStem, Insception, Lifebank, Progenics Cord Blood Cryobank, and Stem Sciences Inc.) range from discussing options with the client, in the case of low volume collection, to discarding—at the bank's discretion—samples that fail to meet standards. Some private banks are affiliated with companies that carry out research with UCB; in such cases, "discarding" the samples may involve using them for research. If that is the case, private banks should be encouraged to seek consent from donors prior to such disposal, or at least to include clear disclosure concerning this possibility in the storage contract, and to anonymize any samples used in research. Private banks should also be encouraged to offer donors the option of donating samples unsuitable for transplantation to a public bank for research purposes.

Recommendation 5

If a sample is unsuitable for clinical use, or when donors decide to terminate storage of a UCB sample, private cord blood banks should be encouraged to offer donors the possibility of donating UCB to a public bank or for research.

REBs reviewing research proposals that use UCB obtained from private cord blood banks should, in addition to ensuring that parental consent meets applicable ethical and legal rules, obtain a copy of the document by which the private bank claims authority to supply the UCB sample.

CLINICAL TRIALS

It is crucial for further development of effective therapies that researchers publish the outcomes, whether positive or negative, of all clinical trials. This ethical obligation is recognized in the Helsinki Declaration.[15] The registration of clinical trials has been proposed as one way to combat publication bias.[16] Arguments have recently been made for the creation of clinical trial registry systems for stem-cell based therapies.[17] Investigators involved in clinical trials of stem cells derived from UCB should publish the results of such trials and participate in voluntary clinical trial registration when available, even in the absence of mandatory requirements. In addition, REBs should make participation in clinical trial registries and publication of results conditions of their approval of such clinical trials.

Recommendation 6

The outcomes of all clinical trials involving UCB, whether positive or negative, should be published. Investigators conducting such clinical trials should participate in voluntary clinical trial registries when available, and REBs should require such participation, as well as publication of the results, when reviewing such clinical trials.

CONCLUSION

The promise and potential of UCB already demonstrated in research and the need for further development of these current therapeutic uses, as well as of other potential uses of stem cells contained in UCB, weigh strongly in favour of the active pursuit of UCB research to bring its promise to fruition. However, the expanded research use of UCB triggers ethical and legal issues that must be addressed. The adoption of these recommendations as guidelines and their implementation can be the first steps towards facilitating the research with UCB that will help to realize its potential for improving health.

ACKNOWLEDGEMENTS

We wish to acknowledge funding from The Stem Cell Network of Canada (Catalyst Grant) and to thank in particular Dr Jacques Galipeau and the participants in the SCN Montreal 2008 workshop, "The Use of Umbilical Cord Blood in Research," as well as thank the Policy Development Committee of The Stem Cell Network of Canada for their helpful comments. The opinions are those of the authors alone.

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