Remote Patient Management: The Future Is G.R.E.E.N.

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Abstract

Peritoneal dialysis is the ideal field where remote patient management (RPM) techniques can be experimented and implemented for a better care. Real-time feedback on patients and machine signals allow for rapid and effective correction of prescription and troubleshooting. Recent results have spurred new interest in this area, where new technology and new options appear to open interesting scenarios for the future. The acronym G.R.E.E.N. describes the initials of the disciplines that are likely to characterize the future of this area of care and research. G for genetics: patient genotyping will allow in the future to expand the application of precision medicine solutions in response to remote monitoring signals. R for robotics: the mechanical actuation of operations normally carried out by a care giver will permit to take maximum advantage of bidirectional interactions between remote signals and remote feedback on dialysis equipment. E for E-health and Information communication technology. Remote monitoring will provide the basis for specific algorithms that can be further implemented and improved by artificial intelligence networks. This will provide support in the decision-making process and will even provide the basis for automated feedback operations. E for eco-compatibility: home therapies with remote monitoring will contribute to save fuel consumption and will provide environment-friendly solutions. N for nanosciences: this interesting area of research will offer a new spectrum of biomaterials and will enable possible uses of nanofluids. The application of advanced RPM with a G.R.E.E.N. approach is likely to provide significant benefits for the future with cost reduction, early detection and resolution

of problems, improved treatment compliance, reduction of patient's access to hospital center for technical and clinical complications, increased confidence of patients treated at home with higher incidence and prevalence of home therapies, and consequent improvement in patient's quality of life.

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Introduction

Peritoneal dialysis (PD) is a form of renal replacement therapy, ideally designed to be carried out at home with maximal patient independence and self-confidence [1, 2]. In spite of these advantages, periodic hospital visits are required for control and verification of adherence to prescription [3]. In recent years, a significant support to home-based therapies has been provided by telemedicine (TM)TM. In fact, the application of remote patient management (RPM) and bi-directional computer-based communication between the hospital headquarter and the patient environment (devices and therapies) have permitted to follow patients at home and significantly reduce their access to the hospital. TM includes a series of tools that provide remote transmission, interpretation and storage of clinical parameters and useful diagnostic images, as well as a 2-way communication between medical teams and patients. In the field of home-based therapies, PD represents a typical example where a complex set of devices, techniques, and quantitative parameters can be the substrate for information exchange via computer networks. In this field, TM and remote monitoring techniques may improve care through prevention and early identification of problems, with consequent timely interventions. This has an important reflection on prognosis, outcomes, and ultimately patient's quality of life [4]. As in the case of other chronic diseases (heart failure, diabetes, and hypertension) [5, 6], RPM may contribute not only to improve the quality of care, but also to reduce direct and indirect costs [7–9], with a significant benefit to the healthcare system [10]. The future of few year ago represents the present of today. The novel automated cyclers for automated PD (APD) are now connected with a modem to a cloud-based network and enables patients to receive and transmit data through a TM platform from and to a PD center (RM-APD). RM of patients on APD with this platform offers the potential benefits of accurate monitoring of the therapy, improved patient safety through surveillance of critical stages of the treatment, early detection of problems or limited compliance to prescription. Furthermore, the 2-way communication system with interactive interface allows a fast trouble shooting: the physicians can change the prescription using the remote connection, reducing the need for frequent in-person visits to the PD center [11].

Previous studies have underlined the potential of TM and RPM for chronic kidney disease patients in improving the quality of life, decreasing the hospital readmission and emergency room visits, and potentially decreasing the costs [12–14]. Recent studies have confirmed this and have demonstrated a significant utility of this technology in patients undergoing PD at home [15–17]. Wallace et al. [18] reported that replacing the face-to-face encounter with a telehealth monitor can reduce patient driving time, time spent in waiting rooms, and travel costs. Makhija et al. [19] performed a study based on a simulated environment and estimated the reduction of healthcare resource utilization and associated costs by early intervention using RM on APD patients. Our group confirmed previous findings where RM can improve collaborative care between patients and the team, and improve patient compliance [20]. In general, we can say that all studies report long-term benefits of the 2-way communication system with improved follow-up of outpatients and significant savings. It is particularly difficult to predict how the future will develop in this area, but we can try to imagine some areas where TM and remote monitoring can further improve the quality of care in PD patients.

The Future of RPM in PD

The application of RPM in PD opens new possible interesting scenarios. New trends and new sciences will probably affect the way we manage patients in this area of medicine. In particular, we can make a short overview of the most interesting aspects of modern medicine that will have a significant impact on home-based therapies like PD. Furthermore, each of these new areas of science will modify our ability to take care of patients as a consequence of new technologies and improved understanding of pathophysiological mechanisms of complications. The acronym G.R.E.E.N. describes the initials of the disciplines that are likely to characterize the future of this area of care and research: G for genetics, R for Robotics, E for E-health and Information communication technology, E for Eco-compatible solutions, N for Nanosciences (Fig. 1).

Genetics

There is a general trend to move beyond patient's phenotype, analyzing the genotype and identifying epigenetic factors affecting the course of disease. The application of genetics to patient care will come as a bonus in the evolution of genomics. Definition of single patient genotype will allow us to study the associations with complications or specific peritoneal transport characteristics, capacity of expression of aquaporins on the peritoneal membrane, and immune

body fluids and in the PD effluent. Specific tests of enzyme function will help to explain different transport characteristics of the living peritoneal membrane. In this view, RPM may contribute to immediate modifications of therapy prescription or even future dialysate composition, enabling to administer enzymatic replacement therapy or other gene-based treatments.

Robotics

The future of PD and RPM will likely include medical robots. The transition to this advanced technology may come earlier than expected due to improvements in robotics as a science. There are obvious safety concerns for machines replacing people in patient care, but the benefits are tempting. We can easily imagine a PD cyclor with mechanical components designed to help PD catheter connection, bag exchange or other simple maneuvers. The robotic cyclor will not need sleep or food and will perform specific tasks with the same accuracy hundreds of times. These actions will be performed by ergonomically optimized actuators that may accomplish desired tasks, send feedback messages and signals to the headquarters via computer, and receive information and orders to modify on-demand therapy prescription. The mechanical actuation of PD operations normally carried out by a care giver will permit to take maximum advantage of robotic applications driven by bidirectional interactions between remote signals and remote feedback on dialysis equipment via TM platforms.

In more advanced future scenarios, a human-like robotic nurse will take full control of the home dialysis patient without the risk of burn out or being overwhelmed by physically and mentally daunting tasks. The nurse robots will even take blood samples or perform i.v. infusions. However, the robots will not operate autonomously. They will always be the tool for physicians and nurses to remotely interact with patients, check on their conditions, and control further actions. This will virtually eliminate most of the time-consuming home visits that will become unnecessary. Of course, safety issues are very important, and even the most advanced and sophisticated robots cannot operate without a human control. In this sense, RPM becomes quintessential to guarantee safety, and appropriate therapeutic interventions and access to signals and remote control should only be a prerogative of fully authorized personnel. Once these aspects are taken care, robotics can greatly improve the quality of life of home-PD patients and their caregivers.

In future, advanced robotic care may include catheter and connections handling, injections of antibiotics or drugs, exit site maintenance, and care. Catheter malfunction as well as other problems can be remotely managed with a set of automatic or remotely authorized troubleshooting. The robotic apparatus may

present greater reach and flexibility, capacity of millimetric incisions or operations, and other very precise tasks.

Change is often scary, and robotics in healthcare is a big one. It has the potential to do so much good: to bring medical care to regions where even today there is none to be found; to make the production and distribution of pharmaceuticals cheaper and more efficient; to lighten the load of medical professionals; to help people walk again. To reap the benefits and avoid the potential dangers of such a technological revolution, we need to keep informed about the strides that science makes so that we can better prepare and adapt to the not-so-distant future where robots play a crucial role and work closely with us.

E-Health and Information/Communication Systems

E-health and TM are disciplines that permit PD patients in remote areas to have access to high-quality emergency consultations. Remote monitoring will provide a series of information and signals that will likely be the basis for specific algorithms of feedback. These will be further implemented and improved by artificial intelligence networks. This will provide support in the decision-making process and even provide the basis for automated feedback operations. Furthermore, the easy bidirectional communication between the machine and the hospital will allow a complete and consistent data collection with the accumulation of important information. These parameters derived from hundreds of treatments will populate a patient-specific or center-specific database that will allow to answer appropriate queries and to perform pragmatic trials. Electronic medical records will become a repository for an extensive experience that may allow comparison between patients, populations or even different centers. Data can also be utilized for quality assurance and continuous quality improvement programs, offering information on performance on target or above/below the desired level. If results are satisfactory, a continuous improvement will further ameliorate the performance of the center. If results are unsatisfactory, a complete analysis of the distribution and granularity of data will be required to decide if a series of outliers will be screened or a change of policy will be required. Further information will be offered by specific devices such as bioimpedance and fluid status analysis, scales and nutrition parameters, EKG signals, and PA measurement and so on. These will complete the set of information offered by the cyclor and will provide the basis for active biofeedback in terms of therapy prescription and medications. In this area, we will find a further help by artificial intelligence-driven protocols, and we will count on virtual healthcare teams that will provide guidance and advise for best practice.

Eco-Compatibility

Every effort should be made to save the blue planet. Multiple effects on the environment can be prevented by simple yet important actions in everyday practice. The increment of the percent of patients placed on home-based therapies will provide the basis for environment-friendly solutions. Patients will have an increased self-confidence with a RPM support. RPM and remote assistance will contribute to a sense of safety and care that will increase the population treated at home. Significant savings in terms of fuel consumption and travelling will convince the patient of the benefits of the technique, maintaining the attention to self-administered maneuvers high and accurate. The downstream effects will be a longer technique survival and a significant improvement of quality of life for many patients. The reduction of traffic and energy requirement for cars to transport patient from and to the hospital will contribute to lower the CO₂ emission and relevant pollution. Further, patients will travel less for a lower rate of hospitalization episodes. The future should also consider a lower level of water consumption, utilization of bio-degradable bags and circuits, use of solar-powered cyclers for environmentally safe dialysis. If these aspects are important for the patient and life at home, they can also apply to hospitals that must become greener. This concept connects 2 important societal concerns that are rarely addressed in combination: sustainable development and health promotion. Hospitals, as central healthcare providers, can minimize their negative side effects and improve health gain by ecological building design, improved energy efficiency, ecological purchasing or environmental management systems. Again, RPM can be a key factor to help hospitals and reduce their impact on the environment.

Nanosciences

The use of nanotechnology offers some exciting possibilities in medicine and in PD as well. Some techniques can only be imagined for the future, while others are at various stages of testing, or actually being used today. Nanotechnology in medicine involves applications of nanoparticles, nanofluids or nano-robots to make repairs at the cellular level. Nanotechnology could revolutionize the way we detect problems and treat PD patients in the future, and the interactions with RPM seem to be limitless. There are numerous projects in progress to develop microbots that can travel through bodily fluids to deliver medication exactly to where it is needed, or even to repair damaged cells. Capsules containing nanorobots can be ingested by the patient and dissolved in the patient's stomach. Remotely controlled with the help of magnetic fields, nanorobots can patch up wounds in the stomach or perform other actions. A similar concept can be envisaged for nanorobots injected into the peritoneal cavity. Future applications

of nanomedicine will be based on the ability to build nanorobots. In the future, these nanorobots could actually be programmed to repair specific diseased cells, functioning in a similar way to antibodies in our natural healing processes. In fact the step following bacterial detection will be the infusion of a healing PD solution where the specifically instructed nanorobots may operate a programmed cell repair. Though most of these are only theories today, tomorrow we could very well be fighting off infections with the help of nanobots that are built to mimic our white blood cells, only doing a much faster and effective job of destroying bacteria. Nanorobots could send signals and information to a remote headquarter, and feedback actions can be planned by a bidirectional communication protocol.

Other aspects related to the use of nanomedicine in PD include application of PD solutions designed as nanofluids. A nanofluid is a fluid containing nanometer-sized particles, called nanoparticles. These fluids are engineered colloidal suspensions of nanoparticles in a base fluid with specific thermal and optical properties. The nanoparticles used in nanofluids are typically made of metals, oxides, carbides or carbon nanotubes. Nano-materials used so far in nanofluid synthesis include metallic particles, oxide particles, carbon nanotubes, graphene nano-flakes, and ceramic particles. Since the base fluid may be water, the development of nano PD solution for the future with different properties and functions should be possible. Among other applications of nanotechnology in medicine, the use of nanoparticles to deliver drugs, heat, light or other substances to specific types of cells (such as cancer cells but in our case, it could be peritoneal mesothelial cells) is of great interest. Specifically engineered particles are attracted to diseased cells, which allows direct treatment of those cells. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease. Nanoparticles may also play a role as nano-lubricants, and this would be of great advantage to preserve the surface of the peritoneal membrane. Bacterial or virus antibodies attached to carbon nanotubes could be used to defeat infections before they spread to the peritoneum but at the same time such nanoparticles may send specific signals collected by an efficient RPM system to alert the treating team. Nanoparticles could also detect levels of urea or other toxins in the peritoneal fluid, providing real-time peritoneal equilibration tests and transport information. The same can be true for glucose or the utilized osmotic agents. Nanoparticles can even be engineered as micro gels to generate a direct osmotic function and improve peritoneal ultrafiltration. Progressive dilution of the particles could be detected as a quantitative measure of trans-mesothelial ultrafiltration by a remote monitoring system. Nanoparticles could be used for early diagnosis of peritonitis. The nanoparticles attach to molecules in the peritoneal fluid indicating the start of an infection. When the sample is

scanned for Raman scattering, the nanoparticles enhance the Raman signal, allowing the detection of molecules indicating an infectious disease at a very early stage. Furthermore, early detection of peritoneal membrane damage could be made possible by nanoparticles functionalized to attach to the type of protein generated by damaged mesothelial cells. When proteins accumulate on the nanorod, the color of the nanorod shifts and the problem is detected. Nanomaterial can be used to create bacterial-resistant surfaces for PD catheters. At the same time, specific quantum dots could be created to avoid biofilm formation and to treat antibiotic-resistant bacterial species. A nanoparticle cream has been shown to fight staph infections, and this may be used to treat exit site contamination. This will help to preserve catheter integrity and prolong its life cycle.

Nanofluids could be used for sensing applications. Nanofluid-based ultra-sensitive optical sensor may change its color on exposure to extremely low concentrations of toxic cations. The sensor is useful in detecting minute traces of cations in industrial and environmental samples, and it could be a perfect tool for PD solutions. These sensors are designed for magnetic detection of nanodroplets with magnetic grains suspended in water. At a fixed magnetic field, a light source illuminates the nanofluid where the color of the nanofluid changes depending on the cation concentration. This color change occurs within a second after exposure to cations, much faster than other existing cation sensing methods. All these signals can be sent to a RPM central with the possibility of specific feedback actions.

Finally, nanotechnology can be the basis for miniaturization of circuits and actuators with the possibility to develop a true wearable cyclor for continuous PD therapy. Together with hardware modifications, nanotubes and nanoparticles might be functionalized to act as perfect sorbents for dialysate regeneration.

Conclusions

The nice thing about writing on the future is that your imagination can be limitless because whatever is science fiction today will be the reality of tomorrow. This is something we have experienced in the past, and many of today's innovations were not even thinkable a few years ago. Among these innovations, RPM and TM represent an area of enormous interest for the present. The supposed benefits of this new technology have been demonstrated in recent studies and publication [17–20] and what was described as a dream a few months ago is a reality today. Moving forward, thanks to the scientific alliance with side disciplines, we may say that the future is G.R.E.E.N.

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