Assessment of Gastrointestinal Motility in Renal Transplant Recipients by Alternate Current Biosusceptometry


ABSTRACT

Background. Gastrointestinal (GI) complications are common after renal transplantation, mainly owing to immunosuppressive therapy. Assessment of GI transit time can facilitate rational management of these disorders.

Objective. We evaluate the GI transit parameters in renal transplant recipients taking tacrolimus, azathioprine, and prednisone with the use of the alternate current biosusceptometry (ACB) technique and compared them with healthy volunteers.

Methods. Ten renal transplant recipients and 10 healthy volunteers were enrolled in this study. After an overnight fast, patients and volunteers ingested a standard meal containing magnetic markers. The biomagnetic monitoring was performed at 10-minute intervals for at least 8 hours to obtain gastric emptying as well as the colonic arrival time–intensity curves. Mean gastric emptying time (MGET), mean colon arrival time (MCAT), and mean small intestinal transit time (MSITT) were quantified and compared between control and patient groups with results expressed as mean ± SD.

Results. The MGET measured by the ACB technique was 48 ± 31 minutes and 197 ± 50 minutes for patients and healthy subjects, respectively. MSITT and MCAT values calculated for patients versus volunteers were 171 ± 71 minutes versus 197 ± 71 minutes and 219 ± 83 minutes versus 373 ± 52 minutes, respectively. Renal transplant recipients showed significantly faster; gastric emptying and colon arrival times (P < .001) compared with normal volunteers; however, small intestinal transit time was not significantly different (P = .44).

Conclusions. In stable renal transplant recipients, the GI transit parameters were significantly faster than in normal healthy volunteers. ACB sensors are versatile technologies that can be used for clinical research, because they offer an excellent opportunity to evaluate GI transit in a noninvasive manner without the use of ionizing radiation.
Nowadays, alternative techniques based on biomagnetic field detection have been developed for GI motility studies.\(^5\)–\(^7\) Alternate current biosusceptometry (ACB) is a noninvasive and radiation-free technique that uses induction coils to measure biomagnetic fields resulting from ferromagnetic sources in response to an applied magnetic field.\(^8\)–\(^11\) With recent improvements in instrumental sensitivity, its ease of use, and growing interest from diverse fields, the magnetic sensors have been recognized as valuable tools for biomedical, pharmaceutical, and clinical applications.

The aims of the present study were to examine the GI transit parameters in renal transplant recipients taking tacrolimus, azathioprine, and prednisone as immunosuppressive therapy with the use of the ACB technique and to compare the results with those in healthy volunteers.

METHODS

Instrumentation

Alternate current biosusceptometry works as a double magnetic flux transformer with air nucleus. A single-sensor ACB is composed of pairs of induction coils separated by a fixed baseline.\(^8\)\(^,\)\(^11\) Each pair of coils consists of excitation (outer) and detection (inner) coils in a first-order gradiometric relationship. The excitation coil generates a magnetic field and induces equal magnetic flux in the detection coils; thus, when a ferromagnetic sample is the sensor, an imbalance in the voltage occurs due to the changes in the differential flux between the detection coils. This biomagnetic sensor measures the signals generated by the magnetic flux variation between these coils through lock-in amplifiers. Additional technical details have been reported earlier.\(^11\)\(^,\)\(^12\) Magnetic signals detected by the ACB sensor depend on the surface area of the detection coil, number of turns, rate of change of the magnetic flux (ie applied field), amount of ferromagnetic material, and distances among the sensors and the magnetic sample. This device does not need to be operated in magnetically shielded rooms. The ferromagnetic material remains inert and cannot be absorbed by the GI tract.

Subjects

The Ethics Committee of the Universidade Estadual de Ciências da Saúde de Alagoas approved the study protocol, and trials were conducted in accordance with the Declaration of Helsinki and its revisions. Ten renal allograft recipients (8 men and 2 women, mean age, 43 ± 6.4 years; age range, 34–51 years; mean time after transplantation, 78 ± 33 months; [range, 31–117 months]) and 10 healthy volunteers (6 men and 4 women; mean age, 25 ± 6.5 years; age range, 20–38 years) who had signed informed consent were enrolled in the study. All of the patients had stable renal function and were receiving prednisone (PRED; Geolab, Brazil), azathioprine (AZA; Cristália, Brazil), and tacrolimus (FK506; Prograf, Jansen-Cilag, Brazil) as triple immunosuppressive therapy. At the time of the study, none of the subjects had a history of GI disease or medications that might affect the GI motor function.

Biomagnetic Measurements and Data Analysis

The GI transit study was performed in the morning after an overnight fast. Subjects consumed a standard 420-kcal breakfast (bread, ham, cheese, 300 mL orange juice). Five minutes after eating, the subjects ingested the magnetic markers, consisting of 4 hard gelatin capsules (size 00) filled with 1.50 g ferrite powder (53 ≤ θ ≤ 75 μm; Imag, Brazil) with 200 mL of water, and the biomagnetic monitoring was started immediately. A single-sensor ACB was used to monitor a square point matrix (5 × 5) drawn around the gastric and colonic regions. Each monitoring had 120 seconds duration and was recorded at 10-minutes intervals for at least 8 hours to obtain the magnetic field distribution. These matrices were mathematically interpolated and processed to obtain sequential images.\(^12\)\(^,\)\(^13\) Gastric emptying as well as the colonic arrival time–intensity curves were obtained. The statistical moment was obtained through the temporal average pondered by time-intensity curves, normalized by area under curve.\(^14\) By using this approach, the following GI transit parameters were calculated: mean gastric emptying time (MGET), defined as the amount of magnetic material that emptied from the stomach at time t (min) and was calculated by the area under emptying curve; mean colon arrival time (MCAT), defined as the increase of amount of magnetic material that arrived in colon at time t (min) and calculated by the area between cecum arrival curve until maximal cumulative values; mean small intestinal transit time (MSITT), quantified as the difference between MCAT and MGET. All the results were expressed as mean ± SD. Values of MGET, MCAT, and MSITT were compared between the control and patient groups with the use of the unpaired Student t test. A P value of <.05 was considered to be statistically significant. All signals and images were analyzed in Matlab (Mathworks, USA) and Origin (OriginLab, USA).

RESULTS

Demographics, transplantation-related characteristics, allograft function, and the GI transit parameters for both groups are summarized in Table 1.

The MGET measured by the ACB technique was 48 minutes (range, 15–118) and 197 minutes (range, 71–278) for patients and healthy subjects, respectively. MSITT and MCAT values calculated for patients versus control volunteers were 171 minutes (107–218) versus 197 minutes (71–278) and 219 minutes (122–346) versus 373 minutes (271–448), respectively. In the renal transplant recipients, gastric emptying and colon arrival time were significantly
faster ($P < .001$) compared with normal volunteers; however, small intestinal transit time was not significantly different ($P = .44$; Fig 1). Figure 2 depict the gastric emptying profiles for 2 representative subjects.

**DISCUSSION**

The choice of maintenance immunosuppressive therapy after renal transplantation to prevent allograft rejection is not devoid of side effects. Despite GI complications often being associated with immunosuppressive regimens, motility disorders have been scantily studied after renal transplantation.\(^1,16\) Few studies have assessed GI transit in patients treated with immunosuppressive agents such as cyclosporine, FK506, mycophenolate, or sirolimus.\(^17,19\)

Furthermore, all of those studies were performed with the use of scintigraphy or \(^{13}\)C breath tests. Although those techniques are not invasive, the main drawback of scintigraphic studies is radiation exposure, which makes it less acceptable when repeated evaluations are necessary.\(^4,20\) The \(^{13}\)C breath tests use ingestion of stable isotopes and detection of exhaled \(^{13}\)CO\(_2\) as an indirect measurement of gastric emptying and transit time. Although the results are similar to those obtained with the gold standard, the high costs of producing \(^{13}\)C-labeled meals is high. Moreover, a mass spectrometer, which is needed to analyze the samples, is expensive.\(^21\)

To overcome such technical shortcomings, alternate methods based on biomagnetic field detection have been developed. ACB is a noninvasive and radiation-free technique currently available for monitoring a number of GI physiologic parameters.\(^10,13,22–24\)

In the present study, ACB was used for the first time to evaluate GI transit parameters in renal transplant recipients.
taking triple maintenance immunosuppressive therapy comprising of PRED, AZA, and FK506. All of the patients enrolled in the study had stable renal function, as presented in Table 1. The results showed that gastric emptying and colon arrival were significantly faster compared with normal healthy volunteers (Fig 1). On the other hand, the MSITT was quite consistent between the groups, although individual values varied widely. As reported earlier, small intestinal transit time in humans seems to be relatively constant and appears to be less influenced by prandial state, age, or sex.25

Regarding our findings, it has been supposed that FK506 has a potential prokinetic effect on the GI transit parameters. It is worth highlighting that FK506 is a macrolide and, like all structurally related compounds, induces interdigestive activity contraction (phase III), and this effect is mediated by interaction with motilin receptors in the GI tract.17,26 This pronounced effect may be observed in the mean time needed to emptying the stomach when comparing a renal transplant recipient with a normal volunteer (Fig 2).

In summary, our data showed that in stable renal transplant recipients, the GI transit parameters were significantly faster compared with normal healthy volunteers. Notwithstanding, there are still gaps in our knowledge regarding various aspects concerning the role of maintenance immunosuppression therapy on GI motility in renal transplant recipients. ACB sensors are versatile technologies that can be used for a wide range of applications. For clinical research, this method offers an excellent opportunity to evaluate GI transit in a noninvasive manner without the use of ionizing radiation.

REFERENCES