Changes in intestinal electrical activity during ischaemia correlate to pathology

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Summary

The gastrointestinal tract possesses an omnipresent electrical slow wave called the basic electrical rhythm (BER). It has been shown that the frequency of the BER falls during intestinal ischaemia. The correlation between changes in the BER and pathology that occur during acute ischaemia are not completely understood. To study this, the electrical activity of the ileum in 14 adult male rabbits was recorded during ischaemia. At baseline, 60, 120 and 210 minutes of ischaemia, segments of bowel were resected for histopathologic evaluation. The BER frequency was determined using the Fast Fourier Transformation (FFT) spectral analysis. The BER amplitude and FFT spectral power were also determined. The results showed significant decrease ($p<0.05$, Student's T-test) in the BER frequency, amplitude, and spectral power at all time points. Between 60 and 120 minutes, while there was a decrease in BER activity the pathologic grade remained the same (focal loss of surface epithelium). By 210 minutes of ischaemia when the BER could not be recorded, there was diffuse mucosal infarction. The results indicate that changes in the electrical activity of the bowel during acute mesenteric ischaemia occurred prior to the pathologic changes. The presence of electrical activity indicates that there was viable bowel. Thus it should be possible to use recordings of electrical activity to evaluate bowel viability during acute ischaemia.

Keywords: ***Intestinal ischaemia, Basic electrical rhythm, Pathology.***

Résumé

L'artère gastrointestinal posséde une vague électrique lente et omniprésente appelée rythme électrique normal (Basic Electrical Rhythm, BER). Il a été démontré que la fréquence du rythme (BER) descend pendant la déficience de sang dans l'intestin. La corrélation entre les changements du BER et la pathologie qui se produit durant la déficience de sang accentuée n'est pas complètement comprise. Pour ètudier ceci, l'activité électrique de la partie intestinale de 14 cobayes males adultes était relevée durant la deficience de sang. Des segments internes étaient examinés à la baseline et à 60, 120, 210 minutes de la déficience et soumis à l'évaluation histopathologique. La fréquence du BER était déterminée en utilisant la transformation rapide Fourier (Fast Fourier Transformation, FFT). L'amplitude du BER et le pouvoir spectral de la FFT étaient aussi déterminés. Les resultats ont montré une diminution signifiante ($p<0.05$ Student's T-test) dans la fréquence l'amplitude et le pouvoir spectral du BER aux points de tout temps. Entre 60 et 120 minutes pendant qu'il y avait une diminution en activité du rythme, le grade pathologique reste la même infarction focal de muchose. A 210 minutes de deficience quand le rythme n'a pas pu enregistré, il y avait une diffuse de muchose d'infarction. Les resultats indiquent que les changements dans l'activité électrique de la cavité intestinale durant la déficience accentuée se passé avant les, changements pathologiques aux points de tout temps. La présence d'activité électrique indique que la cavité intestinale était viable. Ainsi, il sera possible d'utiliser l'enregistrement de l'activité électrique pour évaluer la viabilité durant la déficience de sang accentuée et la reperfusion.

Introduction

The electromyographic activity of the gastrointestinal tract is an important criterion of viability of the intestine[1,2]. the basic electrical rhythm (BER) is an electrical slow wave that is present all the time in the gastrointestinal tract, even in the absence of detectable mechanical activity of the bowel. It is constant for any given part of the gastrointestinal tract. It is known that decrease in the frequency of the BER can be caused by hypothermia, hypoxia and hypothyroidsm. Observations have been made in previous studies that show a decrease in the electrical activity of the bowel during arterial ischaemia[1,3,4,5]. Transient tachyarrhythmias (frequency >2 times normal BER frequency) have also been noted at some point during the process of ischaemia[6]. The relationship between changes in the BER and pathology that occur during acute ischaemia is not completely understood. Correlation of the changes in electrical activity and pathology will be important in establishing the role of electrical measurements in evaluating bowel viability during and after vascular assault such as occurs in acute mesenteric ischaemia. This study was, therefore, carried out to correlate the small intestinal electrical activity and histopathologic changes in acute intestinal ischaemia

Materials and methods

Fourteen adult male New Zealand rabbits weighing 3 to 4 kg were studied after an overnight fast. General anaesthesia was induced using acepromazine (0.5mg/kg) and Ketamine (40mg/kg). An intravenous line was then established in an ear vein. This served for infusion of subsequent doses of ketamine for maintenance of anaesthesia and for administration of fluids to maintain hydration. The rabbit was placed on a heating pad to maintain its temperature, which was checked periodically using a rectal thermometer. Mid-line incision was used to gain access into the abdomen. A 15 cm segment of ileum was identified and isolated by ligating and transecting it proximally and distally but with its mesentery and segmental vascular supply intact. This was done to eliminate any intramural blood supply from subjacent bowel during the experiment. A biopsy of this ileal segment was done. Bipolar serosal electrodes were sutured to the ileal segment and the abdominal wound was closed. The leads from the electrodes were connected to the data acquisition system, which consisted of a Beckman amplifier (Beckman Instruments, Inc., Model R612) equipped with an analogue-to-digital convertor (Biopac Systems, Model MP100) and an Apple Powerbook 170 (Apple Computer, Inc.) utilising Acknowledge 3.2.1 software (Biopac Systems). Baseline recordings of ileal electrical

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activity were performed for 20 minutes. The abdomen was opened again and the blood supply to the ileal segment was ligated to induce ischaemia. The abdomen was closed. Continuous recordings were done through out this period and the subsequent 210 minutes of ischaemia. Biopsies of the experimental bowel segment were done at 60, 120 and 210 minutes of ischaemia. The abdomen was opened and then closed each time a biopsy was taken. The animal was euthanised at the end of the experiment.

A pathologist, who had no knowledge of the specimen identity, performed microscopic examination of haematoxylin and eosin sections of the biopsies. The specimens were graded on a scale of 0 – 6 (no pathologic change to transmural necrosis) using a modification of the Swerdlow and Antonioli system[7] (Table 1). The histopathologic grades were recorded as mean ± SEM. The BER frequency (cycles per minute, cpm) at the different time points were determined using the Fast Fourier Transformation (FFT)) spectral analysis technique and recorded as the mean ± SEM. The FFT examines 5-minute segments of the electrical recordings and determines the dominant frequency. The BER amplitude and FFT spectral power were determined, normalised and expressed as the mean ± SEM. Statistical significance was calculated using the Student's T–test, with significance defined as $p<0.05$.

Results

The mean values of the different parameters of electrical activity during the experiment are shown in Table 2. The BER frequency decreased from 13.5 ± 0.6cpm at onset of ischaemia to 8.5 ± 0.7cpm at 60 minutes of ischaemia. It decreased further to 7.7 ± 0.5 cpm by 120 minutes and was not detectable at 210 minutes. There was a dramatic decrease in the normalised values of the amplitude and spectral power. The amplitude decreased to 0.45±0.1 and 0.22±0.03, while the spectral power decreased to 0.46±0.3 and 0.24±0.09 at 60 and 120 minutes of ischaemia respectively. Electrical activity was not detectable at 210 minutes. The changes in electrical parameters were statistically significant ($p<0.05$) at all the time points. The graphs in Figures 1,2, and 3 show the pattern of change of these parameters. There is very close similarity in the patterns for the BER amplitude and spectral power.

Table 1 Histopathologic scoring based on a modification of the Swerdlow and Antonioli system[7]

Grade	Histology
0	No pathologic change
1	Focal loss of surface epithelium
2	Mucosal infarction • extensive loss of surface epithelium • loss of variable amounts of lamina propira • sparing of basal glands • intact muscularis mucosae
3	Submucosal infarction •variable necrosis of submucosa • complete mucosal necrosis • intact muscuularis mucosae
4	Mural infarction • loss of muscularis mucosae • complete necrosis of mucosa and submucosa
5	Mural infarction • involvement of inner layer of muscularis propria • complete necrosis of mucosa and submucosa
	Transmural necrosis of entire bowel wall.

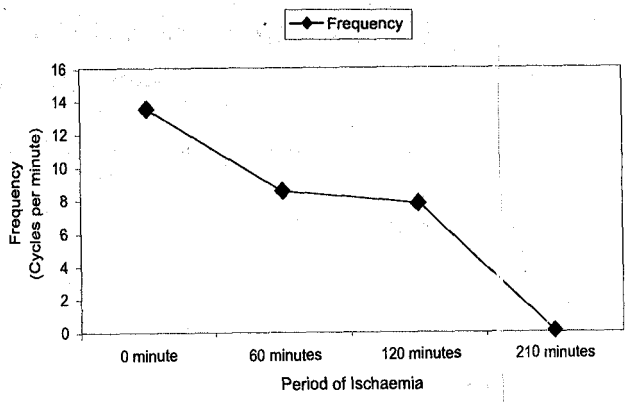

Fig. 1 ***BER frequency at baseline and during the period of ischaemia. After onset of ischaemia, there was gradual decrease in the BER frequency until it became uundetectable at 210 minutes.***

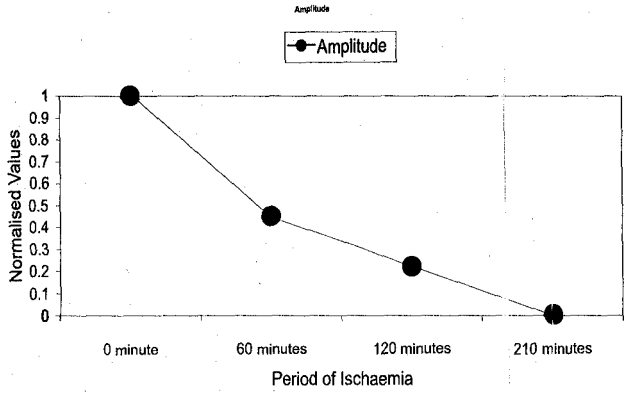

Fig. 2 ***BER amplitude at baseline and during the period of ischaemia. The values of the amplitude were normalised. After the induction of ischaemia, there was progressive reduction of the amplitude until electrical activity became undetectable.***

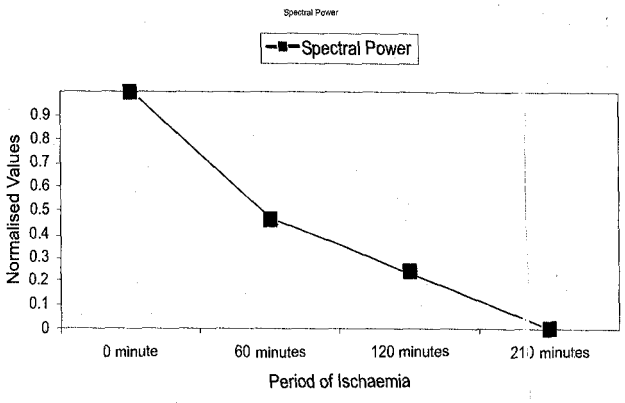

Fig. 3 ***BER spectral power at baseline and during the period of ischaemia. The value of the spectral power were normalised. After inducing ischaemia, there was progressive reduction of the spectral power until elctrical activity became undetectable. There is close similarity in the patterns of change of the amplitude and spectral power.***

Microscopic examination of the bowel revealed focal loss of surface epithelium (grade 1) from 60 to 120 minutes of ischaemia, and diffuse mucosal infarction (grade 2) after 210 minutes of ischaemia. The values of the pathologic grades are shown in Table 3.

Table 2 Change in BER parameters at baseline and during ischaemia

Ischaemia time	0 minute	60 minutes	120 minutes	210 minutes
frequency cpm	13.5±0.6	8.5±0.7	7.7±0.5	0
Amplitude	1±0.3	0.45±0.1	0.22 ± 0.03	0
Spectral power	1±0.39	0.46±0.3	0.24±0.09	0

Values are expressed in mean ± SEM
the amplitute and spectral power values were normalised.
All parameters decreased significantly at all time points ($p<0.05$, Student's T-test).
BER = basic electrical rhythm
cpm = cycles per minute.

Table 3 Histopathologic grade of the bowel at different ischaemia times

Ischaemia time	0 minute	60 minutes	120 minutes	210 minutes
Histologic grade	0	1 ± 0.3	1.6 ± 0.8	2 ± 0

Discussion

The results of this experiment demonstrate clearly the changes in electrical activity during acute mesenteric ischaemia. They confirm earlier observations that the frequency of the BER decreases during mesenteric ischaemia. The decrease in the frequency and amplitude of the BER occur early after the onset of ischaemia, being significantly so at 60 minutes. At this time, the pathologic changes were limited to focal loss of surface epithelium (grade 1). Even at 120 minutes of ischaemia when the BER frequency had decreased further, the pathologic change was still grade 1. It was not until after 120 minutes that there was diffuse mucosal injury. This lag is even more evident when the pathologic change is compared with the change in amplitude of the BER that is observed through out the study period. At 210 minutes of ischaemia the pathologic change was still limited to the mucosa (grade 2), even though the electrical activity could not be recorded. This demonstrates the sensitivity of the electrical recordings in showing alterations of bowel integrity during ischaemia well before histopathologic evidence becomes apparent. It can thus be concluded that the presence of BER during acute intestinal ischaemia is evidence of bowel viability. Whether this inference can be extended to the state of the intestine during reperfusion will require ischaemia reperfusion studies.

Mesenteric ischaemia had continued to be a clinical challenge in terms of its evaluation and diagnosis. The morbidity and mortality associated with it have remained high mainly because of delayed diagnosis[8,9]. The non-specificity of the clinical features contributes to this delay in diagnosis. Clinical judgement and adjuvant techniques used to assess bowel viability in acute mesenteric ischaemia lack sensitivity and/or specificity or do not have established clinical utility[10,11,12]. Mesenteric angiography is invasive, requires expertise in invasive radiology and may not demonstrate venous infarction occurring with volvulus or mechanical bowel obstruction. Moreover, the contrast load given during angiography can be harmful to the kidneys and such invasive tests often delay definitive surgical treatment. The changes that are detected by magnetic resonance imaging occur late in the disease process and such changes are also present in other disease processes which induce bowel oedema. Biochemical indices are indicative only in the late stages[13], and even then are not specific[14]. Recourse is usually made to exploratory laparotomy for diagnosis. Gangrenous bowel is easily recognisable at laparotomy and it is then resected. However, bowel of questionable viability poses a dilemma as to whether or not to resect. Intra-operative diagnostic techniques include Doppler and fluorescein angiography to determine the viability of marginal segments of bowel. Consequently, second-look laparotomies are done in order to confirm that non-viable bowel has not been left behind in the attempt to preserve bowel at initial laparotomy[11].

Measurements of gastrointestinal electrical activity, therefore, have the prospects of serving a useful role in the determination of bowel viability[12]. Experiments have been carried out to measure the magnetic fields related to the electrical activity of the gastrointestinal tract[15]. These magnetic field measurements have been compared and found to correlate quite well with the electrical activity[16]. These findings have been utilised in investigations to non-invasively detect mesenteric ischaemia using a superconducting quantum interference device.[5-17]. Therefore, elucidation of the relationship between electrical activity and pathology should be useful in further studies on non-invasive detection of intestinal ischaemia.

The results of this experiment lead to the conclusions that during acute intestinal ischaemia (1) electrical changes occur before the pathologic manifestation, and (2) the presence of electrical activity is evidence of bowel viability. Thus, it should be possible to use electrical recordings to monitor the viability of the bowel. A useful role can be found for the use of these electrical activity parameters in the intraoperative and peri-operative monitoring of bowel viability, particularly in situations where at initial or re-laparotomy the bowel viability is in doubt and a decision has to be taken about resection. Further studies will also need to be carried out to characterise the electrical changes that occur in the very early stages of ischaemia and in ischaemia-reperfusion scenarios.

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