Thesis points of a PhD doctorial thesis

Effect of glutamine-rich and glutamine-poor diet in necrotizing pancreatitis and after oesophageal cancer

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2002
Introduction and literature

The place of nutrition in the therapy

Lusk (1928): „I think, we were right, if we had explained the phenomenon of nutrition in the following way: what kind of materials would be destroyed in different circumstances and how much of different nutriments had to be demolished to keep the function of the organism.”

What does clinical enteral nutrition mean?
It means artificial nutrition of patients, who are unable to eat, or it is forbidden them to eat because of any illness, or they have deficiencies in some of different nutrients. Enteral nutrition is preferred to parenteral, depending on hemodynamics, type of the disease, digestive and adsorptive function of the gastrointestinal tract. Enteral feeding is more simply, cost-effective, physiological and the primary role of the liver in digestion, synthesis, decomposition against poisoning remains.

Only the natural food contains all the necessary components which are needed. Special nutrients or chemically defined oligopeptides, macromolecules are mixed to prepare clinical enteral diet. Our aim is to ensure enough calory intake, carbohydrates, proteins, vitamins and trace elements. Some diseases need special supply. In some illnesses the absence or equilibrium disturbance of special components is remarkable, selective, tissue-specific nutriments are necessary.

Psychosomatic harmonia, physical activity, supply with food saves against several diseases. In the third millennium our lifestyle is a challenge for our genoms too, adopted in millions of years to our life. There are few injuries of civilisation, where the alterations did not cause any harm.

Significance of enteral nutrition in inflammatory and tumorous diseases.
The malnutrition of tumorous patient is caused by many factors. It alters the quality of life, decreases the survival of the patient. The daily energy supply is 25 Kcal/kg with electrolutes, with 0.2 g/kg nitrogen intake, carbohydrate and fat supply. Appropriate nutrition results decreasing of growth of tumour. The on complicating question of medical doctors is, who cure cancer patients is, whether the feeding resulted in growth of the tumour or not. What kind of optimal composition and amount of food would ensure the metabolism of the patient?

Hypocaloric nutriment with increased protein content is advised for septic patients in the early phase of the disease, that is 200 g/day carbohydrate, 1.2-2 g/kg protein. The demand is in close connection with the release of infectious and hormone mediators in the early phase of the sepsis. CO$_2$ production in consequence of carbohydrate metabolism, or steatosis and liver damage following fat metabolism would cause more side effects, than the advantage of the calory intake.

The role of glutamine in the nutrition and in the increase of defence mechanisms of the organism is; Attention has been made by Wernerman to the role of glutamine. Glutamine is one of the 5 most important free amino acids, which build up our proteins. Alfa-ketoglutarate means its carbon skeleton, creating the Krebs cycle also. It plays role in the synthesis of the nucleotids and is the main transporter of ammonia from the peripheral tissues. It can be synthesised by all cells of the body, but in stress situation it may become essential and the organism cannot produce glutamine enough. The optimal glutamine content influences the system and the mucosa of the gut. The lack of glutamine may cause disturbance in the organ function. Lymphocytes and macrophages of the immune-system of the gut need energy and amino acids to the synthesis of the protein, but glutamine is their most important energy source, more than the sugar is.

Glutamine decreases infectious attachment of the cancer patients. Glutamine-rich diet causes increased demolish of glutamine in only malnourished patients. Maybe it is caused by a bad glutamine supply and an altered function of the guts.

The role of retinol-binding protein and prealbumin in determination of the nutritional status and immune-function of the body. The follow-up of nutritional status is possible with measuring of body weight, body mass index and with the help of sensitive indicators of of the protein nutrition - prealbumin and transferrin. Another sensitive marker of nutritional status is the retinol-binding protein. Its serum level depends on the vitamin „A” suppling of the body. The retinol vitamin „A”
is a micronutrient, which has a key role in the defence mechanism of the organism. It is responsible for the integrity of the intestines and for optimal amount of circulating immune-globulins.

**My aims are four folds**

1. My primary aim was to compare the effect of glutamine-rich jejunal nutrition in necrotizing pancreatitis and in cancer patients after oesophagectomy.
   
   a./ I checked how the patients tolerate the nutriment depending on osmolarity and speed of dosage of the diet.
   
   b./ Changes in laboratory data were measured in a 10-day period.
   
   c./ Anthropometric changes in consequence of the diet were measured.
   
   d./ Time of intensive care and clinical stay, complications, results of 1,5 year follow up in connection with the nutrition were examined.
   
   e./ The alterations are connected to the diets which are similar and which differ in the two types of the diseases; in necrotizing pancreatitis and after oesophageal resection.

2. My secondary aim was to compare the effect of glutamine-poor jejunal nutrition in necrotizing pancreatitis and in cancer patients after oesophagectomy.

   a./ I checked how the patients tolerate the nutriment depending on osmolarity and speed of dosage of the diet.
   
   b./ Changes in laboratory data were measured in a 10-day period.
   
   c./ Anthropometric changes, in consequence of the diet were measured.
   
   d./ Time of intensive care and clinical stay, complications, results of 1,5 year follow up connected with the nutrition were examined.
   
   e./ The alterations are connected to the diets which are similar and which differ in the two types of the diseases; in necrotizing pancreatitis and after oesophageal resection.

3. On the basis of the above I can affirm that the results will lead to therapeutic values in healing necrotizing pancreatitis and oesophageal cancer.

4. I can firm that prealbumin and retinol-binding protein has a predictive value in the every day praxis.

**Patients and methods**

*Laboratory investigations*

Elektrolytes, blood picture, parameters of coagulation, liver and kidney function, fat metabolism were regularly monitored. Measurements for nutritional status - albumin, prealbumin, retinol-binding protein, transferrin and fibrinogen level - were carried out preoperatively, on the first, 4th and 10th postoperative days. On the same days C-reactive acute phase protein, the amount of humoral immunity-parameters: IgG, IgA, IgM, IgE and complement components C3 and C4 were analysed. Peripheral cells were analysed to characterise cellular immunity: T cells - CD3+, CD4+ helper and CD8+ cytotoxic cells, B cells: - CD19+ cells and the ratio of CD56 - natural killer cells. The activity of peripheral phagocytes was determined by whole blood chemiluminescence measurement.

*Body mass index investigation*
The changes in BMI and in composition of the body were measured with multi-frequency bio-impedance analyser.

Statistical analysis
Paired T test was performed to compare laboratory data measured in different periods. The "p" values less than 0.05 were considered statistically significant.

Scores
In case of cancer patients with oesophageal tumour Apache II's score, in patients, suffering from necrotizing pancreatitis Ranson's score and Apache II's score were applied.

Composition of different diets in 100 mls nutriment:

- Glutamine-rich diet: energy: 125 kcal, protein: 7,5 g, glutamine: 1,3 g, arginine: 0,8 g, cystein: 0,7 g, fat: 4,17 g, carbohydrate: 14,5 g, fibre, osmolarity: 380 mosm/ l.
- Glutamine-poor diet: energy: 100 kcal, protein: 4,1 g, fat: 4,17 g, carbohydrate: 14,5 g, fibre, osmolarity: 250 mosm/ l.

Patients:

59 patients were investigated from years 1998-to 2000. There was performed a randomised, blind trial. In the perioperative and postoperative period pathogenesis and laboratory data of 19 patients suffering from necrotizing pancreatitis (14 men and 5 women) and 40 patients resected for oesophageal cancer (33 men and 7 women) were followed up. We investigated the glutamine-rich diet has more beneficial effect in clinical outcome or in significant laboratory changes in patients with necrotizing pancreatitis or in patients resected for oesophageal cancer. The same method was applied in two other groups of patients, who suffered from pancreatic necrosis and were resected for oesophageal cancer as well. It has been measured whether the glutamine-poor diet influences more beneficial the parameters of patients with necrotizing pancreatitis or those of resected patients for oesophageal cancer.

Patients with glutamine-rich diet:

11 patients were treated for necrotizing pancreatitis and received glutamine-rich diet. The cause of pancreatitis was alcohol abuse in 7 cases, gallstone in 3 cases, bacterial infection in one case. The mean value of Apache II’s score was 2,36 (2-5). The Ranson’s score by admittance was: 3,1 (3-5), in 48 hours: 3,6 (3-5).

26 patients resected for oesophageal cancer were nutrited with glutamine-rich diet as well. The mean value of Apache II’s score was: 4,57 (0-15).

Patients with glutamine-poor diet:

8 patients were treated for necrotizing pancreatitis and received glutamine-poor diet. The cause of pancreatitis was alcohol abuse in 6 cases, gallstone in 2 cases. The mean value of Apache II’s score was 3,5 (2-7). The Ranson’s score by admittance was: 3,1 (3-4), in 48 hours: 3,9 (3-6).

14 patients resected for oesophageal cancer were nutrited with glutamine-rich diet as well. The mean value of Apache II’s score was: 2,5 (0-8).

Jejunal nutrition and method of laboratory investigations:
There were used two types of diets. Patients treated for pancreatic necrosis received nasojejunal feeding tube to get the diet, inserted endoscopically to the second jejunum loop. The patients with oesophageal resection got the catheter intraoperatively. The built up of the enteral nutrition was carried out in 4-5 days continuously with the help of a pump. On the postoperative first day the patients received 500 ml tea with the speed of 20 ml/hour. Nutriment was applied on the postoperative second day only and the planned 1500-2000 ml dosage was reached on the 4th postoperative day. Concerning the glutamine-rich nutriment 0,8 g/kg/day protein was the initial dosage. The 2,5 g/kg/day protein dosage was reached on the 4th day. Using the glutamine-poor diet the initial dosage of protein was 0,4 g/kg/day and on the 4th day we reached the 1,3 g/kg/day protein intake. The 25 kcal/kg/day energy demand was ensured by carbohydrate and fat infusions as long as it was necessary to reach the same calory intake with jejunal nutrition. Jejunaly feeding was continued depending on the recovery time of the normal pancreatic functions. The oesophagectomised patients were allowed to drink tea having performed the successful swallowing probe, but their jejunal feeding could be finished with a possibility of an oral eating. Nutritional status, immune-laboratory parameters and clinical progress were followed and measured preoperatively, on the second, 4th and 10th postoperative days of the treatment.

**Results**

Changes in connection with enteral nutrition were measured. Groups of patients were chosen to comprehend the use of the applied nutriments, because the patients could only get our diet. Patients with necrotizing pancreatitis and cancer patients with oesophagectomy were the two groups of investigated patients. Results of patients with inflammatory and tumorous disease were nutriment with isocaloric, isonitrogenous diet and were investigated.

Nutritional status of patients fed with glutamine-rich nutriment became scarcely impaired body mass index decreased 0,9 % in both groups, in the necrotizing pancreatitis and in the resected patients for oesophageal cancer. The intensive stay of patients with pancreatitis (compare 11,3 days to 10,3) and the clinical stay (compare 28,9 days to 24,8) was longer than the stay of patients with resected oesophagus. The number of complications was greater in pancreatitis, than in resected patients for oesophageal cancer (compare 81 % to 69 %). The mortality in the hospital was greater in pancreatitis than in oesophageal cancer patients (compare 27 % to 19 %). After having left the clinic the 1,5 year survival of the patients was 100 % in necrotizing pancreatitis and the mortality in the same period was 3,8% in the resected patients for oesophageal cancer. In the glutamine-rich group parameters, characteristic for protein metabolism and defence mechanism increased significantly in necrotizing pancreatitis: the PRA values and the RBP values also, the values mentioned latter were 0,1 % near to the significance. After oesophageal resection the serum protein, RBP, PRA and IgG values increased significantly on the 4th postoperative day, the serum protein values on the 10th day.

I assume that the glutamine-poor diet results in the following; the decrease of body mass index is similar to the results of both glutamine rich nutriment groups (compare 0,44 kg/m² in pancreatitis to 0,76 kg/m² in oesophageal resection). The number of intensive care days is 4 times greater, the number of clinical days is two times greater in the pancreatic group than in the oesophageal cancer group. The rate of complications in pancreatitis was 63 %, while 50 % in resected patients for oesophageal cancer. The mortality in the hospital was 25 % in pancreatitis, while 14 % in oesophageal cancer patients. No patient with pancreatitis died in 1,5 year, two oesophageal cancer patients were lost, that means 14 % mortality. In necrotizing pancreatitis: the PRA, RBP and IgG values increased significantly in the postoperative period. After oesophageal resection significant increase of serum protein, albumin and IgG levels could be measured.

**Conclusion**
Results of 59 patients were analysed. There is forbidden to eat in necrotizing pancreatitis and after oesophageal resection. These patients would be able to eat, but it is not allowed for them to so. The majority of oesophageal cancer patients is malnourished for difficulties on nutrition. The disease itself and the operation increase their caloric and protein demand. Their metabolism is catabolic.

On an offer for diet of the literature I have choose the nutriments mentioned above. The supply of proteins must be carried out with specific composition of amino acids. 1.5-2 g/ kg daily protein intake is recommended, that means 0,2-0,3 g/ kg nitrogen. We have to ensure the essential amino acids, but there are amino acids, which become essential in stress situation, for example the glutamine. In stress situation the glutamine reserves are purged from the cells of the skeletal muscles and this process is followed by the break-down of the proteins. The latter one has to be prohibited, or supplied. Fiber containing diets were chosen, because concerning the literature fibre enough with fruits, vegetables, vitamins, antioxydants, flavonides and phyto-oestrogens saves the intestines against tumour, the organism against hypertension and coronary disease.

Glutamine-rich diet was given in an inflammatory disease, in necrotizing pancreatitis and to patients suffering from oesophageal cancer. The patients of the two types of illness were chosen, because members of both diseases might suffer from secondary immune-deficiency, which allowed the propagation of an inflammation to a necrosis and spreading of a tumour. The therapy in both diseases means the rest and the disconnection of the the same part of the gastrointestinal tract. Both diseases have the same nutritive therapy: feeding into the jejunum. I wanted to compare, how the response of the patients to the same glutamine –rich diet was. By use of glutamine-poor diet I measured, how the behaviour of groups of patients with necrotizing pancreatitis and those with oesophagectomy was. Concerning the literature, let feed the patient enterally, if it were possible, because the enteral nutrition would save the patient from the bacterial translocation, development of multy organ failure, would decrease mortality and would be cost effective. In sepsis, in therapy of tumorous patients, with help of the glutamine-rich feeding, patients treated with chemotherapy and cobalt irradiation have longer survival, shorter clinical stay.

**Summary**

Malnutrition, prolonged wound healing, secondary infections, mortality of patients made me become interested in doing something to supply the energy and protein currency of patients in the postoperative period. Patients could be found in our clinic to realise the plan. I wanted to gain values, expressed mathematically to make sure about therapeutic value of nutrition. Processing the results of the patients my findings, specially in connection with the glutamine-rich diet and use in the clinical practice are the following:

1. Effects of glutamine-rich diet in the postoperative treatment of necrotizing pancreatitis and oesophagectomy were compared.

   a./ Diet with 380 mmol/ l osmolarity was well tolerated. Continuously, with a volume slowly increasing pumped diet helped to avoid side effects like feeling bloated, producing loose stool. Inaccurate maneging of the nutriment may cause such signs. The tolerance of the patient was taken into consideration. There was not necessary to dilute the diet, the latter wold danger the roules of sterility.

   b./ The glutamine-rich diet resulted significant increase in serum protein and RBP results of patients with necrotizing pancreatitis and after oesophagectomy. PRA values were only elevated in necrotizing pancreatitis. IgG results increased only in the oesophagectomised group. The positive
answer of the patients with necrotizing pancreatitis to the glutamine-rich diet was more expressed
than the reaction of the oesophagectomised group. Enterally glutamine enriched diet seems to be
really effective, when it is given in a big dosage. I gave it in a 25g/ day dosage in a nutriment
containing 1,3 g/ 100 ml glutamine. Maximally 2000 ml/ day diet was pumped to the second
jejunum loop of the patients. The effect of the diet is not so evident, as the effect of the dipeptiven
given intravenously.

c./ After 10-day treatment the body mass index of both groups - necrotizing pancreatitis and
oesophagectomised patients - decreased with 0,9 %. It is a small weight loss.

d./ Intensive (compare 11,3 days to 10,3 days) and clinical (compare 28,9 days to 24,8 days)
stay was longer in the patients with necrotizing pancreatitis. The number of complications was
greater in the pancreatic group, than in the oesophagectomised (compare 81 % to 69 %). The
mortality in the clinic was greater in the group with necrotizing pancreatitis (compare 27 % to 19
%). The 1,5 year survival was 100 % in the group with pancreatitis, 3,8 % in the
oesophagectomised group.

e./ My results did not convince me of the fact, that the jejunaly applied glutamine,
administered concerning our dosage arms the patients with the advantages I wrote in my work
about the glutamine. The increase of RBP and PRA values of patients fed with glutamine-rich diet
in pancreatitis and after oesophagectomy is impressing because these results are predictive for the
outcome and relapses of the patients. The PRA is the best marker of nutritional status and its
decrease (being negative acute phase protein) showes the progress of the inflammatory process.

2./ I measured surprising good values using the glutamine-poor diet.

a./ Fibre containing diet with 250 mmol/ l osmolarity was well tolerated, similar to results in
patients, who received glutamine-rich diet. Correct use of diet helped to avoid frequent and loose
produce of stool.

b./ Significant elevation of PRA, RBP and IgG results call for being paied attention to worth
for feeding. Should we have had the opportunity to feed with lower protein and glutamine content,
we should do it. The nutrition itself activates the gastrointestinal tract and the GI immune-barrier
protects against infections. Significant increase in the serum protein and IgG results of the
oesophagectomised patients were measured. The PRA, RBP results of oesophagectomised patients
did not change significantly. Maybe, answer of an inflammatory or septic disease resulted
mathematically more expressed alterations, than those of tumour patients. That is why immune-
reaction and protein increase of patients with necrotizing pancreatitis more convincing than the
ones in oesophagectomised is.

c./ After a 10-day treatment the body mass index of both groups - necrotizing pancreatitis
and oesophagectomised patients - decreased with 0,9 %.

d./ In the group with pancreatitis the number of intensive days is 4 times greater and the
clinical days are two times greater, than in oesophagectomised patients. The rate of complications
was 63 % in the pancreatic group, 50 % in the oesophagectomised group. The mortality in the clinic
was 25 % in necrotizing pancreatitis, 1,4 % after oesophagectomy. Nobody has died in 1,5 year in
the group with pancreatitis, the number of oesophagectomised decreased with 2 persons. The rate of
mortality was 3,8 %.

3. What I can declare is, that diet with smaller protein and glutamine content can be utilised as well.
Our intestines are one of the most important immune-organ. They work on the influence of the
nutriment representing all advantages of a functioning barrier and serve the local and systemic
immune-defence. Concerning my data, if I had no possibility to the immune-nutrition, then I would
propose to try to ensure the energy and protein supply. The recommended dosage of the glutamine
is 30 g/ kg/ day, for it becomes early essential in stress situation.
4. In the judgement of the nutritional status near the body mass index, count of lymphocytes, serum protein, serum albumin and antropometric alterations there is useful to follow up the changes of the quick indicators of malnutrition: the PRA and the RBP. These tests demonstrate in case of extensive operations, sepsis and tumours not only the nutritional status, but the decrease of their values can be negative prognostic sign of progress, or relapse of the disease. The microelement vitamin „A” is notable in the defence mechanism of the organism. It is responsible for the gut integrity and for the circulating amount of immune-globulins. Patients with low retinol-binding protein may be impaired and we have to think of their impaired bowel function as well. The costs of measurement are acceptable and one measurement pro week may have predictive importance.
**Publication on subject of the PhD thesis**

1. **Hallay J**, Kovács G, Szatmári K, Bakó A, Szentkereszty Zs, Lakos G, Sipka , Sápy P:
   Tápláltsági állapot és immunológiai paraméterek változása nasojejunalis szondán át táplált acut pancreas necrosisban szenvedő betegekben.

   A tápláltsági állapot és az immunológiai paraméterek változása különböző tápszerekkel jejunalisan táplált nyelőcső resektált betegekben.

3. **J Hallay**, G Kovács, K Szatmári, A Bakó, Zs Szentkereszty, G Lakos, S Sipka, P Sápy:
   Early jejunal nutrition and changes in the immunological parameters of patients with acute pancreatitis
   Impact factor: 0,937

4. **J Hallay**, G Kovács, S Sz Kiss, M Farkas, G Lakos, S Sipka, E Bodolay, P Sápy:
   Changes in the Nutritional State and Immune.Serological Parameters of Oesophagectomized Patients Fed Jejunaly with Glutamine-poor and Glutamine-rich Nutriments
   Impact factor: 0,937

5. **J Hallay**, G Kovács, S Sz Kiss, D Czakó, P Sápy, G Lakos, S Sipka:
   Effects of a glutamine-rich diet in oesophagectomised patients.

   Jejunális táplálás nekrotizáló pancreatitisben, illetve nyelőcső resektiot követően.

**Impact factors : 1.874**
Other publications

7. Szentkereszty Zs, Kerekes L, **Hallay J**, Czakó D, Sápy P:
   CT guided percutaneous peripancreatic drainage: a possible therapy in acute necrotizing pancreatitis
   Impact factor: 0,937

8. Szentkereszty Zs, Kotán R, Kerekes L, **Hallay J**:
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9. **Hallay J**, Bobók I, Szokol M, Lakatos L:
   Bartter-szindróma gyermekkorban

10. **Hallay J**, Aranyosi J, Nagy B, Váradi V:
    Brietal ( Methohexital) narcosissal szerzett tapasztalataink a gyermek bronchoscopiában
    Anaesthesiológia és Intenzív Therapia 1986. 16: 29-34.

11. Sz Kiss S, **Hallay J**, Németh É, Vezendi S:
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12. Bóni J, **Hallay J**, Györffy Á, Nemes Z, Sápy P:
    A herediter haemorrhagiás teleangiectasia, mint vérzésforrás az alsó gastroenteralis tractusból

13. Z Galajda, I Mikó, **J Hallay**, T Maros, Á Péterffy, I Furka
    Why the internal mammary artery is an ideal graft for myocardial revascularisation? ( An experimental model with omentoplasty)

14. Takács I, Varga G, **Hallay J**, Szappanos M, Sápy P:
    Fokális májbetegség miatt végzett resectiok eredményei.

**Impact factors : 0,937**
Abstracts of congress presentations

1. Gy Kovács, J Hallay, A Bakó, L Kerekes, P Sápy:
   Data of septico-toxic state caused by necrotizing pancreatitis
   Impact factor: 1,3

2. Kerekes L, Kovács Gy, Szentkereszty Zs, Hallay J, Sápy P:
   Septicus állapotot okozó nekrotizáló pancreatitis kezelési tapasztalatai.
   Magy Seb. 1998. 51: 131

3. J Hallay, A Bakó, M Szappanos, P Sápy, S Sz Kiss, S Sipka:
   Importance of early jejunal feeding in necrotising pancreatitis and after esophagectomy.
   Impact factor: 0,204

4. G Kovács, J Hallay, A Bakó, Gy Kovács, S Sipka, P Sápy:
   Data of septico-toxic condition caused by necrotizing pancreatitis
   Impact factor: 0,204

5. Zs Szentkereszty, J Hallay, P Sápy, L Kerekes:
   How to get better result in the treatment of acute necrotizing pancreatitis.
   Impact factor: 0,204

6. Szentkereszty Zs Kerekes L, Hallay J, Tóth P, Sápy P:
   The role of CT guided percutaneous peripancreatic drainage in the treatment of acute necrotizing pancreatitis.
   Hep-Gastroenterol. 2000. Suppl. 2, 47: 156-156
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7. Lakos G, Hallay J, Kovács G, Szatmári K, Bakó A, Szentkereszty Zs, Sipka S, Sápy P:
   The effect of jejunal nutrition on nutritional and immunological parameters of patients with acute necrotising pancreatitis
   Impact factor: 1,744

8. J Hallay, G Kovács, Gy Kovács, S Sz Kiss, Zs Szentkereszty, P Sápy, G Lakos, S.Sipka:
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Impact factors: 9.369

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7. Nábrádi Z, Kiss I S, **Hallay J**:  
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8. **Hallay J**, Kaló I, Gyulaházi J, Kiss I S, Árkossy P, Móréné:  
   Légzésfunkciós paraméterek és véráció változások thoracotomián átesett betegekben a  
   fájdalomcsillapítás tükřében  
   Magyar Aneszteziológiai és Intenzív Terápiás Társaság Kongresszusa1992 Absztraktok: 24-  
   24.

9. **J Hallay**, Z Galajda, J Csongor, I Furka, I Mikó:  
   Drug absorption from the epidural space in animal model with dogs  
   XVII. World Congress on Diseases of the Chest  
   Impact factor: 1,582

10. Z Galajda, T Bara, T Maros, **J Hallay** :  
   A new experimental method for aortocoronary bypass graft protection with omentoplasty.  
   VIIth. Annual Meeting Cardiac Surgery: Current Issues  
   Impact factor: 1,582

11. Bóni J, Nábrádi Z, **Hallay J**, Sápy P:  
   Elektív colorectalis carcinoma miatt végzett vastagbél műtéteink az antibioticus profilaxis  
   tükřében  

**Impact factors: 3,164**