

Can a Single Dose Corticosteroid Reduce the Incidence of Post-ERCP Pancreatitis?: A Randomized, Prospective Control Study

Kris Kwanngern MD*, Prawes Tiypattanaputi MD*,
Mongkol Wanitpukdeedecha MD*, Patpong Navicharern MD*

* Department of Surgery, Faculty of Medicine, Chulalongkorn University

Background: Acute pancreatitis is one of the complications after Endoscopic retrograde cholangio pancreatography (ERCP) and it could be fatal. Several drugs were used to prevent or decrease this complication. Corticosteroid is one of the medications which may have such potential. It is affordable and available everywhere.

Objectives: To compare the incidence of post-ERCP pancreatitis in patients receiving single dose corticosteroid prior to the procedure with that of the control group.

Research design: A prospective randomized controlled double-blinded study.

Material and Method: A total of 120 patients were randomized to receive either intravenous hydrocortisone 100 mg. or normal saline 1 hour prior to the procedure. The serum amylase levels were recorded 4 and 24 hours after the procedure. Abdominal pain and back pain were also recorded. Patients were diagnosed as having post-ERCP pancreatitis if ones had new or worsened epigastric pain with or without radiation to the back combined with elevation of serum amylase more than 2.5 times the upper limit.

Results: The overall incidence of pancreatitis was 6.67% with 1.64% in the study group compared with 11.86% in the control group ($p = 0.031$). The groups were similar with regard to age, gender, type of procedure performed (diagnostic or therapeutic), difficulty of cannulation, concentration of contrast media and pre operative amylase level.

Conclusion: The results of the present trial indicate that hydrocortisone could reduce the risk of post-ERCP pancreatitis.

Keywords: Endoscopic retrograde cholangiopancreatographys ERCP, Steroid, Pancreatitis

J Med Assoc Thai 2005; 88(Suppl 4): 42-5

Full text. e-Journal: <http://www.medassochai.org/journal>

Endoscopic retrograde cholangio pancreatography (ERCP) and endoscopic sphincterotomy (EST) are useful tools for diagnostic and treatment of various biliary pancreatic diseases. Acute pancreatitis is a serious complication after such procedures⁽¹⁻³⁾ with the incidence of 1-5%⁽²⁻⁴⁾ and it could be fatal^(5,6). Serum amylase may be increased without clinical manifestation of acute pancreatitis in 40-50% of the post ERCP patients. Several drugs used to prevent this complication showed unclear results and most of the medications used were expensive such as somatostatin and its analogues^(7,8).

Correspondence to : Navicharern P, Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Steroid was one of the drugs studied for this purpose. It was affordable and widely available. Some studies showed that preoperative use of steroid resulted in a decreased incidence of post-ERCP pancreatitis⁽⁹⁾, some studies did not⁽¹⁰⁻¹⁴⁾. Among the studies that failed to show the benefit, some used oral form of prednisolone which might not be appropriate.

The aim of this randomized control study was to determine whether the prophylactic use of single dose intravenous hydrocortisone can reduce the incidence of serum amylase elevation or incidence of acute pancreatitis or both in patients undergoing ERCP (whether for diagnostic purpose only or followed by therapeutic procedures).

Material and Method

During a two-year period, 120 patients without exclusion criteria (Table 1) scheduled for ERCP at the department of surgery, King Chulalongkorn Memorial Hospital were randomly allocated to two groups (randomized block system) who underwent double-blinded treatment with hydrocortisone or placebo. The study was approved by the Ethical Committee, Faculty of Medicine, Chulalongkorn university. Informed consent was obtained in every case.

Serum amylase levels were measured before the procedures. The patients in the experimental group received 100 mg. hydrocortisone intravenously an hour before the procedure while the isovolumic normal saline was delivered to the control cases.

Serum amylase levels were measured 4 and 24 hours after the procedure. The abdominal pain and back pain were also observed and recorded.

The patients were diagnosed as having pancreatitis when they had elevation of serum amylase more than 2.5 times normal together with new or worsened epigastric or subcostal pain with or without radiation to the back.

Statistical analysis

Quantitative data of the two groups were compared by student's T-test. Comparison between two groups of qualitative data was performed with Chi Square test or Fisher's Exact test. A p-value of <0.05 was considered to be statistical significant.

Results

A total of 120 patients were included in the present study. 61 were in the experimental group receiving hydrocortisone and 59 were in the control group.

The overall incidence of pancreatitis was 6.67% (1.6% in the experimental group, 11.9% in the control group)

Statistical comparison of the groups revealed no significant differences. (Table 2 and 3, $P > 0.05$)

The preoperative amylase level, and the level at 4 and 24 hours after the procedures were not

Table 1. Exclusion criteria

- | |
|---|
| 1. Unco-operative patients |
| 2. Contraindication for hydrocortisone administration such as : |
| 2.1 Allergy to hydrocortisone |
| 2.2 Peptic ulcer |
| 2.3 Glaucoma |
| 2.4 Congestive heart failure |
| 2.5 Systemic fungal infection |

different between the two groups (Table 4).

There was no difference in the number of patients with serum amylase level > 550 mg% at 4 and 24 hours after ERCP between steroid and control groups (Table 5).

According to the definition of post ERCP pancreatitis which combined both elevation in serum amylase level greater than 2.5 times the upper limit of normal value and new or worsened epigastric and/or subcostal pain, there were 7 patients (11.9%) in the control group who suffered from such condition while there was only one patients (1.6%) from the group pretreated with hydrocortisone. The difference was statistical significant ($p = 0.031$) (Table 5).

Discussion

Acute pancreatitis is one of the serious complications after ERCP^(3,7) and various kinds of medications had been used to prevent the problem. Even among the same group of medications, the results were still unclear. There were differences in the forms of the medication, routes of administration, dosages and timing⁽⁷⁻¹⁴⁾.

Steroid was one of the medications used. It is cheap and available everywhere. Corticosteroids have been determined to affect a number of factors involved in the process of tissue inflammation.

For acute pancreatitis, steroid significantly elevate C1 esterase inhibitor levels which suppress trypsin activation⁽⁹⁾ it also have been shown to induce the synthesis of lipomodulin which subsequently decrease the synthesis of prostaglandins and leukotrienes⁽⁹⁾.

Table 2. Characteristics of the patients

| | Control Group | Steroid Group | p-value |
|----------------------------|---------------|---------------|---------|
| Total number of patients | 59 | 61 | |
| Mean age | 59.27± 15.35 | 55.75±17.92 | > 0.05 |
| Sex (M/F) | 28/31 | 30/31 | |
| Preoperative amylase (mg%) | 221.9±210.48 | 240.98±158.25 | > 0.05 |

Table 3. Details of the procedures

| | Control Group | Steroid Group |
|---------------------------------------|---------------|---------------|
| Procedure | | |
| - Diagnostic | 37 | 35 |
| - Therapeutic | 22 | 26 |
| Contrast media | | |
| Concentration | | |
| 1 : 1 | 59 | 59 |
| 1 : 2 | 0 | 1 |
| No dilution | 0 | 1 |
| Number of pancreatic duct cannulation | | |
| 0-5 | 49 | 53 |
| 6-10 | 10 | 7 |
| > 10 | 0 | 1 |

Weiner GR. et al (1995)⁽⁹⁾ demonstrated the decreasing incidence of post-ERCP pancreatitis in patients receiving preprocedure corticosteroid for prevention of allergic reactions. The study was retrospective and the populations were 824 patients with a history of iodine sensitivity.

There were at least 5 RCT up to date using prophylactic steroids⁽¹⁰⁻¹⁴⁾ for this purpose and they could not demonstrate a beneficial results.

The present study was done during the same period as the last 3 studies mentioned⁽¹⁰⁻¹²⁾ with the different kind of steroids, dosages and time of administration. This might explain the difference in the study results.

Conclusion

The results of the present trial indicate that 100 mg. of hydrocortisone given intravenously 1 hour before endoscopic retrograde cholangiopancreatography could reduce the risk of pancreatitis after the procedures.

Acknowledgement

This study was supported by Ratchadapisek Sompotch Fund, Faculty of Medicine, Chulalongkorn University, Thailand.

References

1. Bilbao MK, Dotter CT, Lee RG. Complications of endoscopic retrograde cholangiopancreatography (ERCP): A study of 10,000 cases. *Gastroenterology* 1976; 70: 314-20.
2. Cotton PB, Lehman G, Vennes J. Endoscopic sphincterotomy complications and their management: An attempt at consensus. *Gastrointest Endosc* 1991; 37: 383-92.
3. Freeman ML, Nelson DB, Sherman S. Complications of endoscopic biliary sphincterotomy. *NEJM* 1996; 335: 909-18.
4. Booth FV, Doerr RJ, Khalahi RS. Surgical management of complications of endoscopic sphincterotomy with preceding papillotomy. *Am J Surg* 1990; 159: 132-5.
5. Chen YK, Abdulian JD, Escalante-Glorsky S. Clinical outcome of post-ERCP pancreatitis: Relationship to history of previous pancreatitis. *Am J Gastroent* 1995; 90: 2120-3.
6. Fung AS, Tsiotos GG, Sarr MG. ERCP-Induced acute necrotizing pancreatitis : Is it a more severe disease? *Pancreas* 1997; 15: 217-21.
7. Guelrud M, Mendoza S, Viera L. Somatostatin prevents acute pancreatitis after pancreatic duct sphincter hydrostatic balloon dilatation in patients with idiopathic recurrent pancreatitis. *Gastrointest Endoscopy* 1991; 37: 44-7.
8. Arcidiacono R, Gambitta P, Rossi A. The use of a long-acting somatostatin analogue (octreotide) for prophylaxis of acute pancreatitis after endoscopic

Table 4. Serum amylase level

| Amylase (mg%) | Control Group | Steroid Group | p-value |
|------------------|---------------|----------------|---------|
| Preoperative | 221.90±210.48 | 240.98±158.25 | > 0.05 |
| 4 hrs.post ERCP | 747.86±739.44 | 678.34±748.80 | > 0.05 |
| 24 hrs.post ERCP | 643.90±790.14 | 644.93±1047.40 | > 0.05 |

Table 5. Number of patients with elevation of serum amylase and pancreatitis

| | Control Group | Steroid Group | p-value |
|-------------------|---------------|---------------|---------|
| Amylase > 550 mg% | | | |
| At 4 hrs. | 23 (39%) | 19 (31.1%) | > 0.05 |
| At 24 hrs. | 16 (27.1%) | 13 (21.3%) | > 0.05 |
| Pancreatitis | 7 (11.9%) | 1 (1.6%) | 0.031 |

- sphincterotomy. *Endoscopy* 1994; 26: 715-8.
9. Weiner GR, Geenen JE. Use of corticosteroids in the prevention of post-ERCP pancreatitis. *Gastrointest Endosc* 1995; 42: 579-83.
 10. Dumot JA, Conwell DL, O'Connor JB. Pretreatment with methyl prednisolone to prevent ERCP-Induced pancreatitis : A randomized, multicenter, placebo-controlled clinical trial. *Am J Gastroenterol* 1998; 93: 61-5.
 11. De Palma GD, Catanzano C. Use of corticosteroids in the prevention of post-ERCP pancreatitis: Results of a controlled prospective study. *Am J Gastroenterol* 1999; 94: 982-5.
 12. Budzynska A, Marek T, Nowak A. A prospective randomized, placebo-controlled trial of prednisolone and allopurinol in the prevention of ERCP-Induced pancreatitis. *Endoscopy* 2001; 33: 766-72.
 13. Manolakopoulos S, Avgerinos A, Ulachogiannakos J. Octreotide versus hydrocortisone versus placebo in the prevention of post-ERCP pancreatitis: A multicenter randomized controlled trial. *Gastrointest Endosc* 2002; 55: 470-5.
 14. Sherman S, Blaut U, Watkins JL. Does prophylactic administration of corticosteroid reduce the risk and severity of post-ERCP pancreatitis: A randomized, prospective, multicenter study. *Gastrointest Endosc* 2003; 58: 23-9.

การให้ยา corticosteroid 1 ครั้งก่อนทำหัตถการ endoscopic retrograde cholangio pancreatography จะสามารถลดอุบัติเหตุน้ำหนักอ้วนอักเสบเฉียบพลันภายหลังหัตถการได้หรือไม่

กฤษณ์ ขวัญเงิน, ประเวศ ดิยะพัฒน์พุดิ, มงคล วณิชภักดีเดชา, พัฒน์พงศ์ นาวิเจริญ

เหตุผลการทำวิจัย: การทำหัตถการ endoscopic retrograde cholangiopancreatography อาจทำให้เกิดภาวะแทรกซ้อนสำคัญคือ ภาวะตับอ่อนอักเสบ ซึ่งแม้พบไม่บ่อย (1-5%) แต่อาจมีความรุนแรงถึงชีวิตได้ ความพยายามในการป้องกันภาวะดังกล่าวให้น้อยลง ด้วยการให้ยาต่างๆ ยังได้ผลสรุปที่ไม่แน่นอน corticosteroid เป็นยาตัวหนึ่งที่มีแนวโน้มอาจลดภาวะดังกล่าวลงได้ ยามีราคาไม่แพงและหาได้ทั่วไป

วัตถุประสงค์: เพื่อเปรียบเทียบอุบัติการณ์ของการเกิดตับอ่อนอักเสบภายหลังการทำหัตถการ endoscopic retrograde cholangio pancreatography ระหว่างกลุ่มที่ได้รับยา hydrocortisone ก่อนการทำหัตถการกับกลุ่มที่ได้รับ normal saline ปริมาตรเท่ากัน

สถานที่ทำการศึกษา: ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

รูปแบบการวิจัย: Double blinded randomized control trial

วิธีการศึกษาและวัดผล: ระหว่างระยะเวลา 2 ปี ผู้ป่วย 120 ราย ที่เข้ารับการหัตถการ ERCP ได้รับการสุ่มแยกเป็น 2 กลุ่ม (randomized block system) กลุ่มทดลองมี 61 ราย ได้รับยา hydrocortisone 100 mg เข้าหลอดเลือดดำก่อนการทำหัตถการ 1 ชั่วโมง ส่วนกลุ่มควบคุมมี 59 ราย ได้รับ normal saline ปริมาตรเท่ากัน ทำการเจาะระดับของ serum amylase ก่อนการผ่าตัด และ 4 ชั่วโมง กับ 24 ชั่วโมงหลังการผ่าตัด รวมทั้งบันทึกอาการปวดท้อง หลังทำหัตถการนำมาเปรียบเทียบกัน

ผลการศึกษา: อุบัติการณ์รวมของการเกิดตับอ่อนอักเสบเฉียบพลันหลังผ่าตัดอยู่ที่ 6.67% เป็นผู้ป่วยในกลุ่มทดลองเพียง 1.6% ส่วนผู้ป่วยในกลุ่มควบคุมมีอุบัติการณ์ 11.9% ซึ่งต่างกันอย่างมีนัยสำคัญทางสถิติ

สรุป: การให้ยา hydrocortisone 100 mg. เข้าหลอดเลือดดำก่อนการทำหัตถการ ERCP 1 ชั่วโมง สามารถลดอุบัติการณ์ของการเกิดตับอ่อนอักเสบหลังการทำหัตถการได้
