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1 **Feeding management before gastrointestinal studies in pigs**

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12

13 **Abstract**

14 Pigs are used to model humans in gastrointestinal studies because of their comparable
15 size, physiology and behaviour: both are monogastric omnivores. A porcine surgical
16 model for testing novel, tethered ultrasound capsule **endoscopes** (USCE) required a
17 clean, motile small intestine. Recommendations for human gastrointestinal tract
18 preparation before the mechanically similar process of video capsule endoscopy
19 describe using oral purgatives while high carbohydrate drinks are recommended
20 before colorectal surgery. Reports of gastrointestinal preparation of pigs exist but lack
21 technical details i.e. administration, efficacy, side-effects.

22 This report details **feeding a high-energy liquid diet to eleven female** pigs undergoing
23 surgery and USCE which was readily accepted, easily administered, produced a clean,
24 motile small intestine and caused no detectable physiological/behavioural
25 abnormalities.

26

27 **Keywords**

28 Pigs, Anaesthesia, Food Withdrawal, Refinement, Gastrointestinal Tract, Capsule
29 Endoscopy, Colorectal Surgery

30 **Introduction**

31 Preparatory measures before gastrointestinal (GI) endoscopy aim to provide a view of
32 the intestinal mucosa unobscured by turbid liquid or food material, both of which
33 reduce diagnostic value. ¹ Similar measures reduce post-surgical complications such as
34 wound dehiscence or anastomotic leakage. ² Pigs and humans are both monogastric
35 omnivores and similar pre-endoscopic preparation should be required, but opinions
36 regarding pre-procedural preparation for video capsule endoscopy (VCE) remain
37 divided.

38 In humans, overnight provision of a liquid diet does not worsen small intestinal
39 conditions compared to oral purgatives (sodium picosulphate/magnesium sulphate or
40 polyethylene glycol) ¹ which are used for mechanical bowel preparation to empty the
41 GI tract of faeces. However, oral purgative administration is not routine before VCE;
42 preparation should be guided by patient/clinical requirements ³ and consideration of
43 pre-existing co-morbidities and peri-operative antibiosis are considered more
44 important in avoiding complications. ²

45 Comparable pre-operative preparation for laboratory pigs is sparsely described and
46 lacks technical details. ⁴ Complan® (liquid meal replacer) has been used to prepare
47 pigs' GI tract before endoscopic surgery ⁵ and a combination of an "electrolyte-rich

48 liquid” and mechanical bowel preparation has been used before anastomotic surgery
49 in minipigs. ⁶ Both methods were used for 48 hours pre-surgery without
50 complications/results reported.

51 A clean, empty yet motile bowel was desired in terminally anaesthetized pigs in studies
52 involving stomata formation and ultrasound capsule endoscopy (USCE) ⁷ prototype
53 testing. Here, the development of a method using a high-energy liquid diet to prepare
54 commercial pigs is detailed.

55 **Materials and Methods**

56 Following ethical approval by Roslin Institute's AWERB, studies were conducted under
57 PPL:PF5151DAF. Eleven female, commercial hybrid pigs, body mass 47 [35 – 50] kg, age
58 14 [11 – 14] weeks were delivered < 7 days before study. Pigs were pair-housed
59 without straw or ingestible bedding. Rubber matting and heat lamps were used to
60 maintain environmental conditions, which were enriched with dog toys and traffic
61 cones.

62 A commercially available “dietetic feed source” (“Glutalyte[®]”; Norbrook, Newry) for
63 use in calves with digestive disturbances was the chosen liquid diet. Prepared
64 according to the manufacturer’s recommendations, it was provided in shallow troughs
65 from arrival so accustomisation could occur. Initially 2 L was offered to each pen (2

66 pigs) every 12 hours. Concentrated feed (“ABN Pig Rearer Pellets”; ABN Feeds, Cupar,
67 Fife) was offered twice daily until 36 – 48 hours before anaesthetic induction. After
68 concentrate feeding stopped, Glutalyte® was offered at an increased rate (4 L/pen
69 every 12 hours) until pre-anaesthetic medication was administered (figure 1); water
70 was always available *ab libitum*.

71 Intramuscular sedation comprising midazolam (0.25 mgkg⁻¹; “Hypnovel”, Roche),
72 morphine (0.25 mgkg⁻¹; “Morphine Sulphate”, Martindale, Essex) medetomidine (7
73 µgkg⁻¹; “Medetor”, Dechra, Shrewsbury) and ketamine (7 mgkg⁻¹; “Ketamidor”,
74 Chanelle) preceded induction/maintenance of anaesthesia with isoflurane (“IsoFlo”;
75 Abbot, Maidenhead) vaporised in medical air/oxygen. Blood glucose (BG) was
76 monitored intermittently during anaesthesia (standard institution practice); after
77 surgery pigs were euthanized using pentobarbital (“Pentoject 20%”; Animalcare, York)
78 without recovery from anaesthesia.

79 Descriptive statistics are stated as (median [range]).

80 **Results**

81 Anaesthesia duration 5 (4 – 11) hours. Glucose supplementation was required in 1/11
82 animals when BG = 2.4 mmol L⁻¹ during surgery (normal > 4.7 mmol L⁻¹ ⁸) but
83 normalised after intravenous supplementation (60 – 300 mg kg⁻¹ hour⁻¹; “Glucose

84 Intravenous Infusion 50% w/v"; Hameln, Gloucester). The small intestinal lumen was
85 consistently empty of ingesta, and peristaltic motion was observed during surgery. No
86 pigs showed abnormal behaviours prior to anaesthesia. All studies were completed
87 successfully.

88 **Discussion/Conclusion**

89 Providing a liquid diet in preparation for GI surgery helped maintain normal
90 physiology, avoided oral purgatives and caused no observable undesirable effects on
91 the pigs' behaviour.

92 Initially, replacement of ingestible bedding with rubber mats in 2 m² pens caused
93 problems with soiling as pigs lay in faeces-contaminated areas. Doubling pen size and
94 elevating sleeping areas allowed pigs to choose distinct sleeping and dunging areas,
95 greatly improving cleanliness. Provision of robust manipulatable objects contributed to
96 normal behaviour.

97 Since liquid or electrolyte-rich diets prepare the porcine GI tract adequately for surgery
98 ^{5,6} and a clear liquid diet provides suitable conditions for VCE in humans, ¹ it was
99 decided to base GI preparation on a liquid diet. Mechanical bowel preparation using
100 oral purgatives was avoided as their usefulness is questionable ^{1,3} and can cause
101 adverse side effects in humans ¹. Bowel preparation using prolonged food withdrawal

102 was also undesirable because of adverse welfare effects. Glutalyte® was chosen
103 because of its high content of carbohydrate (75.7% dextrose w/w) and glutamine.
104 Dextrose provides calories without fibre, avoiding accumulation of intraluminal
105 contents, and glutamine is a “conditionally essential” nutrient for enterocytes during
106 periods of stress.¹⁰ Pigs found Glutalyte® palatable, consuming the majority of liquid
107 offered.

108 Physiological normality and translational relevance were attained in several ways.
109 Blood glucose remained within normal limits in 10/11 pigs, minimising requirements
110 for glucose supplementation and adverse effects of hypo- or hyperglycaemia on GI
111 motility.⁹ Gastrointestinal motility was deemed normal/acceptable by investigators
112 throughout the study. The GI lumen was empty, expediting stomata surgery, allowing
113 the USCE prototype an unobscured examination field, and replicating conditions
114 expected in humans.

115 Limitations included: lack of a control group, no measurement of Glutalyte® intake/pig
116 and no specific assessment was undertaken regarding behavioural changes potentially
117 associated with an impoverished environment. Only female pigs were used according
118 to the demands of the primary study.

119 Providing a high carbohydrate liquid diet to pigs as the sole energy source for 36 – 48
120 hours before gastrointestinal surgery and USCE produced a clean, motile small
121 intestine which was suitable for the experiment performed. With appropriate
122 environmental adaptation, pigs demonstrated neither adverse behaviours nor
123 physiological abnormalities. Therefore, this proved a successful way to prepare
124 laboratory pigs for gastrointestinal surgery and capsule endoscopy studies whilst
125 avoiding aversive procedures i.e., purgative administration and food withdrawal.

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154

155 Ethical Statement

156 This study reports technical details of the non-regulated husbandry and preparation of
157 animals undergoing subsequent regulated procedures.

158

159 Declaration of Conflicting Interests

160 The authors declare no potential conflicts of interest with respect to research,
161 authorship, and/or publication of the article.

162

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